ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 10 micrograms solution for injection in pre-filled syringe.
Aranesp 15 micrograms solution for injection in pre-filled syringe.
Aranesp 20 micrograms solution for injection in pre-filled syringe.
Aranesp 30 micrograms solution for injection in pre-filled syringe.
Aranesp 40 micrograms solution for injection in pre-filled syringe.
Aranesp 50 micrograms solution for injection in pre-filled syringe.
Aranesp 60 micrograms solution for injection in pre-filled syringe.
Aranesp 80 micrograms solution for injection in pre-filled syringe.
Aranesp 100 micrograms solution for injection in pre-filled syringe.
Aranesp 130 micrograms solution for injection in pre-filled syringe.
Aranesp 150 micrograms solution for injection in pre-filled syringe.
Aranesp 300 micrograms solution for injection in pre-filled syringe.
Aranesp 500 micrograms solution for injection in pre-filled syringe.

Aranesp 10 micrograms solution for injection in pre-filled pen.
Aranesp 15 micrograms solution for injection in pre-filled pen.
Aranesp 20 micrograms solution for injection in pre-filled pen.
Aranesp 30 micrograms solution for injection in pre-filled pen.
Aranesp 40 micrograms solution for injection in pre-filled pen.
Aranesp 50 micrograms solution for injection in pre-filled pen.
Aranesp 60 micrograms solution for injection in pre-filled pen.
Aranesp 80 micrograms solution for injection in pre-filled pen.
Aranesp 100 micrograms solution for injection in pre-filled pen.
Aranesp 130 micrograms solution for injection in pre-filled pen.
Aranesp 150 micrograms solution for injection in pre-filled pen.
Aranesp 300 micrograms solution for injection in pre-filled pen.
Aranesp 500 micrograms solution for injection in pre-filled pen.

Aranesp 25 micrograms solution for injection in vial.
Aranesp 40 micrograms solution for injection in vial.
Aranesp 60 micrograms solution for injection in vial.
Aranesp 100 micrograms solution for injection in vial.
Aranesp 200 micrograms solution for injection in vial.
Aranesp 300 micrograms solution for injection in vial.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Aranesp 10 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 10 micrograms of darbepoetin alfa in 0.4 mL (25 mcg/mL).
Aranesp 15 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 15 micrograms of darbepoetin alfa in 0.375 mL (40 mcg/mL).
Aranesp 20 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 20 micrograms of darbepoetin alfa in 0.5 mL (40 mcg/mL).
Aranesp 30 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 30 micrograms of darbepoetin alfa in 0.3 mL (100 mcg/mL).
Aranesp 40 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 40 micrograms of darbepoetin alfa in 0.4 mL (100 mcg/mL).
Aranesp 50 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 50 micrograms of darbepoetin alfa in 0.5 mL (100 mcg/mL).
Aranesp 60 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 60 micrograms of darbepoetin alfa in 0.3 mL (200 mcg/mL).
Aranesp 80 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 80 micrograms of darbepoetin alfa in 0.4 mL (200 mcg/mL).

Aranesp 100 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 100 micrograms of darbepoetin alfa in 0.5 mL (200 mcg/mL).
Aranesp 130 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 130 micrograms of darbepoetin alfa in 0.65 mL (200 mcg/mL).
Aranesp 150 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 150 micrograms of darbepoetin alfa in 0.3 mL (500 mcg/mL).
Aranesp 300 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 300 micrograms of darbepoetin alfa in 0.6 mL (500 mcg/mL).
Aranesp 500 micrograms solution for injection in pre-filled syringe
Each pre-filled syringe contains 500 micrograms of darbepoetin alfa in 1 mL (500 mcg/mL).

Aranesp 10 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 10 micrograms of darbepoetin alfa in 0.4 mL (25 mcg/mL).
Aranesp 15 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 15 micrograms of darbepoetin alfa in 0.375 mL (40 mcg/mL).
Aranesp 20 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 20 micrograms of darbepoetin alfa in 0.5 mL (40 mcg/mL).
Aranesp 30 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 30 micrograms of darbepoetin alfa in 0.3 mL (100 mcg/mL).
Aranesp 40 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 40 micrograms of darbepoetin alfa in 0.4 mL (100 mcg/mL).
Aranesp 50 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 50 micrograms of darbepoetin alfa in 0.5 mL (100 mcg/mL).
Aranesp 60 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 60 micrograms of darbepoetin alfa in 0.3 mL (200 mcg/mL).
Aranesp 80 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 80 micrograms of darbepoetin alfa in 0.4 mL (200 mcg/mL).
Aranesp 100 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 100 micrograms of darbepoetin alfa in 0.5 mL (200 mcg/mL).
Aranesp 130 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 130 micrograms of darbepoetin alfa in 0.65 mL (200 mcg/mL).
Aranesp 150 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 150 micrograms of darbepoetin alfa in 0.3 mL (500 mcg/mL).
Aranesp 300 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 300 micrograms of darbepoetin alfa in 0.6 mL (500 mcg/mL).
Aranesp 500 micrograms solution for injection in pre-filled pen
Each pre-filled pen contains 500 micrograms of darbepoetin alfa in 1 mL (500 mcg/mL).

Aranesp 25 micrograms solution for injection in vial
Each vial contains 25 micrograms of darbepoetin alfa in 1 mL (25 mcg/mL).
Aranesp 40 micrograms solution for injection in vial
Each vial contains 40 micrograms of darbepoetin alfa in 1 mL (40 mcg/mL).
Aranesp 60 micrograms solution for injection in vial
Each vial contains 60 micrograms of darbepoetin alfa in 1 mL (60 mcg/mL).
Aranesp 100 micrograms solution for injection in vial
Each vial contains 100 micrograms of darbepoetin alfa in 1 mL (100 mcg/mL).
Aranesp 200 micrograms solution for injection in vial
Each vial contains 200 micrograms of darbepoetin alfa in 1 mL (200 mcg/mL).
Aranesp 300 micrograms solution for injection in vial
Each vial contains 300 micrograms of darbepoetin alfa in 1 mL (300 mcg/mL).

Darbepoetin alfa is produced by gene-technology in Chinese Hamster Ovary Cells (CHO-K1).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection) in pre-filled syringe.
Solution for injection (injection) in pre-filled pen (SureClick).
Solution for injection (injection) in vial.

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of symptomatic anaemia associated with chronic renal failure (CRF) in adults and paediatric patients (see section 4.2).

Treatment of symptomatic anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy.

4.2 Posology and method of administration

Aranesp treatment should be initiated by physicians experienced in the above mentioned indications.

Posology

Treatment of symptomatic anaemia in adult and paediatric chronic renal failure patients

Anaemia symptoms and sequelae may vary with age, gender, and overall burden of disease; a physician's evaluation of the individual patient's clinical course and condition is necessary. Aranesp should be administered either subcutaneously or intravenously in order to increase haemoglobin to not greater than 12 g/dL (7.5 mmol/L). Subcutaneous use is preferable in patients who are not receiving haemodialysis to avoid the puncture of peripheral veins.

Patients should be monitored closely to ensure that the lowest approved effective dose of Aranesp is used to provide adequate control of the symptoms of anaemia whilst maintaining a haemoglobin concentration below or at 12 g/dL (7.5 mmol/L). Caution should be exercised with escalation of Aranesp doses in patients with chronic renal failure. In patients with a poor haemoglobin response to Aranesp, alternative explanations for the poor response should be considered (see sections 4.4 and 5.1).

Due to intra-patient variability, occasional individual haemoglobin values for a patient above and below the desired haemoglobin level may be observed. Haemoglobin variability should be addressed through dose management, with consideration for the haemoglobin target range of 10 g/dL (6.2 mmol/L) to 12 g/dL (7.5 mmol/L). A sustained haemoglobin level of greater than 12 g/dL (7.5 mmol/L) should be avoided; guidance for appropriate dose adjustment for when haemoglobin values exceeding 12 g/dL (7.5 mmol/L) are observed are described below. A rise in haemoglobin of greater than 2 g/dL (1.25 mmol/L) over a four week period should be avoided. If it occurs, appropriate dose adjustment should be made as provided.

Treatment with Aranesp is divided into two stages, correction and maintenance phase. Guidance is given separately for adult and paediatric patients.

Adult patients with chronic renal failure

Correction phase:

The initial dose by subcutaneous or intravenous administration is 0.45 mcg/kg body weight, as a single injection once weekly. Alternatively, in patients not on dialysis, the following initial doses can also be administered subcutaneously as a single injection: 0.75 mcg/kg once every two weeks or 1.5 mcg/kg once monthly. If the increase in haemoglobin is inadequate (less than 1 g/dL (0.6 mmol/L) in four weeks) increase the dose by approximately 25%. Dose increases must not be made more frequently than once every four weeks.

If the rise in haemoglobin is greater than 2 g/dL (1.25 mmol/L) in four weeks reduce the dose by approximately 25%. If the haemoglobin exceeds 12 g/dL (7.5 mmol/L), a dose reduction should be considered. If the haemoglobin continues to increase, the dose should be reduced by approximately 25%. If after a dose reduction, haemoglobin continues to increase, the dose should be temporarily withheld until the haemoglobin begins to decrease, at which point therapy should be reinitiated at approximately 25% lower than the previous dose.

The haemoglobin should be measured every one or two weeks until it is stable. Thereafter the haemoglobin can be measured at longer intervals.

Maintenance phase:

In dialysis patients, Aranesp may continue to be administered as a single injection once weekly or once every two weeks. Dialysis patients converting from once weekly to once every other week dosing with Aranesp should initially receive a dose equivalent to twice the previous once weekly dose.

In patients not on dialysis, Aranesp may continue to be administered as a single injection once weekly or once every two weeks or once monthly. For patients treated with Aranesp once every two weeks, after the target haemoglobin has been achieved, Aranesp may then be administered subcutaneously once monthly using an initial dose equal to twice the previous once every two week dose.

Dosing should be titrated as necessary to maintain the haemoglobin target.

If a dose adjustment is required to maintain haemoglobin at the desired level, it is recommended that the dose is adjusted by approximately 25%.

If the rise in haemoglobin is greater than 2 g/dL (1.25 mmol/L) in four weeks reduce the dose by approximately 25%, depending on the rate of increase. If the haemoglobin exceeds 12 g/dL (7.5 mmol/L), a dose reduction should be considered. If the haemoglobin continues to increase, the dose should be reduced by approximately 25%. If after a dose reduction, haemoglobin continues to increase, the dose should be temporarily withheld until the haemoglobin begins to decrease, at which point therapy should be reinitiated at approximately 25% lower than the previous dose.

After any dose or schedule adjustment the haemoglobin should be monitored every one or two weeks. Dose changes in the maintenance phase of treatment should not be made more frequently than every two weeks.

When changing the route of administration the same dose must be used and the haemoglobin monitored every one or two weeks so that the appropriate dose adjustments can be made to keep the haemoglobin at the desired level.

Clinical studies have demonstrated that adult patients receiving r-HuEPO one, two or three times weekly may be converted to once weekly or once every other week Aranesp. The initial weekly dose of Aranesp (mcg/week) can be determined by dividing the total weekly dose of r-HuEPO (IU/week) by 200. The initial every other week dose of Aranesp (mcg/every other week) can be determined by

dividing the total cumulative dose of r-HuEPO administered over a two-week period by 200. Because of individual variability, titration to optimal therapeutic doses is expected for individual patients. When substituting Aranesp for r-HuEPO the haemoglobin should be monitored every one or two weeks and the same route of administration should be used.

Paediatric population with chronic renal failure

Treatment of paediatric patients younger than 1 year of age has not been studied in randomised clinical trials (see section 5.1).

Correction phase:

For patients ≥ 1 year of age, the initial dose by subcutaneous or intravenous administration is 0.45 mcg/kg body weight, as a single injection once weekly. Alternatively, in patients not on dialysis, an initial dose of 0.75 mcg/kg may be administered subcutaneously as a single injection once every two weeks. If the increase in haemoglobin is inadequate (less than 1 g/dL (0.6 mmol/L) in four weeks) increase the dose by approximately 25%. Dose increases must not be made more frequently than once every four weeks.

If the rise in haemoglobin is greater than 2 g/dL (1.25 mmol/L) in four weeks reduce the dose by approximately 25%, depending on the rate of increase. If the haemoglobin exceeds 12 g/dL (7.5 mmol/L), a dose reduction should be considered. If the haemoglobin continues to increase, the dose should be reduced by approximately 25%. If after a dose reduction, haemoglobin continues to increase, the dose should be temporarily withheld until the haemoglobin begins to decrease, at which point therapy should be reinitiated at approximately 25% lower than the previous dose.

The haemoglobin should be measured every one or two weeks until it is stable. Thereafter the haemoglobin can be measured at longer intervals.

Correction of anaemia in paediatric patients with once monthly Aranesp dosing frequency has not been studied.

Maintenance phase:

For paediatric patients ≥ 1 year of age, in the maintenance phase, Aranesp may continue to be administered as a single injection once weekly or once every two weeks. Patients < 6 years of age may need higher doses for maintenance of haemoglobin than patients above that age. Dialysis patients converting from once weekly to once every other week dosing with Aranesp should initially receive a dose equivalent to twice the previous once weekly dose.

In patients ≥ 11 years of age not on dialysis, once the target haemoglobin has been achieved with once every two week dosing, Aranesp may be administered subcutaneously once monthly using an initial dose equal to twice the previous once every two week dose.

Clinical data in paediatric patients has demonstrated that patients receiving r-HuEPO two or three times weekly may be converted to once weekly Aranesp, and those receiving r-HuEPO once weekly may be converted to once every other week Aranesp. The initial weekly paediatric dose of Aranesp (mcg/week) can be determined by dividing the total weekly dose of r-HuEPO (IU/week) by 240. The initial every other week dose of Aranesp (mcg/every other week) can be determined by dividing the total cumulative dose of r-HuEPO administered over a two-week period by 240. Because of individual variability, titration to optimal therapeutic doses is expected for individual patients. When substituting Aranesp for r-HuEPO the haemoglobin should be monitored every one or two weeks and the same route of administration should be used.

Dosing should be titrated as necessary to maintain the haemoglobin target.

If a dose adjustment is required to maintain haemoglobin at the desired level, it is recommended that the dose is adjusted by approximately 25%.

If the rise in haemoglobin is greater than 2 g/dL (1.25 mmol/L) in four weeks reduce the dose by approximately 25%, depending on the rate of increase. If the haemoglobin exceeds 12 g/dL (7.5 mmol/L), a dose reduction should be considered. If the haemoglobin continues to increase, the dose should be reduced by approximately 25%. If after a dose reduction, haemoglobin continues to increase, the dose should be temporarily withheld until the haemoglobin begins to decrease, at which point therapy should be reinitiated at approximately 25% lower than the previous dose.

Patients starting dialysis during treatment with Aranesp should be closely monitored for adequate control of their haemoglobin.

After any dose or schedule adjustment the haemoglobin should be monitored every one or two weeks. Dose changes in the maintenance phase of treatment should not be made more frequently than every two weeks.

When changing the route of administration the same dose must be used and the haemoglobin monitored every one or two weeks so that the appropriate dose adjustments can be made to keep the haemoglobin at the desired level.

Treatment of symptomatic chemotherapy-induced anaemia in cancer patients

Aranesp should be administered by the subcutaneous route to patients with anaemia (e.g. haemoglobin concentration ≤ 10 g/dL (6.2 mmol/L)) in order to increase haemoglobin to not greater than 12 g/dL (7.5 mmol/L). Anaemia symptoms and sequelae may vary with age, gender, and overall burden of disease; a physician's evaluation of the individual patient's clinical course and condition is necessary.

Due to intra-patient variability, occasional individual haemoglobin values for a patient above and below the desired haemoglobin level may be observed. Haemoglobin variability should be addressed through dose management, with consideration for the haemoglobin target range of 10 g/dL (6.2 mmol/L) to 12 g/dL (7.5 mmol/L). A sustained haemoglobin level of greater than 12 g/dL (7.5 mmol/L) should be avoided; guidance for appropriate dose adjustments for when haemoglobin values exceeding 12 g/dL (7.5 mmol/L) are observed are described below.

The recommended initial dose is 500 mcg (6.75 mcg/kg) given once every three weeks, or once weekly dosing can be given at 2.25 mcg/kg body weight. If the clinical response of the patient (fatigue, haemoglobin response) is inadequate after nine weeks, further therapy may not be effective.

Aranesp therapy should be discontinued approximately four weeks after the end of chemotherapy.

Once the therapeutic objective for an individual patient has been achieved, the dose should be reduced by 25 to 50% in order to ensure that the lowest approved dose of Aranesp is used to maintain haemoglobin at a level that controls the symptoms of anaemia. Appropriate dose titration between 500 mcg, 300 mcg, and 150 mcg should be considered.

Patients should be monitored closely, if the haemoglobin exceeds 12 g/dL (7.5 mmol/L), the dose should be reduced by approximately 25 to 50%. Treatment with Aranesp should be temporarily discontinued if haemoglobin levels exceed 13 g/dL (8.1 mmol/L). Therapy should be reinitiated at approximately 25% lower than the previous dose after haemoglobin levels fall to 12 g/dL (7.5 mmol/L) or below.

If the rise in haemoglobin is greater than 2 g/dL (1.25 mmol/L) in 4 weeks, the dose should be reduced by 25 to 50%.

Method of administration

Aranesp may be administered subcutaneously by the patient or a carer after being trained by a doctor, nurse or pharmacist.

Aranesp 10, 15, 20, 30, 40, 50, 60, 80, 100, 130, 150, 300, 500 micrograms solution for injection in pre-filled syringe
Aranesp is administered either subcutaneously or intravenously as described in the posology.
Rotate the injection sites and inject slowly to avoid discomfort at the site of injection.
Aranesp is supplied ready for use in a pre-filled syringe.

Aranesp 10, 15, 20, 30, 40, 50, 60, 80, 100, 130, 150, 300, 500 micrograms solution for injection in pre-filled pen
Aranesp in a pre-filled pen is only for subcutaneous administration.
Rotate the injection sites to avoid discomfort at the site of injection.
Aranesp is supplied ready for use in a pre-filled pen.

Aranesp 25, 40, 60, 100, 200, 300 micrograms solution for injection in vial
Aranesp is administered either subcutaneously or intravenously as described in the posology.
Rotate the injection sites and inject slowly to avoid discomfort at the site of injection.
Aranesp is supplied ready for use in a vial.

The instructions for use, handling and disposal are given in section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Poorly controlled hypertension.

4.4 Special warnings and precautions for use

General

In order to improve the traceability of erythropoiesis-stimulating agents (ESAs), the trade name of the administered ESA should be clearly recorded (or stated) in the patient file.

Blood pressure should be monitored in all patients, particularly during initiation of Aranesp therapy. If blood pressure is difficult to control by initiation of appropriate measures, the haemoglobin may be reduced by decreasing or withholding the dose of Aranesp (see section 4.2). Cases of severe hypertension, including hypertensive crisis, hypertensive encephalopathy, and seizures, have been observed in CRF patients treated with Aranesp.

In order to ensure effective erythropoiesis, iron status should be evaluated for all patients prior to and during treatment and supplementary iron therapy may be necessary.

Non-response to therapy with Aranesp should prompt a search for causative factors. Deficiencies of iron, folic acid or vitamin B12 reduce the effectiveness of ESAs and should therefore be corrected. Intercurrent infections, inflammatory or traumatic episodes, occult blood loss, haemolysis, severe aluminium toxicity, underlying haematologic diseases, or bone marrow fibrosis may also compromise the erythropoietic response. A reticulocyte count should be considered as part of the evaluation. If typical causes of non-response are excluded, and the patient has reticulocytopenia, an examination of the bone marrow should be considered. If the bone marrow is consistent with PRCA, testing for anti-erythropoietin antibodies should be performed.

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported in association with epoetin treatment. More severe cases have been observed with long-acting epoetins.
At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, Aranesp should be withdrawn immediately and an alternative treatment considered. If the patient has developed a severe cutaneous skin reaction such as SJS or TEN due to the use of Aranesp, treatment with Aranesp must not be restarted in this patient at any time.

Pure red cell aplasia caused by neutralising anti-erythropoietin antibodies has been reported in association with ESAs, including Aranesp. This has been predominantly reported in patients with CRF treated subcutaneously. These antibodies have been shown to cross-react with all erythropoietic proteins, and patients suspected or confirmed to have neutralising antibodies to erythropoietin should not be switched to Aranesp (see section 4.8).

A paradoxical decrease in haemoglobin and development of severe anaemia associated with low reticulocyte counts should prompt to discontinue treatment with epoetin and perform anti-erythropoietin antibody testing. Cases have been reported in patients with hepatitis C treated with interferon and ribavirin, when epoetins are used concomitantly. Epoetins are not approved in the management of anaemia associated with hepatitis C.

Active liver disease was an exclusion criteria in all studies of Aranesp, therefore no data are available from patients with impaired liver function. Since the liver is thought to be the principal route of elimination of darbepoetin alfa and r-HuEPO, Aranesp should be used with caution in patients with liver disease.

Aranesp should also be used with caution in those patients with sickle cell anaemia.

Misuse of Aranesp by healthy persons may lead to an excessive increase in packed cell volume. This may be associated with life-threatening complications of the cardiovascular system.

The needle cap of the pre-filled syringe or pre-filled pen contains dry natural rubber (a derivative of latex), which may cause allergic reactions.

Aranesp should be used with caution in patients with epilepsy. Convulsions have been reported in patients receiving Aranesp.

The reported risk of thrombotic vascular events (TVEs) should be carefully weighed against the benefits to be derived from treatment with darbepoetin alfa particularly in patients with pre-existing risk factors for TVE, including obesity and prior history of TVEs (e.g., deep venous thrombosis, pulmonary embolism, and cerebral vascular accident).

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

<u>Chronic renal failure patients</u>

In patients with chronic renal failure, maintenance haemoglobin concentration should not exceed the upper limit of the target haemoglobin concentration recommended in section 4.2. In clinical studies, an increased risk of death, serious cardiovascular or cerebrovascular events including stroke, and vascular access thrombosis was observed when ESAs were administered to target a haemoglobin of greater than 12 g/dL (7.5 mmol/L).

Caution should be exercised with escalation of Aranesp doses in patients with chronic renal failure, since high cumulative epoetin doses may be associated with an increased risk of mortality, serious cardiovascular and cerebrovascular events. In patients with a poor haemoglobin response to epoetins, alternative explanations for the poor response should be considered (see sections 4.2 and 5.1).

Controlled clinical trials have not shown significant benefits attributable to the administration of epoetins when haemoglobin concentration is increased beyond the level necessary to control symptoms of anaemia and to avoid blood transfusion.

Supplementary iron therapy is recommended for all patients with serum ferritin values below 100 mcg/L or whose transferrin saturation is below 20%.

Serum potassium levels should be monitored regularly during Aranesp therapy. Potassium elevation has been reported in a few patients receiving Aranesp, though causality has not been established. If an elevated or rising potassium level is observed then consideration should be given to ceasing Aranesp administration until the level has been corrected.

Cancer patients

Effect on tumour growth

Epoetins are growth factors that primarily stimulate red blood cell production. Erythropoietin receptors may be expressed on the surface of a variety of tumour cells. As with all growth factors, there is a concern that epoetins could stimulate the growth of tumours. In several controlled studies, epoetins have not been shown to improve overall survival or decrease the risk of tumour progression in patients with anaemia associated with cancer.

In controlled clinical studies, use of Aranesp and other ESAs have shown:

- shortened time to tumour progression in patients with advanced head and neck cancer receiving radiation therapy when administered to target a haemoglobin of greater than 14 g/dL (8.7 mmol/L), ESAs are not indicated for use in this patient population.

- shortened overall survival and increased deaths attributed to disease progression at 4 months in patients with metastatic breast cancer receiving chemotherapy when administered to target a haemoglobin of 12-14 g/dL (7.5-8.7 mmol/L).

- increased risk of death when administered to target a haemoglobin of 12 g/dL (7.5 mmol/L) in patients with active malignant disease receiving neither chemotherapy nor radiation therapy. ESAs are not indicated for use in this patient population.

- an observed 9% increase in risk for PD or death in the epoetin alfa plus SOC group from a primary analysis and a 15% increased risk that cannot be statistically ruled out in patients with metastatic breast cancer receiving chemotherapy when administered to achieve a haemoglobin concentration range of 10 to 12 g/dL (6.2 to 7.5 mmol/L).

- non-inferiority of darbepoetin alfa to placebo for overall survival and progression free survival in patients with advanced stage non-small cell lung cancer receiving chemotherapy when administered to a target haemoglobin of 12 g/dL (7.5 mmol/L) (see section 5.1).

In view of the above, in some clinical situations blood transfusion should be the preferred treatment for the management of anaemia in patients with cancer. The decision to administer recombinant erythropoietins should be based on a benefit-risk assessment with the participation of the individual patient, which should take into account the specific clinical context. Factors that should be considered in this assessment should include the type of tumour and its stage; the degree of anaemia; life-expectancy; the environment in which the patient is being treated; and patient preference (see section 5.1).

In patients with solid tumours or lymphoproliferative malignancies, if the haemoglobin value exceeds 12 g/dL (7.5 mmol/L), the dosage adaptation described in section 4.2 should be closely respected, in

order to minimise the potential risk of thromboembolic events. Platelet counts and haemoglobin level should also be monitored at regular intervals.

4.5 Interaction with other medicinal products and other forms of interaction

The clinical results obtained so far do not indicate any interaction of darbepoetin alfa with other substances. However, there is potential for an interaction with substances that are highly bound to red blood cells e.g. cyclosporin, tacrolimus. If Aranesp is given concomitantly with any of these treatments, blood levels of these substances should be monitored and the dosage adjusted as the haemoglobin rises.

4.6 Pregnancy and lactation

Pregnancy

There are no adequate and well-controlled studies with Aranesp in pregnant women.

Animal studies do not indicate direct harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. No alteration of fertility was detected.

Caution should be exercised when prescribing Aranesp to pregnant women.

Breast-feeding

It is unknown whether Aranesp is excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Aranesp therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Aranesp has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Identified adverse reactions associated with Aranesp are hypertension, stroke, thromboembolic events, convulsions, allergic reactions, rash/erythema and pure red cell aplasia (PRCA); see section 4.4.

Injection site pain was reported as attributable to treatment in studies where Aranesp was administered via subcutaneous injection. The injection site discomfort was generally mild and transient in nature and occurred predominantly after the first injection.

Tabulated list of adverse reactions

Incidence of adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).

Data are presented separately for CRF and cancer patients reflecting the different adverse reaction profile in these populations.

Chronic renal failure patients

Data presented from controlled studies included 1,357 patients, 766 who received Aranesp and 591 patients who received r-HuEPO. In the Aranesp group, 83% were receiving dialysis and 17% were not receiving dialysis. Stroke was identified as an adverse reaction in an additional clinical study (TREAT, see section 5.1).

Incidence of adverse reactions from controlled clinical studies and post-marketing experience are:

MedDRA system organ class	**Subject incidence**	**Adverse reaction**
Blood and lymphatic system disorders	Not known[2]	Pure red cell aplasia
Immune system disorders	Very common	Hypersensitivity[a]
Nervous system disorders	Common	Stroke[b]
	Uncommon[1]	Convulsions
Cardiac disorders	Very common	Hypertension
Vascular disorders	Uncommon	Thromboembolic events[c]
	Uncommon[1]	Dialysis vascular access thrombosis[d]
Skin and subcutaneous tissue disorders	Common	Rash/erythema[e]
	Not known[2]	SJS/TEN, erythema multiforme, blistering, skin exfoliation
General disorders and administration site conditions	Common	Injection site pain
	Uncommon[1]	Injection site bruising Injection site haemorrhage

Source: Includes 5 randomised, double-blind, active-controlled studies (970200, 970235, 980117, 980202, and 980211) except for the adverse reaction of stroke which was identified as an adverse reaction in the TREAT study (study 20010184).

[1] Adverse reactions identified in the post-marketing environment. Per the Guideline on Summary of Product Characteristics (Revision 2, September 2009), frequency of adverse reactions identified in the post-marketing setting was determined using the "Rule of three".

[2] Frequency cannot be estimated from the available data.

[a] Hypersensitivity events includes all events under the hypersensitivity SMQ.

[b] Stroke events includes PT haemorrhagic stroke, ischaemic stroke, cerebrovascular accident, and stroke in evolution.

[c] Thromboembolic events adverse reaction includes PT embolism arterial, thrombophlebitis, thrombosis, venous thrombosis limb.

[d] Dialysis vascular access thrombosis includes all adverse reactions under the dialysis vascular access thrombosis AMQ

[e] Rash/erythema adverse reaction includes PT rash, rash pruritic, rash macular, rash generalised, erythema.

Cancer patients

Adverse reactions were determined based on pooled data from eight randomised, double-blind, placebo-controlled studies of Aranesp with a total of 4,630 patients (Aranesp 2,888, placebo 1,742). Patients with solid tumours (e.g., lung, breast, colon, ovarian cancers) and lymphoid malignancies (e.g., lymphoma, multiple myeloma) were enrolled in the clinical studies.

Incidence of adverse reactions from controlled clinical studies and post-marketing experience are:

MedDRA system organ class	**Subject incidence**	**Adverse reaction**
Immune system disorders	Very common	Hypersensitivity[a]
Nervous system disorders	Uncommon[1]	Convulsions
Cardiac disorders	Common	Hypertension
Vascular disorders	Common	Thromboembolic events[b], including pulmonary embolism

MedDRA system organ class	Subject incidence	Adverse reaction
Skin and subcutaneous tissue disorders	Common	Rash/erythema[c]
	Not known[2]	SJS/TEN, erythema multiforme, blistering, skin exfoliation
General disorders and administration site conditions	Common	Oedema[d]
	Common	Injection site pain[e]
	Uncommon[1]	Injection site bruising Injection site haemorrhage

[1] ADRs identified in the post marketing environment. Per the Guideline on Summary of Product Characteristics (Revision 2, September 2009), frequency of ADRs identified in the post marketing setting was determined using the "Rule of three".
[2] Frequency cannot be estimated from the available data.
Source: includes 8 randomised, double-blind, placebo-controlled studies (980291-schedule 1 and 2, 980297, 990114, 20000161, 20010145, 20030232, and 20070782)
[a] Hypersensitivity events includes all events under the hypersensitivity SMQ.
[b] Thromboembolic events adverse reactions includes PT embolism, thrombosis, deep vein thrombosis, jugular vein thrombosis, venous thrombosis, arterial thrombosis, pelvic venous thrombosis, peripheral embolism, pulmonary embolism, as well as thrombosis in device from SOC product issues.
[c] Rash adverse reactions includes PT rash, rash pruritic, rash generalised, rash papular, erythema, exfoliative rash, rash maculo-papular, rash vesicular as well as rash pustular from SOC Infections and Infestations.
[d] Oedema: includes PT Oedema Peripheral, Oedema, Generalised Oedema, Oedema due to Cardiac Disease, Face oedema
[e] Injection site pain adverse reaction includes PT injection site pain, administration site pain, catheter site pain, infusion site pain and vessel puncture site pain.

Description of selected adverse reactions

Chronic renal failure patients

Stroke was reported as common in CRF patients in TREAT (see section 5.1).

In isolated cases, neutralising anti-erythropoietin antibody mediated pure red cell aplasia (PRCA) associated with Aranesp therapy have been reported predominantly in patients with CRF treated subcutaneously. In case PRCA is diagnosed, therapy with Aranesp must be discontinued and patients should not be switched to another recombinant erythropoietic protein (see section 4.4).

The frequency of all hypersensitivity reactions was estimated from clinical trial data as very common in CRF patients. Hypersensitivity reactions were also very common in the placebo groups. There have been reports, from post-marketing experience, of serious hypersensitivity reactions including anaphylactic reaction, angioedema, allergic bronchospasm, skin rash and urticaria associated with darbepoetin alfa.

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported (see section 4.4).

Convulsions have been reported in patients receiving darbepoetin alfa (see section 4.4). The frequency is estimated from clinical trial data as uncommon in CRF patients.

In CRF patients on haemodialysis, events of vascular access thrombosis (such as vascular access complication, arteriovenous fistula thrombosis, graft thrombosis, shunt thrombosis, arteriovenous fistula site complication, etc.) have been reported in post-marketing data. The frequency is estimated from clinical trial data as uncommon.

Cancer patients

Hypertension has been observed in cancer patients in post-marketing experience (see section 4.4). The frequency is estimated from clinical trial data as common in cancer patients and was also common in the placebo groups.

Hypersensitivity reactions have been observed in cancer patients in post-marketing experience. The frequency of all hypersensitivity reactions was estimated from clinical trial data as very common in cancer patients. Hypersensitivity reactions were also very common in the placebo groups. There have been reports of serious hypersensitivity reactions including anaphylactic reaction, angioedema, allergic bronchospasm, skin rash and urticaria associated with darbepoetin alfa.

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported (see section 4.4).

Convulsions have been reported in patients receiving darbepoetin alfa in post-marketing experience (see section 4.4). The frequency is estimated from clinical trial data as uncommon in cancer patients. Convulsions were common in the placebo groups.

Paediatric chronic renal failure population

In all paediatric CRF studies, there were no additional adverse reactions identified for paediatric patients compared to those previously reported for adult patients (see section 5.1).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

The maximum amount of Aranesp that can be safely administered in single or multiple doses has not been determined. Therapy with Aranesp can result in polycythaemia if the haemoglobin is not carefully monitored and the dose appropriately adjusted. Cases of severe hypertension have been observed following overdose with Aranesp (see section 4.4).

In the event of polycythaemia, Aranesp should be temporarily withheld (see section 4.2). If clinically indicated, phlebotomy may be performed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-anaemic preparations, other anti-anaemic preparations, ATC Code: B03XA02.

Mechanism of action

Human erythropoietin is an endogenous glycoprotein hormone that is the primary regulator of erythropoiesis through specific interaction with the erythropoietin receptor on the erythroid progenitor cells in the bone marrow. The production of erythropoietin primarily occurs in and is regulated by the kidney in response to changes in tissue oxygenation. Production of endogenous erythropoietin is impaired in patients with chronic renal failure and the primary cause of their anaemia is due to

erythropoietin deficiency. In patients with cancer receiving chemotherapy the etiology of anaemia is multifactorial. In these patients, erythropoietin deficiency and a reduced response of erythroid progenitor cells to endogenous erythropoietin both contribute significantly towards their anaemia.

Pharmacodynamic effects

Darbepoetin alfa stimulates erythropoiesis by the same mechanism as the endogenous hormone. Darbepoetin alfa has five N-linked carbohydrate chains whereas the endogenous hormone and recombinant human erythropoietins (r-HuEPO) have three. The additional sugar residues are molecularly indistinct from those on the endogenous hormone. Due to its increased carbohydrate content darbepoetin alfa has a longer terminal half-life than r-HuEPO and consequently a greater *in vivo* activity. Despite these molecular changes, darbepoetin alfa retains a very narrow specificity for the erythropoietin receptor.

Clinical efficacy and safety

Chronic renal failure patients

Patients with CRF experienced greater risks for death and serious cardiovascular events when administered ESAs to target higher versus lower haemoglobin levels (13.5 g/dL (8.4 mmol/L) versus 11.3 g/dL (7.1 mmol/L); 14 g/dL (8.7 mmol/L) versus 10 g/dL (6.2 mmol/L) in two clinical studies.

In a randomised, double-blind correction study (n = 358) comparing once every two week and once monthly dosing schedules in patients with CRF not on dialysis, darbepoetin alfa once monthly dosing was non-inferior to once every two week dosing for correcting anaemia. The median (quartile 1, quartile 3) time to achieve haemoglobin correction (≥ 10.0 g/dL and ≥ 1.0 g/dL increase from baseline) was 5 weeks for both once every two week (3, 7 weeks) and once monthly dosing (3, 9 weeks). During the evaluation period (weeks 29-33), the mean (95% CI) weekly equivalent dose was 0.20 (0.17, 0.24) mcg/kg in the once every two week arm and 0.27 (0.23, 0.32) mcg/kg in the once monthly arm.

In a randomised, double-blind, placebo-controlled study (TREAT) of 4,038 CRF patients not on dialysis with type 2 diabetes and haemoglobin levels ≤ 11 g/dL, patients received either treatment with darbepoetin alfa to target haemoglobin levels of 13 g/dL or placebo (with darbepoetin alfa rescue at haemoglobin less than 9 g/dL). The study did not meet either primary objective of demonstrating a reduction in risk for all-cause mortality or cardiovascular morbidity (darbepoetin alfa vs placebo; HR 1.05, 95% CI (0.94, 1.17)), or all-cause mortality or end stage renal disease (ESRD) (darbepoetin alfa vs placebo; HR 1.06, 95% CI (0.95, 1.19)). Analysis of the individual components of the composite endpoints showed the following HR (95% CI): death 1.05 (0.92, 1.21), congestive heart failure (CHF) 0.89 (0.74, 1.08), myocardial infarction (MI) 0.96 (0.75, 1.23), stroke 1.92 (1.38, 2.68), hospitalisation for myocardial ischaemia 0.84 (0.55, 1.27), ESRD 1.02 (0.87, 1.18).

Pooled post-hoc analyses of clinical studies of ESAs have been performed in chronic renal failure patients (on dialysis, not on dialysis, in diabetic and non-diabetic patients). A tendency towards increased risk estimates for all-cause mortality, cardiovascular and cerebrovascular events associated with higher cumulative ESA doses independent of the diabetes or dialysis status was observed (see sections 4.2 and 4.4).

Paediatric population

In a randomised clinical study 114 paediatric patients aged 2 to 18 with chronic kidney disease receiving or not receiving dialysis who were anaemic (haemoglobin < 10.0 g/dL) and not being treated with an ESA were administered darbepoetin alfa weekly (n = 58) or once every two weeks (n = 56) for the correction of anaemia. Haemoglobin concentrations were corrected to ≥ 10 g/dL in > 98% ($p < 0.001$) of paediatric patients administered darbepoetin alfa once weekly and 84% ($p = 0.293$) once every two weeks. At the time haemoglobin ≥ 10.0 g/dL was first achieved, the mean (SD) weight-

adjusted dose was 0.48 (0.24) mcg/kg (range: 0.0 to 1.7 mcg/kg) weekly for the once weekly group and 0.76 (0.21) mcg/kg (range: 0.3 to 1.5 mcg/kg) biweekly for the once every two week group.

In a clinical study in 124 paediatric patients with chronic kidney disease receiving or not receiving dialysis aged 1 to 18, patients that were stable on epoetin alfa were randomised to receive either darbepoetin alfa administered once weekly (subcutaneously or intravenously) using a dose conversion ratio of 238:1 or to continue with epoetin alfa therapy at the current dose, schedule, and route of administration. The primary efficacy endpoint [change in haemoglobin between baseline and the evaluation period (week 21-28)] was comparable between the two groups. The mean haemoglobin for r-HuEPO and darbepoetin alfa at baseline was 11.1 (SD 0.7) g/dL and 11.3 (SD 0.6) g/dL, respectively. The mean haemoglobin at week 28 for r-HuEPO and darbepoetin alfa was 11.1 (SD 1.4) g/dL and 11.1 (SD 1.1) g/dL, respectively.

In an European observational registry study which enrolled 319 paediatric patients with chronic kidney disease (13 (4.1%) patients < 1 year of age, 83 (26.0%) patients 1-< 6 years of age, 90 (28.2%) patients 6-< 12 years of age, and 133 (41.7%) patients ≥ 12 years of age) receiving darbepoetin alfa, mean haemoglobin concentrations ranging between 11.3 and 11.5 g/dL and mean weight-adjusted darbepoetin alfa doses remained relatively constant (between 2.31 mcg/kg month and 2.67 mcg/kg month) over the study period for the entire study population.

In these studies, no meaningful differences were identified between the safety profile for paediatric patients and that previously reported for adult patients (see section 4.8).

Cancer patients receiving chemotherapy

EPO-ANE-3010, a randomised, open-label, multicentre study was conducted in 2,098 anaemic women with metastatic breast cancer, who received first line or second line chemotherapy. This was a non inferiority study designed to rule out a 15% risk increase in tumour progression or death of epoetin alfa plus standard of care (SOC) as compared with SOC alone. At the time of clinical data cutoff, the median progression free survival (PFS) per investigator assessment of disease progression was 7.4 months in each arm (HR 1.09, 95% CI: 0.99, 1.20), indicating the study objective was not met. Significantly fewer patients received RBC transfusions in the epoetin alfa plus SOC arm (5.8% versus 11.4%); however, significantly more patients had thrombotic vascular events in the epoetin alfa plus SOC arm (2.8% versus 1.4%). At the final analysis, 1,653 deaths were reported. Median overall survival in the epoetin alfa plus SOC group was 17.8 months compared with 18.0 months in the SOC alone group (HR 1.07, 95% CI: 0.97, 1.18). The median time to progression (TTP) based on investigator-determined progressive disease (PD) was 7.5 months in the epoetin alfa plus SOC group and 7.5 months in the SOC group (HR 1.099, 95% CI: 0.998, 1.210). The median TTP based on IRC-determined PD was 8.0 months in the epoetin alfa plus SOC group and 8.3 months in the SOC group (HR 1.033, 95% CI: 0.924, 1.156).

In a prospective, randomised double-blind, placebo-controlled study conducted in 314 lung cancer patients receiving platinum containing chemotherapy there was a significant reduction in transfusion requirements ($p < 0.001$).

Clinical studies have demonstrated that darbepoetin alfa had similar effectiveness when administered as a single injection either once every three weeks, once every two weeks, or weekly without any increase in total dose requirements.

The safety and effectiveness of once every three weeks dosing of Aranesp therapy in reducing the requirement for red blood cell transfusions in patients undergoing chemotherapy was assessed in a randomised, double-blind, multinational study. This study was conducted in 705 anaemic patients with non-myeloid malignancies receiving multi-cycle chemotherapy. Patients were randomised to receive Aranesp at 500 mcg once every three weeks or 2.25 mcg/kg once weekly. In both groups, the dose was reduced by 40% of the previous dose (e.g., for first dose reduction, to 300 mcg in the once every three weeks group and 1.35 mcg/kg in the once weekly group) if haemoglobin increased by more than 1 g/dL in a 14-day period. In the once every three weeks group, 72% of patients required dose

reductions. In the once weekly group, 75% of patients required dose reductions. This study supports 500 mcg once every three weeks being comparable to once weekly administration with respect to the incidence of subjects receiving at least one red blood cell transfusion from week 5 to the end of treatment phase.

In a prospective, randomised double-blind, placebo-controlled study conducted in 344 anaemic patients with lymphoproliferative malignancies receiving chemotherapy there was a significant reduction in transfusion requirements and an improvement in haemoglobin response ($p < 0.001$). Improvement in fatigue, as measured by the Functional Assessment of Cancer Therapy-fatigue (FACT-fatigue) scale, was also observed.

Erythropoietin is a growth factor that primarily stimulates red blood cell production. Erythropoietin receptors may be expressed on the surface of a variety of tumour cells.

Survival and tumour progression have been examined in five large controlled studies involving a total of 2,833 patients, of which four were double-blind placebo-controlled studies and one was an open-label study. Two of the studies recruited patients who were being treated with chemotherapy. The target haemoglobin concentration in two studies was > 13 g/dL; in the remaining three studies it was 12-14 g/dL. In the open-label study there was no difference in overall survival between patients treated with recombinant human erythropoietin and controls. In the four placebo-controlled studies the hazard ratios for overall survival ranged between 1.25 and 2.47 in favour of controls. These studies have shown a consistent unexplained statistically significant excess mortality in patients who have anaemia associated with various common cancers who received recombinant human erythropoietin compared to controls. Overall survival outcome in the trials could not be satisfactorily explained by differences in the incidence of thrombosis and related complications between those given recombinant human erythropoietin and those in the control group.

In a randomised, double-blind, placebo-controlled phase 3 study 2,549 adult patients with anaemia receiving chemotherapy for the treatment of advanced stage non-small cell lung cancer (NSCLC), were randomised 2:1 to darbepoetin alfa or placebo and treated to a maximum Hb of 12 g/dL. The results showed non-inferiority for the primary endpoint of overall survival with a median survival for darbepoetin alfa versus placebo of 9.5 and 9.3 months, respectively (stratified HR 0.92; 95% CI: 0.83–1.01). The secondary endpoint of progression free survival was 4.8 and 4.3 months, respectively (stratified HR 0.95; 95% CI: 0.87–1.04), ruling out the pre-defined 15% risk increase.

A systematic review has also been performed involving more than 9,000 cancer patients participating in 57 clinical trials. Meta-analysis of overall survival data produced a hazard ratio point estimate of 1.08 in favour of controls (95% CI: 0.99, 1.18; 42 trials and 8,167 patients).

An increased relative risk of thromboembolic events (RR 1.67, 95% CI: 1.35, 2.06; 35 trials and 6,769 patients) was observed in patients treated with recombinant human erythropoietin. There is therefore consistent evidence to suggest that there may be significant harm to patients with cancer who are treated with recombinant human erythropoietin. The extent to which these outcomes might apply to the administration of recombinant human erythropoietin to patients with cancer, treated with chemotherapy to achieve haemoglobin concentrations less than 13 g/dL, is unclear because few patients with these characteristics were included in the data reviewed.

A patient-level data analysis has also been performed on more than 13,900 cancer patients (chemo-, radio-, chemoradio-, or no therapy) participating in 53 controlled clinical trials involving several epoetins. Meta-analysis of overall survival data produced a hazard ratio point estimate of 1.06 in favour of controls (95% CI: 1.00, 1.12; 53 trials and 13,933 patients) and for the cancer patients receiving chemotherapy, the overall survival hazard ratio was 1.04 (95% CI: 0.97, 1.11; 38 trials and 10,441 patients). Meta-analyses also indicate consistently a significantly increased relative risk of thromboembolic events in cancer patients receiving recombinant human erythropoietin (see section 4.4).

5.2 Pharmacokinetic properties

Due to its increased carbohydrate content the level of darbepoetin alfa in the circulation remains above the minimum stimulatory concentration for erythropoiesis for longer than the equivalent molar dose of r-HuEPO, allowing darbepoetin alfa to be administered less frequently to achieve the same biological response.

Chronic renal failure patients

The pharmacokinetics of darbepoetin alfa has been studied clinically in chronic renal failure patients following intravenous and subcutaneous administration. The terminal half-life of darbepoetin alfa is 21 hours (SD 7.5) when administered intravenously. Clearance of darbepoetin alfa is 1.9 mL/hr/kg (SD 0.56) and the volume of distribution (V_{ss}) is approximately equal to plasma volume (50 mL/kg). Bioavailability is 37% with subcutaneous administration. Following monthly administration of darbepoetin alfa, at subcutaneous doses ranging from 0.6 to 2.1 mcg/kg, the terminal half-life was 73 hours (SD 24). The longer terminal half-life of darbepoetin alfa administered subcutaneously compared to intravenously is due to subcutaneous absorption kinetics. In clinical studies, minimal accumulation was observed with either route of administration. In preclinical studies it has been shown that renal clearance is minimal (up to 2% of total clearance), and does not affect the serum half-life.

Data from 809 patients receiving Aranesp in European clinical studies were analysed to assess the dose required to maintain haemoglobin; no difference was observed between the average weekly dose administered via the intravenous or subcutaneous routes of injection.

The pharmacokinetics of darbepoetin alfa in paediatric patients (2 to 16 years) with CRF who were either receiving or not receiving dialysis was assessed for sampling periods up to 2 weeks (336 hours) after one or two subcutaneous or intravenous doses. Where the same sampling duration was used, observed pharmacokinetic data and population pharmacokinetic modelling demonstrated that the pharmacokinetics of darbepoetin alfa was similar for paediatric and adult patients with CRF.

In a phase 1 pharmacokinetic study, following intravenous administration, an approximate 25% difference between paediatric and adult patients in the area under the curve from time 0 to infinity (AUC[0-∞]) was observed; however, this difference was less than the 2-fold range in AUC(0-∞) observed for the paediatric patients. AUC(0-∞) was similar between adult and paediatric patients with CRF following subcutaneous administration. Half-life was also similar between adult and paediatric patients with CRF following both intravenous and subcutaneous administration.

Cancer patients receiving chemotherapy

Following subcutaneous administration of 2.25 mcg/kg to adult cancer patients a mean peak concentration of 10.6 ng/mL (SD 5.9) of darbepoetin alfa was reached at a mean time of 91 hours (SD 19.7). These parameters were consistent with dose linear pharmacokinetics over a wide dose range (0.5 to 8 mcg/kg weekly and 3 to 9 mcg/kg every two weeks). Pharmacokinetic parameters did not change on multiple dosing over 12 weeks (dosing every week or every two weeks). There was an expected moderate (< 2 fold) increase in serum concentration as steady state was approached, but no unexpected accumulation upon repeated administration. A pharmacokinetic study in patients with chemotherapy-induced anaemia treated with 6.75 mcg/kg darbepoetin alfa administered SC every 3 weeks in combination with chemotherapy was conducted which allowed for full characterisation of the terminal half-life. In this study, mean (SD) terminal half-life was 74 (SD 27) hours.

5.3 Preclinical safety data

In all studies in rats and dogs darbepoetin alfa produced marked increases in haemoglobin, haematocrits, red blood cell counts and reticulocytes, which correspond to the expected pharmacological effects. Adverse events at very high doses were all considered to be related to an exaggerated pharmacological effect (decreased tissue perfusion due to increased blood viscosity).

These included myelofibrosis and splenic hypertrophy as well as broadening of the ECG-QRS complex in dogs but no dysrhythmia and no effect on the QT interval were observed.

Darbepoetin alfa did not reveal any genotoxic potential nor did it have any effect on the proliferation of non-haematological cells *in vitro* or *in vivo*. In the chronic toxicity studies no tumourigenic or unexpected mitogenic responses were observed in any tissue type. The carcinogenic potential of darbepoetin alfa has not been evaluated in long-term animal studies.

In studies performed in rats and rabbits no clinically relevant evidence of harmful effects with respect to pregnancy, embryonal/ foetal development, parturition or postnatal development was observed. Placental transfer was minimal. No alteration of fertility was detected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium phosphate monobasic
Sodium phosphate dibasic
Sodium chloride
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of incompatibility studies, this medicinal product must not be mixed or administered as an infusion with other medicinal products.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
Do not freeze.
Keep the container in the outer carton in order to protect from light.

For the purpose of ambulatory use, Aranesp may be removed from storage once for a maximum single period of seven days at room temperature (up to 25ºC). Once removed from the refrigerator and has reached room temperature (up to 25ºC) it must either be used within 7 days or disposed of.

6.5 Nature and contents of container

<u>Aranesp 10 micrograms solution for injection in pre-filled syringe</u>
0.4 mL solution for injection (25 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
<u>Aranesp 15 micrograms solution for injection in pre-filled syringe</u>
0.375 mL solution for injection (40 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
<u>Aranesp 20 micrograms solution for injection in pre-filled syringe</u>
0.5 mL solution for injection (40 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
<u>Aranesp 30 micrograms solution for injection in pre-filled syringe</u>
0.3 mL solution for injection (100 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.

Aranesp 40 micrograms solution for injection in pre-filled syringe
0.4 mL solution for injection (100 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 50 micrograms solution for injection in pre-filled syringe
0.5 mL solution for injection (100 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 60 micrograms solution for injection in pre-filled syringe
0.3 mL solution for injection (200 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 80 micrograms solution for injection in pre-filled syringe
0.4 mL solution for injection (200 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 100 micrograms solution for injection in pre-filled syringe
0.5 mL solution for injection (200 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 130 micrograms solution for injection in pre-filled syringe
0.65 mL solution for injection (200 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 150 micrograms solution for injection in pre-filled syringe
0.3 mL solution for injection (500 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 300 micrograms solution for injection in pre-filled syringe
0.6 mL solution for injection (500 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.
Aranesp 500 micrograms solution for injection in pre-filled syringe
1 mL solution for injection (500 mcg/mL darbepoetin alfa) in a type 1 glass pre-filled syringe with stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled syringes.

The syringes may be presented in either blistered (1- and 4-pack), with or without an automatic needle guard or non-blistered packaging (1-pack only).

The needle cap of the pre-filled syringe contains dry natural rubber (a derivative of latex). See section 4.4.

Aranesp 10 micrograms solution for injection in pre-filled pen
0.4 mL solution for injection (25 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 15 micrograms solution for injection in pre-filled pen
0.375 mL solution for injection (40 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 20 micrograms solution for injection in pre-filled pen
0.5 mL solution for injection (40 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 30 micrograms solution for injection in pre-filled pen
0.3 mL solution for injection (100 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 40 micrograms solution for injection in pre-filled pen
0.4 mL solution for injection (100 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 50 micrograms solution for injection in pre-filled pen
0.5 mL solution for injection (100 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 60 micrograms solution for injection in pre-filled pen
0.3 mL solution for injection (200 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.

Aranesp 80 micrograms solution for injection in pre-filled pen
0.4 mL solution for injection (200 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 100 micrograms solution for injection in pre-filled pen
0.5 mL solution for injection (200 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 130 micrograms solution for injection in pre-filled pen
0.65 mL solution for injection (200 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 150 micrograms solution for injection in pre-filled pen
0.3 mL solution for injection (500 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 300 micrograms solution for injection in pre-filled pen
0.6 mL solution for injection (500 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.
Aranesp 500 micrograms solution for injection in pre-filled pen
1 mL solution for injection (500 mcg/mL darbepoetin alfa) in a pre-filled pen with type 1 glass syringe and stainless steel 27 gauge needle. Pack size of 1 or 4 pre-filled pens.

The needle cap of the pre-filled pen contains dry natural rubber (a derivative of latex). See section 4.4.

Aranesp 25 micrograms solution for injection in vial
1 mL solution for injection (25 mcg/mL darbepoetin alfa) in a type 1 glass vial with fluoropolymer laminated elastomeric stopper and an aluminium seal with flip-off dust cover. Pack size of 1 or 4 vials.
Aranesp 40 micrograms solution for injection in vial
1 mL solution for injection (40 mcg/mL darbepoetin alfa) in a type 1 glass vial with fluoropolymer laminated elastomeric stopper and an aluminium seal with flip-off dust cover. Pack size of 1 or 4 vials.
Aranesp 60 micrograms solution for injection in vial
1 mL solution for injection (60 mcg/mL darbepoetin alfa) in a type 1 glass vial with fluoropolymer laminated elastomeric stopper and an aluminium seal with flip-off dust cover. Pack size of 1 or 4 vials.
Aranesp 100 micrograms solution for injection in vial
1 mL solution for injection (100 mcg/mL darbepoetin alfa) in a type 1 glass vial with fluoropolymer laminated elastomeric stopper and an aluminium seal with flip-off dust cover. Pack size of 1 or 4 vials.
Aranesp 200 micrograms solution for injection in vial
1 mL solution for injection (200 mcg/mL darbepoetin alfa) in a type 1 glass vial with fluoropolymer laminated elastomeric stopper and an aluminium seal with flip-off dust cover. Pack size of 1 or 4 vials.
Aranesp 300 micrograms solution for injection in vial
1 mL solution for injection (300 mcg/mL darbepoetin alfa) in a type 1 glass vial with fluoropolymer laminated elastomeric stopper and an aluminium seal with flip-off dust cover. Pack size of 1 or 4 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The carton contains a package leaflet with the full instructions for use and handling.

The Aranesp (SureClick) pre-filled pen delivers the complete dose of each presentation.

Aranesp is a sterile but unpreserved product. Do not administer more than one dose. Any medicinal product remaining should be disposed of.

Before administration the Aranesp solution should be inspected for visible particles. Only solutions which are colourless, clear or slightly opalescent, should be injected. Do not shake. Allow the container to reach room temperature before injecting.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

8. MARKETING AUTHORISATION NUMBERS

Aranesp 10 micrograms solution for injection pre-filled syringe
EU/1/01/185/001 1 Pack Blister
EU/1/01/185/002 4 Pack Blister
EU/1/01/185/033 1 Pack Unblistered
EU/1/01/185/074 1 blister pack with needle guard
EU/1/01/185/075 4 blister pack with needle guard
Aranesp 15 micrograms solution for injection pre-filled syringe
EU/1/01/185/003 1 Pack Blister
EU/1/01/185/004 4 Pack Blister
EU/1/01/185/034 1 Pack Unblistered
EU/1/01/185/076 1 blister pack with needle guard
EU/1/01/185/077 4 blister pack with needle guard
Aranesp 20 micrograms solution for injection pre-filled syringe
EU/1/01/185/005 1 Pack Blister
EU/1/01/185/006 4 Pack Blister
EU/1/01/185/035 1 Pack Unblistered
EU/1/01/185/078 1 blister pack with needle guard
EU/1/01/185/079 4 blister pack with needle guard
Aranesp 30 micrograms solution for injection pre-filled syringe
EU/1/01/185/007 1 Pack Blister
EU/1/01/185/008 4 Pack Blister
EU/1/01/185/036 1 Pack Unblistered
EU/1/01/185/080 1 blister pack with needle guard
EU/1/01/185/081 4 blister pack with needle guard
Aranesp 40 micrograms solution for injection pre-filled syringe
EU/1/01/185/009 1 Pack Blister
EU/1/01/185/010 4 Pack Blister
EU/1/01/185/037 1 Pack Unblistered
EU/1/01/185/082 1 blister pack with needle guard
EU/1/01/185/083 4 blister pack with needle guard
Aranesp 50 micrograms solution for injection pre-filled syringe
EU/1/01/185/011 1 Pack Blister
EU/1/01/185/012 4 Pack Blister
EU/1/01/185/038 1 Pack Unblistered
EU/1/01/185/084 1 blister pack with needle guard
EU/1/01/185/085 4 blister pack with needle guard
Aranesp 60 micrograms solution for injection pre-filled syringe
EU/1/01/185/013 1 Pack Blister
EU/1/01/185/014 4 Pack Blister
EU/1/01/185/039 1 Pack Unblistered
EU/1/01/185/086 1 blister pack with needle guard
EU/1/01/185/087 4 blister pack with needle guard

Aranesp 80 micrograms solution for injection pre-filled syringe
EU/1/01/185/015 1 Pack Blister
EU/1/01/185/016 4 Pack Blister
EU/1/01/185/040 1 Pack Unblistered
EU/1/01/185/088 1 blister pack with needle guard
EU/1/01/185/089 4 blister pack with needle guard
Aranesp 100 micrograms solution for injection pre-filled syringe
EU/1/01/185/017 1 Pack Blister
EU/1/01/185/018 4 Pack Blister
EU/1/01/185/041 1 Pack Unblistered
EU/1/01/185/090 1 blister pack with needle guard
EU/1/01/185/091 4 blister pack with needle guard
Aranesp 130 micrograms solution for injection pre-filled syringe
EU/1/01/185/069 1 Pack Blister
EU/1/01/185/070 4 Pack Blister
EU/1/01/185/071 1 Pack Unblistered
EU/1/01/185/092 1 blister pack with needle guard
EU/1/01/185/093 4 blister pack with needle guard
Aranesp 150 micrograms solution for injection pre-filled syringe
EU/1/01/185/019 1 Pack Blister
EU/1/01/185/020 4 Pack Blister
EU/1/01/185/042 1 Pack Unblistered
EU/1/01/185/094 1 blister pack with needle guard
EU/1/01/185/095 4 blister pack with needle guard
Aranesp 300 micrograms solution for injection pre-filled syringe
EU/1/01/185/021 1 Pack Blister
EU/1/01/185/022 4 Pack Blister
EU/1/01/185/043 1 Pack Unblistered
EU/1/01/185/096 1 blister pack with needle guard
EU/1/01/185/097 4 blister pack with needle guard
Aranesp 500 micrograms solution for injection pre-filled syringe
EU/1/01/185/031 1 Pack Blister
EU/1/01/185/032 4 Pack Blister
EU/1/01/185/044 1 Pack Unblistered
EU/1/01/185/098 1 blister pack with needle guard
EU/1/01/185/099 4 blister pack with needle guard
Aranesp 10 micrograms solution for injection pre-filled pen
EU/1/01/185/045 – 1 pack
EU/1/01/185/057 – 4 pack
Aranesp 15 micrograms solution for injection pre-filled pen
EU/1/01/185/046 – 1 pack
EU/1/01/185/058 – 4 pack
Aranesp 20 micrograms solution for injection pre-filled pen
EU/1/01/185/047 – 1 pack
EU/1/01/185/059 – 4 pack
Aranesp 30 micrograms solution for injection pre-filled pen
EU/1/01/185/048 – 1 pack
EU/1/01/185/060 – 4 pack
Aranesp 40 micrograms solution for injection pre-filled pen
EU/1/01/185/049 – 1 pack
EU/1/01/185/061 – 4 pack
Aranesp 50 micrograms solution for injection pre-filled pen
EU/1/01/185/050 – 1 pack
EU/1/01/185/062 – 4 pack
Aranesp 60 micrograms solution for injection pre-filled pen
EU/1/01/185/051 – 1 pack
EU/1/01/185/063 – 4 pack

Aranesp 80 micrograms solution for injection pre-filled pen
EU/1/01/185/052 – 1 pack
EU/1/01/185/064 – 4 pack
Aranesp 100 micrograms solution for injection pre-filled pen
EU/1/01/185/053 – 1 pack
EU/1/01/185/065 – 4 pack
Aranesp 130 micrograms solution for injection pre-filled pen
EU/1/01/185/072 – 1 pack
EU/1/01/185/073 – 4 pack
Aranesp 150 micrograms solution for injection pre-filled pen
EU/1/01/185/054 – 1 pack
EU/1/01/185/066 – 4 pack
Aranesp 300 micrograms solution for injection pre-filled pen
EU/1/01/185/055 – 1 pack
EU/1/01/185/067 – 4 pack
Aranesp 500 micrograms solution for injection pre-filled pen
EU/1/01/185/056 – 1 pack
EU/1/01/185/068 – 4 pack
Aranesp 25 micrograms solution for injection vial
EU/1/01/185/100 1 Pack
EU/1/01/185/101 4 Pack
Aranesp 40 micrograms solution for injection vial
EU/1/01/185/102 1 Pack
EU/1/01/185/103 4 Pack
Aranesp 60 micrograms solution for injection vial
EU/1/01/185/104 1 Pack
EU/1/01/185/105 4 Pack
Aranesp 100 micrograms solution for injection vial
EU/1/01/185/106 1 Pack
EU/1/01/185/107 4 Pack
Aranesp 200 micrograms solution for injection vial
EU/1/01/185/108 1 Pack
EU/1/01/185/109 4 Pack
Aranesp 300 micrograms solution for injection vial
EU/1/01/185/110 1 Pack
EU/1/01/185/111 4 Pack

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8 June 2001
Date of latest renewal: 19 May 2006

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Amgen Manufacturing Limited LLC
Road 31 km 24.6
Juncos, PR 00777
Puerto Rico

Name and address of the manufacturers responsible for batch release

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Amgen Technology (Ireland) Unlimited Company
Pottery Road
Dun Laoghaire
Co Dublin
Ireland

Amgen NV
Telecomlaan 5-7
1831 Diegem
Belgium

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (See Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures for Aranesp solution for injection in pre-filled pen**

The MAH shall agree the final educational material with the national competent authority where the pre-filled pen is marketed. Healthcare professionals prescribing Aranesp pre-filled pen will be provided educational materials to facilitate training patients on the correct self-administration of Aranesp.

The healthcare professional's educational material should contain the following key elements:

- Training checklist
  - provides structured training steps for healthcare professionals to train patients/caregivers on the specific preparation and administration steps that they will need to perform using a dummy pen, while following the instructions for use located in the package leaflet.
  - reminds the healthcare professionals to verify that the patients/caregivers can demonstrate using the dummy pen confidently and competently to be able to prepare and administer the medicine successfully when at home.
  - includes information on how to receive further checklists or demonstration device(s).
- A demonstration device
- A poster-size instructions for use (for patients/caregivers with diminished eyesight)
  - includes the instructions for use located in the package leaflet in a way that patients/caregivers with diminished eyesight are informed on how to handle the pen and administer Aranesp appropriately.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 10 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled syringe contains 10 micrograms darbepoetin alfa (25 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/001 1 pack
EU/1/01/185/002 4 pack
EU/1/01/185/074 1 pack with needle guard
EU/1/01/185/075 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 10 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 10 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.4 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 10 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.4 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 10 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 10 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled syringe contains 10 micrograms darbepoetin alfa (25 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/033

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 10 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 10 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 15 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.375 mL pre-filled syringe contains 15 micrograms darbepoetin alfa (40 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/003 1 pack
EU/1/01/185/004 4 pack
EU/1/01/185/076 1 pack with needle guard
EU/1/01/185/077 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 15 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 15 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.375 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 15 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.375 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 15 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.375 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 15 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.375 mL pre-filled syringe contains 15 micrograms darbepoetin alfa (40 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/034

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 15 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 15 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.375 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 20 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled syringe contains 20 micrograms darbepoetin alfa (40 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/005 1 pack
EU/1/01/185/006 4 pack
EU/1/01/185/078 1 pack with needle guard
EU/1/01/185/079 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 20 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 20 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.5 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 20 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.5 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 20 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 20 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled syringe contains 20 micrograms darbepoetin alfa (40 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/035

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 20 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 20 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 30 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled syringe contains 30 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/007 1 pack
EU/1/01/185/008 4 pack
EU/1/01/185/080 1 pack with needle guard
EU/1/01/185/081 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 30 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 30 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.3 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 30 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.3 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 30 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 30 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled syringe contains 30 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/036

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 30 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 30 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 40 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled syringe contains 40 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/009 1 pack
EU/1/01/185/010 4 pack
EU/1/01/185/082 1 pack with needle guard
EU/1/01/185/083 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 40 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 40 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.4 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 40 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.4 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 40 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 40 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled syringe contains 40 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/037

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 40 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 40 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 50 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled syringe contains 50 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/011 1 pack
EU/1/01/185/012 4 pack
EU/1/01/185/084 1 pack with needle guard
EU/1/01/185/085 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 50 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 50 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.5 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 50 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.5 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 50 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 50 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled syringe contains 50 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/038

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 50 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 50 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 60 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled syringe contains 60 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/013 1 pack
EU/1/01/185/014 4 pack
EU/1/01/185/086 1 pack with needle guard
EU/1/01/185/087 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 60 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 60 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.3 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 60 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.3 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 60 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 60 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled syringe contains 60 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/039

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 60 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 60 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 80 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled syringe contains 80 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/015 1 pack
EU/1/01/185/016 4 pack
EU/1/01/185/088 1 pack with needle guard
EU/1/01/185/089 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 80 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 80 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.4 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 80 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.4 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 80 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 80 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled syringe contains 80 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/040

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 80 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 80 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 100 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled syringe contains 100 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/017 1 pack
EU/1/01/185/018 4 pack
EU/1/01/185/090 1 pack with needle guard
EU/1/01/185/091 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 100 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 100 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.5 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 100 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.5 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 100 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 100 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled syringe contains 100 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/041

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 100 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 100 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 130 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.65 mL pre-filled syringe contains 130 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/069 1 pack
EU/1/01/185/070 4 pack
EU/1/01/185/092 1 pack with needle guard
EU/1/01/185/093 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 130 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 130 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.65 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 130 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.65 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 130 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.65 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 130 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.65 mL pre-filled syringe contains 130 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/071

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 130 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 130 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.65 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 150 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled syringe contains 150 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/019 1 pack
EU/1/01/185/020 4 pack
EU/1/01/185/094 1 pack with needle guard
EU/1/01/185/095 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 150 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 150 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.3 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 150 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.3 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 150 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 150 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled syringe contains 150 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/042

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 150 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 150 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 300 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.6 mL pre-filled syringe contains 300 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/021 1 pack
EU/1/01/185/022 4 pack
EU/1/01/185/096 1 pack with needle guard
EU/1/01/185/097 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 300 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 300 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.6 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 300 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
0.6 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 300 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.6 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 300 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.6 mL pre-filled syringe contains 300 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/043

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 300 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 300 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.6 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 500 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL pre-filled syringe contains 500 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.
4 single use pre-filled syringes.
1 single use pre-filled syringe with automatic needle guard.
4 single use pre-filled syringes with automatic needle guards.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Important: read the package leaflet before handling pre-filled syringe.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/031 1 pack
EU/1/01/185/032 4 pack
EU/1/01/185/098 1 pack with needle guard
EU/1/01/185/099 4 pack with needle guard

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 500 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 500 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
1 ml

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

TRAY FOR PRE-FILLED SYRINGE WITH NEEDLE GUARD

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 500 µg injection
Darbepoetin alfa

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

IV/SC
1 ml

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITH TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 500 µg
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 500 micrograms solution for injection in pre-filled syringe
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL pre-filled syringe contains 500 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/044

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 500 micrograms syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL WHEN USED WITHOUT TRAY

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 500 µg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 10 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled pen contains 10 micrograms darbepoetin alfa (25 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/045 1 pack
EU/1/01/185/057 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 10 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 10 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 15 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.375 mL pre-filled pen contains 15 micrograms darbepoetin alfa (40 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/046 1 pack
EU/1/01/185/058 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 15 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 15 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.375 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 20 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled pen contains 20 micrograms darbepoetin alfa (40 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/047 1 pack
EU/1/01/185/059 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 20 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 20 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 30 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled pen contains 30 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/048 1 pack
EU/1/01/185/060 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 30 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 30 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 40 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled pen contains 40 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/049 1 pack
EU/1/01/185/061 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 40 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 40 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 50 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled pen contains 50 micrograms darbepoetin alfa (100 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/050 1 pack
EU/1/01/185/062 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 50 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 50 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 60 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled pen contains 60 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/051 1 pack
EU/1/01/185/063 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 60 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 60 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 80 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.4 mL pre-filled pen contains 80 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/052 1 pack
EU/1/01/185/064 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 80 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 80 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.4 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 100 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 mL pre-filled pen contains 100 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/053 1 pack
EU/1/01/185/065 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 100 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 100 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 130 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.65 mL pre-filled pen contains 130 micrograms darbepoetin alfa (200 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/072 1 pack
EU/1/01/185/073 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 130 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 130 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.65 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 150 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.3 mL pre-filled pen contains 150 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/054 1 pack
EU/1/01/185/066 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 150 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 150 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.3 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 300 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.6 mL pre-filled pen contains 300 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/055 1 pack
EU/1/01/185/067 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 300 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 300 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.6 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 500 micrograms solution for injection in pre-filled pen
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL pre-filled pen contains 500 micrograms darbepoetin alfa (500 micrograms/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

SureClick x1
1 single use pre-filled pen
This box containing 1 pre-filled pen, is part of a 4-multipack
SureClick x4
4 single use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/056 1 pack
EU/1/01/185/068 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Aranesp 500 micrograms pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 500 µg injection
Darbepoetin alfa
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

Amgen Europe B.V.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

VIAL CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 25 micrograms solution for injection in vial
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL vial contains 25 micrograms darbepoetin alfa.

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use vial
4 single use vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/100 1 pack
EU/1/01/185/101 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 25 mcg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

VIAL CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 40 micrograms solution for injection in vial
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL vial contains 40 micrograms darbepoetin alfa.

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use vial
4 single use vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/102 1 pack
EU/1/01/185/103 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 40 mcg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

VIAL CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 60 micrograms solution for injection in vial
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL vial contains 60 micrograms darbepoetin alfa.

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use vial
4 single use vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/104 1 pack
EU/1/01/185/105 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 60 mcg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

VIAL CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 100 micrograms solution for injection in vial
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL vial contains 100 micrograms darbepoetin alfa.

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use vial
4 single use vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/106 1 pack
EU/1/01/185/107 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 100 mcg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

VIAL CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 200 micrograms solution for injection in vial
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL vial contains 200 micrograms darbepoetin alfa.

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use vial
4 single use vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/108 1 pack
EU/1/01/185/109 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 200 mcg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

VIAL CARTON

1. NAME OF THE MEDICINAL PRODUCT

Aranesp 300 micrograms solution for injection in vial
Darbepoetin alfa

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 1 mL vial contains 300 micrograms darbepoetin alfa.

3. LIST OF EXCIPIENTS

Excipients: sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

1 single use vial
4 single use vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous or subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/185/110 1 pack
EU/1/01/185/111 4 pack

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Aranesp 300 mcg injection
Darbepoetin alfa
IV/SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Aranesp 10 micrograms solution for injection in pre-filled syringe
Aranesp 15 micrograms solution for injection in pre-filled syringe
Aranesp 20 micrograms solution for injection in pre-filled syringe
Aranesp 30 micrograms solution for injection in pre-filled syringe
Aranesp 40 micrograms solution for injection in pre-filled syringe
Aranesp 50 micrograms solution for injection in pre-filled syringe
Aranesp 60 micrograms solution for injection in pre-filled syringe
Aranesp 80 micrograms solution for injection in pre-filled syringe
Aranesp 100 micrograms solution for injection in pre-filled syringe
Aranesp 130 micrograms solution for injection in pre-filled syringe
Aranesp 150 micrograms solution for injection in pre-filled syringe
Aranesp 300 micrograms solution for injection in pre-filled syringe
Aranesp 500 micrograms solution for injection in pre-filled syringe
darbepoetin alfa

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet (see section 4).

What is in this leaflet

1. What Aranesp is and what it is used for

Your doctor has given you Aranesp (an anti-anaemic) to treat your anaemia. Anaemia is when your blood does not contain enough red blood cells and the symptoms may be fatigue, weakness and shortness of breath.

Aranesp works in exactly the same way as the natural hormone erythropoietin. Erythropoietin is produced in your kidneys and encourages your bone marrow to produce more red blood cells. The active substance of Aranesp is darbepoetin alfa produced by gene-technology in Chinese Hamster Ovary Cells (CHO-K1).

If you have chronic renal failure

Aranesp is used to treat symptomatic anaemia that is associated with chronic renal failure (kidney failure) in adults and children. In kidney failure, the kidney does not produce enough of the natural hormone erythropoietin which can often cause anaemia.

Because it will take your body some time to make more red blood cells, it will be about four weeks before you notice any effect. Your normal dialysis routine will not affect the ability of Aranesp to treat your anaemia.

If you are receiving chemotherapy

Aranesp is used to treat symptomatic anaemia in adult cancer patients with non-bone marrow cancers (non-myeloid malignancies) who are receiving chemotherapy.

One of the main side effects of chemotherapy is that it stops the bone marrow producing enough blood cells. Towards the end of your chemotherapy course, particularly if you have had a lot of chemotherapy, your red blood cell count may fall making you anaemic.

2. What you need to know before you use Aranesp

Do not use Aranesp:
- if you are allergic to darbepoetin alfa or any of the other ingredients of this medicine listed in section 6.
- if you have been diagnosed with high blood pressure which is not being controlled with other medicines prescribed by your doctor.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Aranesp.

Please tell your doctor if you are **suffering** or **have suffered** from:
- high blood pressure which is being controlled with medicines prescribed by your doctor;
- sickle cell anaemia;
- epileptic fits (seizures);
- convulsions (fits or seizures);
- liver disease;
- significant lack of response to medicines used to treat anaemia;
- an allergy to latex (the needle cap on the pre-filled syringe contains a derivative of latex); or
- hepatitis C.

Special warnings:
- If you have symptoms which include unusual tiredness and a lack of energy this could mean you have pure red cell aplasia (PRCA), which has been reported in patients. PRCA means that the body has stopped or reduced the production of red blood cells which causes severe anaemia. If you experience these symptoms you should contact your doctor who will determine the best course of action to treat your anaemia.

- Take special care with other products that stimulate red blood cell production: Aranesp is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional should always record the exact product you are using.

- If you are a patient with chronic renal failure, and particularly if you do not respond properly to Aranesp, your doctor will check your dose of Aranesp because repeatedly increasing your dose of Aranesp if you are not responding to treatment may increase the risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- Your doctor should try to keep your haemoglobin between 10 and 12 g/dL. Your doctor will check that your haemoglobin does not exceed a certain level, as high haemoglobin concentrations could put you at risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- If you have symptoms which include severe headache, drowsiness, confusion, problems with your eyesight, nausea, vomiting or fits (seizures), it could mean that you have very high blood pressure. If you experience these symptoms you should contact your doctor.

- If you are a cancer patient you should be aware that Aranesp may act as a blood cell growth factor and in some circumstances may have a negative impact on your cancer. Depending on your individual situation a blood transfusion may be preferable. Please discuss this with your doctor.

- Misuse by healthy people can cause life-threatening problems with the heart or blood vessels.

- Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.
  If you develop a serious rash or another of these skin symptoms, stop taking Aranesp and contact your doctor or seek medical attention immediately.

Other medicines and Aranesp

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Cyclosporin and tacrolimus (medicines which suppress the immune system) may be affected by the number of red cells in your blood. It is important to tell your doctor if you are taking either of these medicines.

Using Aranesp with food and drink

Food and drink do not affect Aranesp.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Aranesp has not been tested in pregnant women. It is important to tell your doctor if you:
- are pregnant;
- think you may be pregnant; or
- plan to get pregnant.

It is not known whether darbepoetin alfa is excreted in human milk. You must stop breast-feeding if you use Aranesp.

Driving and using machines

Aranesp should not affect your ability to drive or use machinery.

Aranesp contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Aranesp

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Following blood tests, your doctor has decided you need Aranesp as your haemoglobin level is 10 g/dL or less. Your doctor will tell you how much and how often you must take Aranesp in order to maintain a haemoglobin level between 10 and 12 g/dL. This may vary depending on whether you are an adult or a child.

Injecting Aranesp yourself

Your doctor may decide that it is best for you or a carer to inject Aranesp. Your doctor, nurse or pharmacist will show you how to inject yourself with the pre-filled syringe. Do not try to inject yourself if you have not been trained. **Never inject Aranesp into a vein yourself.**

If you have chronic renal failure

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, Aranesp is given as a single injection, either under your skin (subcutaneous) or into a vein (intravenous).

In order to correct your anaemia, your initial dose of Aranesp per kilogram of your body weight will be either:

- 0.75 micrograms once every two weeks, or
- 0.45 micrograms once weekly.

For adult patients not on dialysis, 1.5 micrograms/kg once monthly may also be used as the initial dose.

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, once your anaemia is corrected you will continue to receive Aranesp given as a single injection, either once a week or once every two weeks. For all adults and paediatric patients ≥ 11 years of age not on dialysis, Aranesp could also be given as an injection once monthly.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose once every four weeks as necessary in order to maintain long term control of your anaemia.

Your doctor will use the lowest effective dose to control the symptoms of your anaemia.

If you do not respond adequately to Aranesp, your doctor will check your dose and will inform you if you need to change doses of Aranesp.

Your blood pressure will also be checked regularly, particularly at the beginning of your treatment.

In some cases, your doctor may recommend that you take iron supplements.

Your doctor may decide to change the way that your injection is given (either under the skin or into a vein). If this changes you will start on the same dose as you have been receiving and your doctor will take blood samples to make sure that your anaemia is still being managed correctly.

If your doctor has decided to change your treatment from r-HuEPO (erythropoietin produced by gene-technology) to Aranesp, they will choose whether you should receive your Aranesp injection once weekly or once every two weeks. The route of injection is the same as with r-HuEPO but your doctor will tell you how much you should take, and when, and may adjust your dose if necessary.

If you are receiving chemotherapy

Aranesp is given as a single injection, either once a week or once every three weeks, under your skin.

In order to correct your anaemia, your initial dose will be:
- 500 micrograms once every three weeks (6.75 micrograms of Aranesp per kilogram of your body weight); or
- 2.25 micrograms (once weekly) of Aranesp per kilogram of your body weight.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose as necessary. Your treatment will continue until approximately four weeks after the end of your chemotherapy. Your doctor will tell you exactly when to stop taking Aranesp.

In some cases, your doctor may recommend that you take iron supplements.

If you use more Aranesp than you should

You could have serious problems if you use more Aranesp than you need, such as very high blood pressure. You should contact your doctor, nurse or pharmacist if this does happen. If you feel unwell in any way you should contact your doctor, nurse or pharmacist immediately.

If you forget to use Aranesp

Do not use a double dose to make up for a forgotten dose.

If you have forgotten a dose of Aranesp, you should contact your doctor to discuss when you should inject the next dose.

If you stop using Aranesp

If you want to stop using Aranesp, you should discuss it with your doctor first.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been experienced by some patients taking Aranesp:

Chronic renal failure patients

Very common: may affect more than 1 in 10 people
- High blood pressure (hypertension)
- Allergic reactions

Common: may affect up to 1 in 10 people
- Stroke
- Pain around the area injected
- Rash and/or redness of the skin

Uncommon: may affect up to 1 in 100 people
- Blood clots (thrombosis)
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection
- Blood clots in a dialysis access

Not known: frequency cannot be estimated from available data
- Pure red cell aplasia (PRCA) – (anaemia, unusual tiredness, lack of energy)

Cancer patients

Very common: may affect more than 1 in 10 people
- Allergic reactions

Common: may affect up to 1 in 10 people
- High blood pressure (hypertension)
- Blood clots (thrombosis)
- Pain around the area injected
- Rash and/or redness of the skin
- Fluid retention (oedema)

Uncommon: may affect up to 1 in 100 people
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection

All patients

Not known: frequency cannot be estimated from available data
- Serious allergic reactions which may include:
  - Sudden life-threatening allergic reactions (anaphylaxis)
  - Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
  - Shortness of breath (allergic bronchospasm)
  - Skin rash
  - Hives (urticaria)
- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. Stop using Aranesp if you develop these symptoms and contact your doctor or seek medical attention immediately (see section 2).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aranesp

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the pre-filled syringe label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Do not use Aranesp if you think it has been frozen.

Keep the pre-filled syringe in the outer carton in order to protect from light.

When your syringe has been removed from the refrigerator and left at room temperature for approximately 30 minutes before injection it must either be used within 7 days or disposed of.

Do not use this medicine if you notice the pre-filled syringe contents are cloudy or there are particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aranesp contains

- The active substance is darbepoetin alfa, r-HuEPO (erythropoietin produced by gene-technology). The pre-filled syringe contains either 10, 15, 20, 30, 40, 50, 60, 80, 100, 130, 150, 300 or 500 micrograms of darbepoetin alfa.
- The other ingredients are sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 and water for injections.

What Aranesp looks like and contents of the pack

Aranesp is a clear, colourless or slightly pearly solution for injection in a pre-filled syringe.

Aranesp is available in packs of 1 or 4 pre-filled syringes. The syringes are provided either with (1- and 4-pack) or without (1-pack) a blister-wrapping. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Amgen Europe B.V.
Minervum 7061
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Marketing Authorisation Holder
Amgen Europe B.V.
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Amgen Technology (Ireland) Unlimited Company
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Manufacturer
Amgen NV
Telecomlaan 5-7
1831 Diegem
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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s.a. Amgen n.v.
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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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7. Instructions for injecting with the Aranesp pre-filled syringe

This section contains information on how to give yourself an injection of Aranesp. It is important that you do not try to give yourself the injection unless you have received training from your doctor, nurse or pharmacist. If you have questions about how to inject, please ask your doctor, nurse or pharmacist for assistance.

How do you or the person injecting you, use the Aranesp pre-filled syringe?

Your doctor has prescribed an Aranesp pre-filled syringe for injection into the tissue just under the skin. Your doctor, nurse or pharmacist will tell you how much Aranesp you need and how frequently it should be injected.

Equipment:

To give yourself an injection you will need:

- a new Aranesp pre-filled syringe; and
- alcohol wipes or similar.

What should I do before I give myself a subcutaneous injection of Aranesp?

1. Remove the pre-filled syringe from the refrigerator. Leave the pre-filled syringe at room temperature for approximately 30 minutes. This will make the injection more comfortable. Do not warm Aranesp in any other way (for example, do not warm it in a microwave or in hot water). Additionally, do not leave the syringe exposed to direct sunlight.

2. Do not shake the pre-filled syringe.

3. Do not remove the cap from the syringe until you are ready to inject.

4. Check that it is the correct dose that your doctor has prescribed.

5. Check the expiry date on the pre-filled syringe label (EXP). Do not use it if the date has passed the last day of the month shown.

6. Check the appearance of Aranesp. It must be a clear, colourless or slightly pearly liquid. If it is cloudy or there are particles in it, you must not use it.

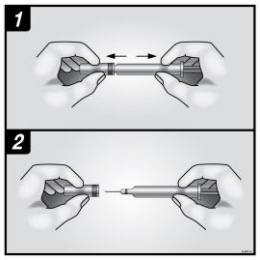
7. Wash your hands thoroughly.

8. Find a comfortable, well-lit, clean surface and put all the equipment you need within reach.

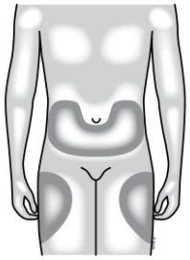
How do I prepare my Aranesp injection?

Before you inject Aranesp you must do the following:

1. To avoid bending the needle, gently pull the cap from the needle without twisting as shown in pictures 1 and 2.
2. Do not touch the needle or push the plunger.
3. You may notice a small air bubble in the pre-filled syringe. You do not have to remove the air bubble before injecting. Injecting the solution with the air bubble is harmless.
4. You can now use the pre-filled syringe.



Where should I give my injection?



The best places to inject yourself are the top of your thighs and the abdomen. If someone else is injecting for you, they can also use the back of your arms.

You may change the injection site if you notice the area is red or sore.

How do I give my injection?

1. Disinfect your skin by using an alcohol wipe and pinch (without squeezing) the skin between your thumb and forefinger.

2. Insert the needle fully into the skin as shown by your doctor, nurse or pharmacist.

3. Inject the prescribed dose subcutaneously as directed by your doctor, nurse or pharmacist.

4. Push the plunger with a slow constant pressure, always keeping your skin pinched, until the syringe is empty.

5. Remove the needle and let go of your skin.

6. If you notice a spot of blood you may gently dab it away with a cotton ball or tissue. Do not rub the injection site. If needed, you may cover the injection site with a plaster.

7. Only use each syringe for one injection. Do not use any Aranesp that is left in the syringe.

Remember: If you have any problems, please do not be afraid to ask your doctor or nurse for help and advice.

Disposing of used syringes

- Do not put the cap back on used needles, as you may accidentally prick yourself.
- Keep used syringes out of the reach and sight of children.
- The used pre-filled syringe should be disposed of in accordance with local requirements. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Package leaflet: Information for the user

Aranesp 10 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 15 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 20 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 30 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 40 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 50 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 60 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 80 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 100 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 130 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 150 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 300 micrograms solution for injection in pre-filled pen (SureClick)
Aranesp 500 micrograms solution for injection in pre-filled pen (SureClick)
darbepoetin alfa

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- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet (see section 4).

What is in this leaflet

1. What Aranesp is and what it is used for

Your doctor has given you Aranesp (an anti-anaemic) to treat your anaemia. Anaemia is when your blood does not contain enough red blood cells and the symptoms may be fatigue, weakness and shortness of breath.

Aranesp works in exactly the same way as the natural hormone erythropoietin. Erythropoietin is produced in your kidneys and encourages your bone marrow to produce more red blood cells. The active substance of Aranesp is darbepoetin alfa produced by gene-technology in Chinese Hamster Ovary Cells (CHO-K1).

If you have chronic renal failure

Aranesp is used to treat symptomatic anaemia that is associated with chronic renal failure (kidney failure) in adults and children. In kidney failure, the kidney does not produce enough of the natural hormone erythropoietin which can often cause anaemia.

Because it will take your body some time to make more red blood cells, it will be about four weeks before you notice any effect. Your normal dialysis routine will not affect the ability of Aranesp to treat your anaemia.

If you are receiving chemotherapy

Aranesp is used to treat symptomatic anaemia in adult cancer patients with non-bone marrow cancers (non-myeloid malignancies) who are receiving chemotherapy.

One of the main side effects of chemotherapy is that it stops the bone marrow producing enough blood cells. Towards the end of your chemotherapy course, particularly if you have had a lot of chemotherapy, your red blood cell count may fall making you anaemic.

2. What you need to know before you use Aranesp

Do not use Aranesp:
- if you are allergic to darbepoetin alfa or any of the other ingredients of this medicine listed in section 6.
- if you have been diagnosed with high blood pressure which is not being controlled with other medicines prescribed by your doctor.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Aranesp

Please tell your doctor if you are **suffering** or **have suffered** from:
- high blood pressure which is being controlled with medicines prescribed by your doctor;
- sickle cell anaemia;
- epileptic fits (seizures);
- convulsions (fits or seizures);
- liver disease;
- significant lack of response to medicines used to treat anaemia;
- an allergy to latex (the needle cap on the pre-filled pen contains a derivative of latex); or
- hepatitis C.

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- Your doctor should try to keep your haemoglobin between 10 and 12 g/dL. Your doctor will check that your haemoglobin does not exceed a certain level, as high haemoglobin concentrations could put you at risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- If you have symptoms which include severe headache, drowsiness, confusion, problems with your eyesight, nausea, vomiting or fits (seizures), it could mean that you have very high blood pressure. If you experience these symptoms you should contact your doctor.

- If you are a cancer patient you should be aware that Aranesp may act as a blood cell growth factor and in some circumstances may have a negative impact on your cancer. Depending on your individual situation a blood transfusion may be preferable. Please discuss this with your doctor.

- Misuse by healthy people can cause life-threatening problems with the heart or blood vessels.

- Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.
  If you develop a serious rash or another of these skin symptoms, stop taking Aranesp and contact your doctor or seek medical attention immediately.

Other medicines and Aranesp

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Cyclosporin and tacrolimus (medicines which suppress the immune system) may be affected by the number of red cells in your blood. It is important to tell your doctor if you are taking either of these medicines.

Using Aranesp with food and drink

Food and drink do not affect Aranesp.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Aranesp has not been tested in pregnant women. It is important to tell your doctor if you:
- are pregnant;
- think you may be pregnant; or
- plan to get pregnant.

It is not known whether darbepoetin alfa is excreted in human milk. You must stop breast-feeding if you use Aranesp.

Driving and using machines

Aranesp should not affect your ability to drive or use machinery.

Aranesp contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Aranesp

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Following blood tests, your doctor has decided you need Aranesp as your haemoglobin level is 10 g/dL or less. Your injection is to be given under the skin (subcutaneous), and so you may use the Aranesp pre-filled pen. Your doctor will tell you how much and how often you must take Aranesp in order to maintain a haemoglobin level between 10 and 12 g/dL. This may vary depending on whether you are an adult or a child.

Injecting Aranesp yourself

Your doctor has decided that the Aranesp pre-filled pen is the best way for you, a nurse or a carer to inject Aranesp. Your doctor, nurse or pharmacist will show you how to inject yourself with the pre-filled pen. Do not try to inject yourself if you have not been trained. **Never inject Aranesp into a vein yourself. The pre-filled pen is designed to inject the area under your skin only.**

For instructions on use of the pre-filled pen, please read the section at the end of this leaflet.

If you have chronic renal failure

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, Aranesp pre-filled pen is given as a single injection, under your skin (subcutaneous).

In order to correct your anaemia, your initial dose of Aranesp per kilogram of your body weight will be either:

- 0.75 micrograms once every two weeks, or
- 0.45 micrograms once weekly.

For adult patients not on dialysis, 1.5 micrograms/kg once monthly may also be used as the initial dose.

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, once your anaemia is corrected you will continue to receive Aranesp given as a single injection, either once a week or once every two weeks. For all adults and paediatric patients ≥ 11 years of age not on dialysis, Aranesp could also be given as an injection once monthly.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose once every four weeks as necessary in order to maintain long term control of your anaemia.

Your doctor will use the lowest effective dose to control the symptoms of your anaemia.

If you do not respond adequately to Aranesp, your doctor will check your dose and will inform you if you need to change doses of Aranesp.

Your blood pressure will also be checked regularly, particularly at the beginning of your treatment.

In some cases, your doctor may recommend that you take iron supplements.

Your doctor may decide to change the way that your injection is given (either under the skin or into a vein). If this changes you will start on the same dose as you have been receiving and your doctor will take blood samples to make sure that your anaemia is still being managed correctly.

If your doctor has decided to change your treatment from r-HuEPO (erythropoietin produced by gene-technology) to Aranesp, they will choose whether you should receive your Aranesp injection once weekly or once every two weeks. The route of injection is the same as with r-HuEPO but your doctor will tell you how much you should take, and when, and may adjust your dose if necessary.

If you are receiving chemotherapy

Aranesp is given as a single injection, either once a week or once every three weeks, under your skin.

In order to correct your anaemia, your initial dose will be:
- 500 micrograms once every three weeks (6.75 micrograms of Aranesp per kilogram of your body weight); or
- 2.25 micrograms (once weekly) of Aranesp per kilogram of your body weight.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose as necessary. Your treatment will continue until approximately four weeks after the end of your chemotherapy. Your doctor will tell you exactly when to stop taking Aranesp.

In some cases, your doctor may recommend that you take iron supplements.

If you use more Aranesp than you should

You could have serious problems if you use more Aranesp than you need, such as very high blood pressure. You should contact your doctor, nurse or pharmacist if this does happen. If you feel unwell in any way you should contact your doctor, nurse or pharmacist immediately.

If you forget to use Aranesp

Do not use a double dose to make up for a forgotten dose.

If you have forgotten a dose of Aranesp, you should contact your doctor to discuss when you should inject the next dose.

If you stop using Aranesp

If you want to stop using Aranesp, you should discuss it with your doctor first.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been experienced by some patients taking Aranesp:

<u>Chronic renal failure patients</u>

Very common: may affect more than 1 in 10 people
- High blood pressure (hypertension)
- Allergic reactions

Common: may affect up to 1 in 10 people
- Stroke
- Pain around the area injected
- Rash and/or redness of the skin

Uncommon: may affect up to 1 in 100 people
- Blood clots (thrombosis)
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection
- Blood clots in a dialysis access

Not known: frequency cannot be estimated from available data
- Pure red cell aplasia (PRCA) – (anaemia, unusual tiredness, lack of energy)

Cancer patients

Very common: may affect more than 1 in 10 people
- Allergic reactions

Common: may affect up to 1 in 10 people
- High blood pressure (hypertension)
- Blood clots (thrombosis)
- Pain around the area injected
- Rash and/or redness of the skin
- Fluid retention (oedema)

Uncommon: may affect up to 1 in 100 people
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection

All patients

Not known: frequency cannot be estimated from available data
- Serious allergic reactions which may include:
  - Sudden life-threatening allergic reactions (anaphylaxis)
  - Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
  - Shortness of breath (allergic bronchospasm)
  - Skin rash
  - Hives (urticaria)
- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. Stop using Aranesp if you develop these symptoms and contact your doctor or seek medical attention immediately (see section 2).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aranesp

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the pre-filled pen label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Do not use Aranesp if you think it has been frozen.

Keep the pre-filled pen in the outer carton in order to protect from light.

When your pen has been removed from the refrigerator and left at room temperature for approximately 30 minutes before injection it must either be used within 7 days or disposed of.

Do not use this medicine if you notice the pre-filled pen contents are cloudy or there are particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aranesp contains

- The active substance is darbepoetin alfa, r-HuEPO (erythropoietin produced by gene-technology). The pre-filled pen contains either 10, 15, 20, 30, 40, 50, 60, 80, 100, 130, 150, 300 or 500 micrograms of darbepoetin alfa.
- The other ingredients are sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 and water for injections.

What Aranesp looks like and contents of the pack

Aranesp is a clear, colourless or slightly pearly solution for injection in a pre-filled pen.

Aranesp (SureClick) is available in packs containing 1 or 4 pre-filled pens. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Marketing Authorisation Holder
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Manufacturer
Amgen Technology (Ireland) Unlimited Company
Pottery Road
Dun Laoghaire
Co Dublin
Ireland

Manufacturer
Amgen NV
Telecomlaan 5-7
1831 Diegem
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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s.a. Amgen n.v.
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Slovenija
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Amgen Slovakia s.r.o.
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Latvija
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Sverige
Amgen AB
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United Kingdom (Northern Ireland)
Amgen Limited
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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

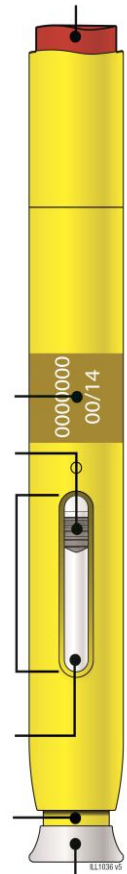
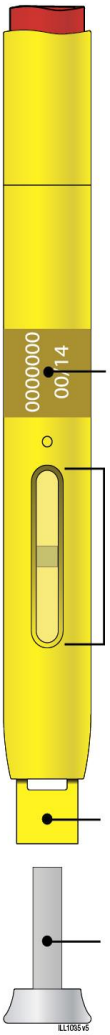
This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

Instructions for use

It is important that you do not try to give the injection unless you or your caregiver has received training from your healthcare provider.

There are additional educational materials available to train you on how to self administer Aranesp pre-filled pen, a dummy demonstration device and a poster-size instructions for use for patients/caregivers with diminished eyesight.

Guide to parts

Before use	**After use**
	

Important: Needle is inside the yellow safety guard.

Important

Before you use the Aranesp SureClick pre-filled pen, read this important information:

Storing your Aranesp SureClick pre-filled pens

- Keep the pre-filled pen and all medicines out of the sight and reach of children.
- Keep the pre-filled pen in the outer carton in order to protect from light or physical damage.
- Store the pre-filled pen in the refrigerator (2ºC – 8ºC).
- Once your pre-filled pen has been removed from the refrigerator, and left at room temperature (up to 25ºC) for approximately 30 minutes before injection, it must either be used within seven days or disposed of.

✘ **Do not** store the pre-filled pen in extreme heat or cold. For example, avoid storing in your car glove box or boot.

✘ **Do not** freeze. Do not use Aranesp if you think it has been frozen.

Using your Aranesp SureClick pre-filled pens

- Your healthcare provider has prescribed the Aranesp pre-filled pen for injection into the tissue just under the skin (subcutaneous use).

✘ **Do not** use the pre-filled pen after the expiry date on the label. The expiry date refers to the last day of that month.

✘ **Do not** shake the pre-filled pen.

✘ **Do not** remove the grey cap from the pre-filled pen until you are ready to inject.

✘ **Do not** use the pre-filled pen if it has been dropped on a hard surface. Part of the pre-filled pen may be broken even if you cannot see the break. Use a new pre-filled pen.

- The grey cap on the pen contains dry natural rubber, which is made from latex. Tell your healthcare provider if you are allergic to latex.

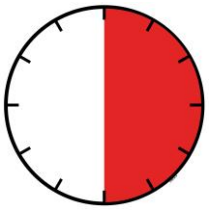
For more information or help, contact your healthcare provider.

Step 1: Prepare

A Remove one pre-filled pen from the carton.

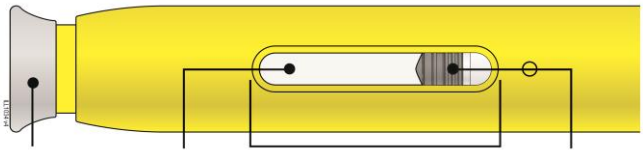
Carefully lift the pre-filled pen straight up out of the carton.
Put the original carton with any unused pre-filled pens back in the refrigerator.
Leave the pre-filled pen at room temperature for at least 30 minutes before injecting.

- ✘ **Do not** put the pre-filled pen back in the refrigerator once it has reached room temperature.
- ✘ **Do not** try to warm the pre-filled pen by using a heat source such as hot water or microwave.
- ✘ **Do not** leave the pre-filled pen in direct sunlight.
- ✘ **Do not** shake the pre-filled pen.
- ✘ **Do not** remove the grey cap from the pre-filled pen yet.



30 minutes

B Inspect the pre-filled pen.



Grey cap on (needle inside) | Medicine | Window | Plunger (location may vary)

Make sure the medicine in the window is a clear and colourless liquid.

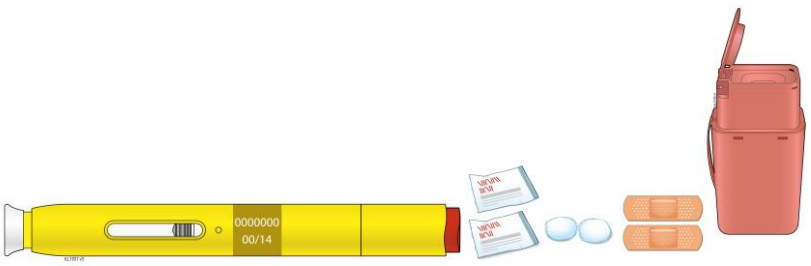
- Check that it is the correct dose that your healthcare provider has prescribed.
- **You may see the plunger in the inspection window at a different location, depending upon the strength.**
- ✘ **Do not** use the pre-filled pen if the medicine is cloudy or discoloured or contains flakes or particles.
- ✘ **Do not** use the pre-filled pen if any part appears cracked or broken.
- ✘ **Do not** use the pre-filled pen if the grey cap is missing or not securely attached.
- ✘ **Do not** use the pre-filled pen if the expiry date printed after EXP on the label has passed.

In all cases, use a new pre-filled pen and contact your healthcare provider.

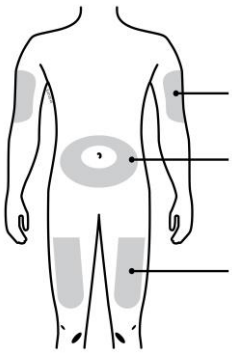
C Gather all the materials needed for your injection.

Wash your hands thoroughly with soap and water.
On a clean, well-lit work surface, place the:

- New pre-filled pen
- Alcohol wipes
- Cotton ball or gauze pad
- Plaster
- Sharps disposal container



D	Prepare and clean your injection site.



Upper arm

Stomach area (abdomen)

Thigh

You can use:

- Your thigh.
- Your stomach area (abdomen), except for a **5 cm (2-inch)** area right around your navel.
- The outer area of upper arm (only if someone else is giving you the injection).

Clean the injection site with an alcohol wipe. Let your skin dry.

✘ **Do not** touch this area again before injecting.

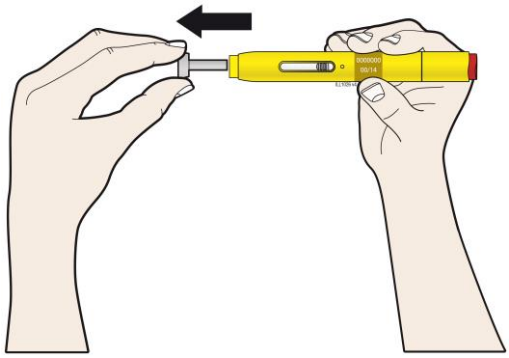
- Choose a different site each time you give yourself an injection. If you want to use the same injection site, make sure it is not the same spot on the injection site you used for a previous injection.

✘ **Do not** inject into areas where the skin is tender, bruised, red, or hard.

- Avoid injecting into raised, thick, red, or scaly skin patches or lesions, or areas with scars or stretch marks.

Important: Follow your healthcare provider's instructions about selecting sites for injection appropriate to you and about changing the site for each injection.

Step 2: Get ready	
E	Pull the grey cap straight off, only when you are ready to inject. **Do not** leave the grey cap off for more than five minutes. This can dry out the medicine.



It is normal to see a drop of liquid at the end of the needle or yellow safety guard.

✘ **Do not** twist or bend the grey cap.

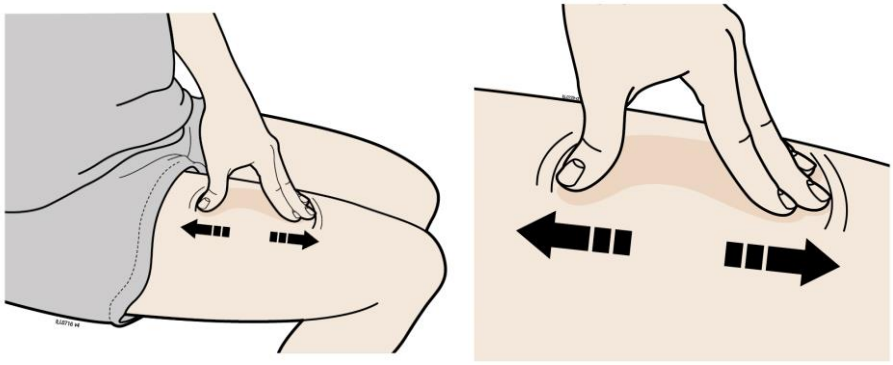
✘ **Do not** put the grey cap back onto the pre-filled pen.

✘ **Do not** remove the grey cap from the pre-filled pen until you are ready to inject.

If you are unable to inject, please contact your healthcare provider immediately.

F	Stretch or pinch your injection site to create a firm surface.

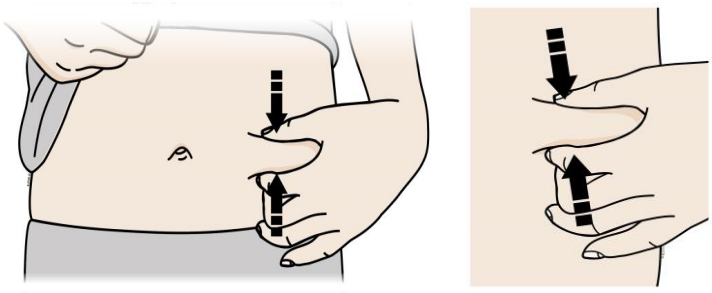
Stretch method



Stretch your skin firmly by moving your thumb and fingers in opposite directions, creating an area about **5 cm (2-inches)** wide.

OR

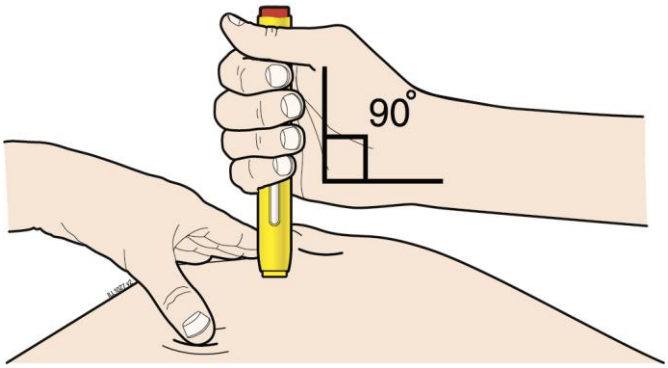
Pinch method



Pinch your skin firmly between your thumb and fingers, creating an area about **5 cm (2-inches)** wide.

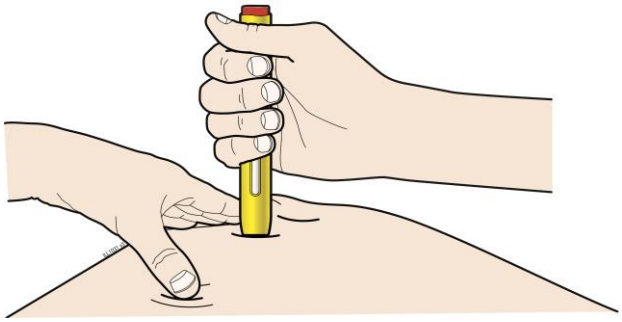
Important: It is important to keep your skin stretched or pinched while injecting.

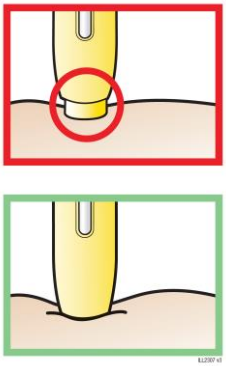
Step 3: Inject	
G	Keep stretching or pinching your skin. With the grey cap off, **place** the pre-filled pen on your skin at 90 degrees.



Important: Do not touch the red start button yet.

H	Firmly **push** the pre-filled pen down onto your skin until it stops moving. The safety guard retracts when pushed onto a firm injection site.

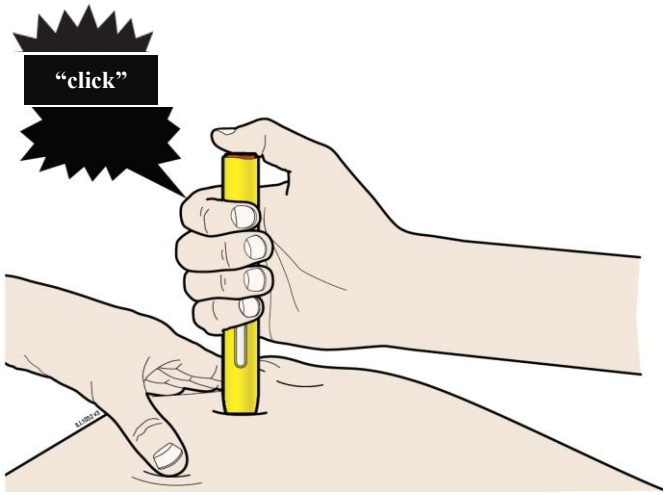




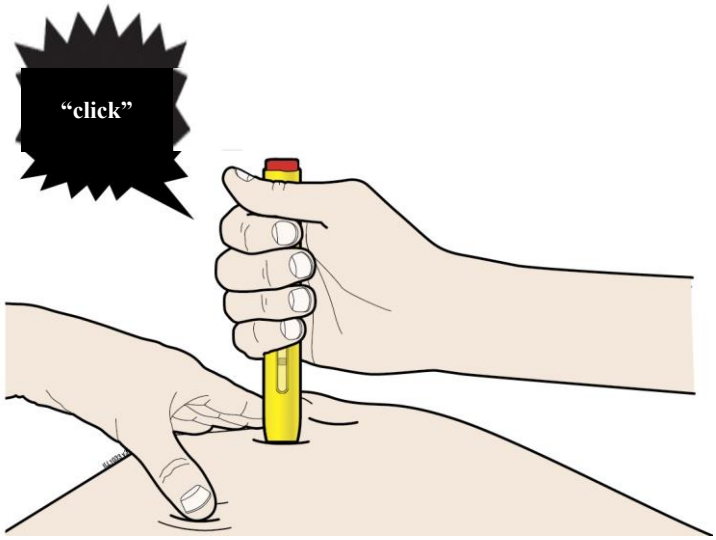
Yellow safety guard retracted.

Important: You must push the pre-filled pen all the way down but do not touch the red start button until you are ready to inject.

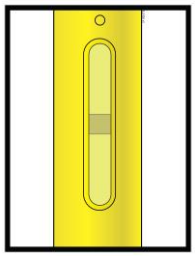
I	When you are ready to inject, **press** the red start button.



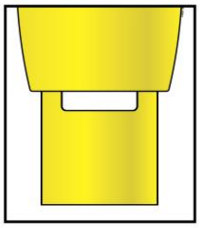
J	Keep **pushing** the pre-filled pen down on your skin. Your injection could take about **15** seconds.



15 seconds



Window turns yellow when the injection is done

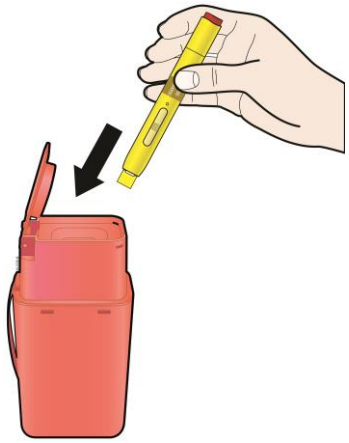


Note: After you remove the pre-filled pen from your skin, the needle will be automatically covered.

Important: When you remove the pre-filled pen, if the window has not turned yellow, or if it looks like the medicine is still injecting, this means you have not received a full dose. Contact your healthcare provider immediately.

K	Examine the injection site.
•	If there is blood, press a cotton ball or gauze pad on your injection site. **Do not** rub the injection site. Apply a plaster if needed.

Step 4: Finish	
L	Dispose of the used pre-filled pen and grey cap.



Put the used pre-filled pen in the sharps disposal container immediately after use.

✘ **Do not** reuse the pre-filled pen.

✘ **Do not** recycle the pre-filled pen or sharps disposal container or throw them into household rubbish.

Talk with your healthcare provider about proper disposal. There may be local guidelines for disposal.

Important: Always keep the sharps disposal container out of the sight and reach of children.

Package leaflet: Information for the user

Aranesp 10 micrograms solution for injection in pre-filled syringe
Aranesp 15 micrograms solution for injection in pre-filled syringe
Aranesp 20 micrograms solution for injection in pre-filled syringe
Aranesp 30 micrograms solution for injection in pre-filled syringe
Aranesp 40 micrograms solution for injection in pre-filled syringe
Aranesp 50 micrograms solution for injection in pre-filled syringe
Aranesp 60 micrograms solution for injection in pre-filled syringe
Aranesp 80 micrograms solution for injection in pre-filled syringe
Aranesp 100 micrograms solution for injection in pre-filled syringe
Aranesp 130 micrograms solution for injection in pre-filled syringe
Aranesp 150 micrograms solution for injection in pre-filled syringe
Aranesp 300 micrograms solution for injection in pre-filled syringe
Aranesp 500 micrograms solution for injection in pre-filled syringe
darbepoetin alfa

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet (see section 4).

What is in this leaflet

1. What Aranesp is and what it is used for

Your doctor has given you Aranesp (an anti-anaemic) to treat your anaemia. Anaemia is when your blood does not contain enough red blood cells and the symptoms may be fatigue, weakness and shortness of breath.

Aranesp works in exactly the same way as the natural hormone erythropoietin. Erythropoietin is produced in your kidneys and encourages your bone marrow to produce more red blood cells. The active substance of Aranesp is darbepoetin alfa produced by gene-technology in Chinese Hamster Ovary Cells (CHO-K1).

If you have chronic renal failure

Aranesp is used to treat symptomatic anaemia that is associated with chronic renal failure (kidney failure) in adults and children. In kidney failure, the kidney does not produce enough of the natural hormone erythropoietin which can often cause anaemia.

Because it will take your body some time to make more red blood cells, it will be about four weeks before you notice any effect. Your normal dialysis routine will not affect the ability of Aranesp to treat your anaemia.

If you are receiving chemotherapy

Aranesp is used to treat symptomatic anaemia in adult cancer patients with non-bone marrow cancers (non-myeloid malignancies) who are receiving chemotherapy.

One of the main side effects of chemotherapy is that it stops the bone marrow producing enough blood cells. Towards the end of your chemotherapy course, particularly if you have had a lot of chemotherapy, your red blood cell count may fall making you anaemic.

2. What you need to know before you use Aranesp

Do not use Aranesp:
- if you are allergic to darbepoetin alfa or any of the other ingredients of this medicine listed in section 6.
- if you have been diagnosed with high blood pressure which is not being controlled with other medicines prescribed by your doctor.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Aranesp.

Please tell your doctor if you are **suffering** or **have suffered** from:
- high blood pressure which is being controlled with medicines prescribed by your doctor;
- sickle cell anaemia;
- epileptic fits (seizures);
- convulsions (fits or seizures);
- liver disease;
- significant lack of response to medicines used to treat anaemia;
- an allergy to latex (the needle cap on the pre-filled syringe contains a derivative of latex); or
- hepatitis C.

Special warnings:
- If you have symptoms which include unusual tiredness and a lack of energy this could mean you have pure red cell aplasia (PRCA), which has been reported in patients. PRCA means that the body has stopped or reduced the production of red blood cells which causes severe anaemia. If you experience these symptoms you should contact your doctor who will determine the best course of action to treat your anaemia.

- Take special care with other products that stimulate red blood cell production: Aranesp is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional should always record the exact product you are using.

- If you are a patient with chronic renal failure, and particularly if you do not respond properly to Aranesp, your doctor will check your dose of Aranesp because repeatedly increasing your dose of Aranesp if you are not responding to treatment may increase the risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- Your doctor should try to keep your haemoglobin between 10 and 12 g/dL. Your doctor will check that your haemoglobin does not exceed a certain level, as high haemoglobin concentrations could put you at risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- If you have symptoms which include severe headache, drowsiness, confusion, problems with your eyesight, nausea, vomiting or fits (seizures), it could mean that you have very high blood pressure. If you experience these symptoms you should contact your doctor.

- If you are a cancer patient you should be aware that Aranesp may act as a blood cell growth factor and in some circumstances may have a negative impact on your cancer. Depending on your individual situation a blood transfusion may be preferable. Please discuss this with your doctor.

- Misuse by healthy people can cause life-threatening problems with the heart or blood vessels.

- Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications. If you develop a serious rash or another of these skin symptoms, stop taking Aranesp and contact your doctor or seek medical attention immediately.

Other medicines and Aranesp

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Cyclosporin and tacrolimus (medicines which suppress the immune system) may be affected by the number of red cells in your blood. It is important to tell your doctor if you are taking either of these medicines.

Using Aranesp with food and drink

Food and drink do not affect Aranesp.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Aranesp has not been tested in pregnant women. It is important to tell your doctor if you:
- are pregnant;
- think you may be pregnant; or
- plan to get pregnant.

It is not known whether darbepoetin alfa is excreted in human milk. You must stop breast-feeding if you use Aranesp.

Driving and using machines

Aranesp should not affect your ability to drive or use machinery.

Aranesp contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Aranesp

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Following blood tests, your doctor has decided you need Aranesp as your haemoglobin level is 10 g/dL or less. Your doctor will tell you how much and how often you must take Aranesp in order to maintain a haemoglobin level between 10 and 12 g/dL. This may vary depending on whether you are an adult or a child.

Injecting Aranesp yourself

Your doctor may decide that it is best for you or a carer to inject Aranesp. Your doctor, nurse or pharmacist will show you how to inject yourself with the pre-filled syringe. Do not try to inject yourself if you have not been trained. **Never inject Aranesp into a vein yourself.**

If you have chronic renal failure

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, Aranesp is given as a single injection, either under your skin (subcutaneous) or into a vein (intravenous).

In order to correct your anaemia, your initial dose of Aranesp per kilogram of your body weight will be either:

- 0.75 micrograms once every two weeks, or
- 0.45 micrograms once weekly.

For adult patients not on dialysis, 1.5 micrograms/kg once monthly may also be used as the initial dose.

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, once your anaemia is corrected you will continue to receive Aranesp given as a single injection, either once a week or once every two weeks. For all adults and paediatric patients ≥ 11 years of age not on dialysis, Aranesp could also be given as an injection once monthly.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose once every four weeks as necessary in order to maintain long term control of your anaemia.

Your doctor will use the lowest effective dose to control the symptoms of your anaemia.

If you do not respond adequately to Aranesp, your doctor will check your dose and will inform you if you need to change doses of Aranesp.

Your blood pressure will also be checked regularly, particularly at the beginning of your treatment.

In some cases, your doctor may recommend that you take iron supplements.

Your doctor may decide to change the way that your injection is given (either under the skin or into a vein). If this changes you will start on the same dose as you have been receiving and your doctor will take blood samples to make sure that your anaemia is still being managed correctly.

If your doctor has decided to change your treatment from r-HuEPO (erythropoietin produced by gene-technology) to Aranesp, they will choose whether you should receive your Aranesp injection once weekly or once every two weeks. The route of injection is the same as with r-HuEPO but your doctor will tell you how much you should take, and when, and may adjust your dose if necessary.

If you are receiving chemotherapy

Aranesp is given as a single injection, either once a week or once every three weeks, under your skin.

In order to correct your anaemia, your initial dose will be:
- 500 micrograms once every three weeks (6.75 micrograms of Aranesp per kilogram of your body weight); or
- 2.25 micrograms (once weekly) of Aranesp per kilogram of your body weight.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose as necessary. Your treatment will continue until approximately four weeks after the end of your chemotherapy. Your doctor will tell you exactly when to stop taking Aranesp.

In some cases, your doctor may recommend that you take iron supplements.

If you use more Aranesp than you should

You could have serious problems if you use more Aranesp than you need, such as very high blood pressure. You should contact your doctor, nurse or pharmacist if this does happen. If you feel unwell in any way you should contact your doctor, nurse or pharmacist immediately.

If you forget to use Aranesp

Do not use a double dose to make up for a forgotten dose.

If you have forgotten a dose of Aranesp, you should contact your doctor to discuss when you should inject the next dose.

If you stop using Aranesp

If you want to stop using Aranesp, you should discuss it with your doctor first.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been experienced by some patients taking Aranesp:

<u>Chronic renal failure patients</u>

Very common: may affect more than 1 in 10 people
- High blood pressure (hypertension)
- Allergic reactions

Common: may affect up to 1 in 10 people
- Stroke
- Pain around the area injected
- Rash and/or redness of the skin

Uncommon: may affect up to 1 in 100 people
- Blood clots (thrombosis)
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection
- Blood clots in a dialysis access

Not known: frequency cannot be estimated from available data
- Pure red cell aplasia (PRCA) – (anaemia, unusual tiredness, lack of energy)

Cancer patients

Very common: may affect more than 1 in 10 people
- Allergic reactions

Common: may affect up to 1 in 10 people
- High blood pressure (hypertension)
- Blood clots (thrombosis)
- Pain around the area injected
- Rash and/or redness of the skin
- Fluid retention (oedema)

Uncommon: may affect up to 1 in 100 people
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection

All patients

Not known: frequency cannot be estimated from available data
- Serious allergic reactions which may include:
  - Sudden life-threatening allergic reactions (anaphylaxis)
  - Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
  - Shortness of breath (allergic bronchospasm)
  - Skin rash
  - Hives (urticaria)
- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. Stop using Aranesp if you develop these symptoms and contact your doctor or seek medical attention immediately (see section 2).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aranesp

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the pre-filled syringe label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Do not use Aranesp if you think it has been frozen.

Keep the pre-filled syringe in the outer carton in order to protect from light.

When your syringe has been removed from the refrigerator and left at room temperature for approximately 30 minutes before injection it must either be used within 7 days or disposed of.

Do not use this medicine if you notice the pre-filled syringe contents are cloudy or there are particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aranesp contains

- The active substance is darbepoetin alfa, r-HuEPO (erythropoietin produced by gene-technology). The pre-filled syringe contains either 10, 15, 20, 30, 40, 50, 60, 80, 100, 130, 150, 300 or 500 micrograms of darbepoetin alfa.
- The other ingredients are sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 and water for injections.

What Aranesp looks like and contents of the pack

Aranesp is a clear, colourless or slightly pearly solution for injection in a pre-filled syringe.

Aranesp is available in packs of 1 or 4 pre-filled syringes with automatic needle guard in a blister wrapping. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Marketing Authorisation Holder
Amgen Europe B.V.
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Manufacturer
Amgen Technology (Ireland) Unlimited Company
Pottery Road
Dun Laoghaire
Co Dublin
Ireland

Manufacturer
Amgen NV
Telecomlaan 5-7
1831 Diegem
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Suomi/Finland
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United Kingdom (Northern Ireland)
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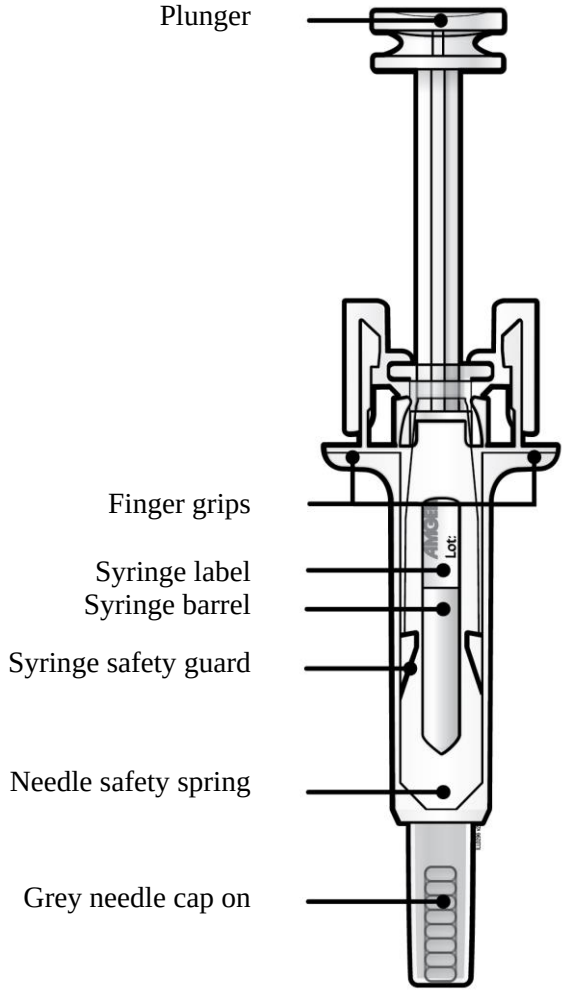
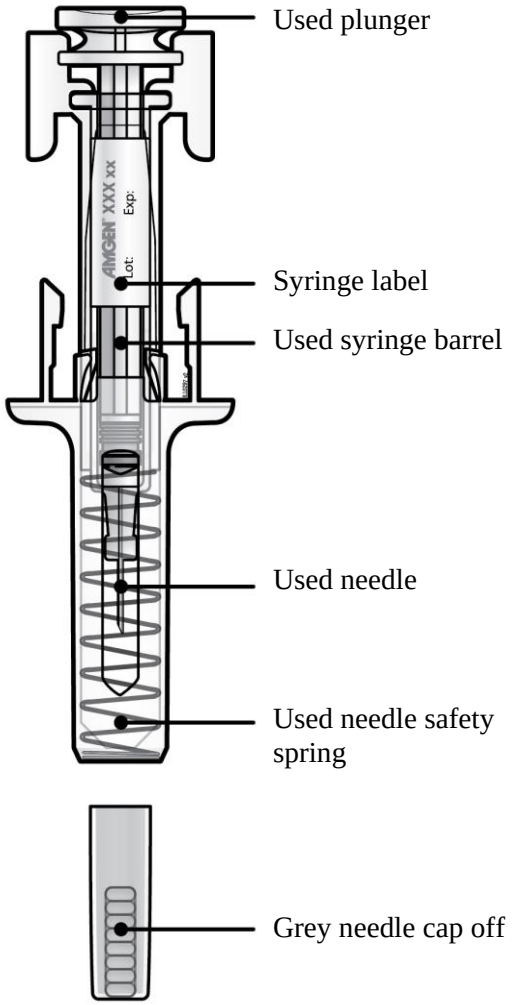
This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

Instructions for use:

Guide to parts	
Before use	After use
	

Important

Before you use an Aranesp pre-filled syringe with automatic needle guard, read this important information:

- It is important that you do not try to give yourself the injection unless you have received training from your doctor or healthcare provider.
- Aranesp is given as an injection into the tissue just under the skin (subcutaneous injection).
- Tell your doctor if you have an allergy to latex. The needle cap on the pre-filled syringe contains a derivative of latex and may cause severe allergic reactions.

✘ **Do not** remove the grey needle cap from the pre-filled syringe until you are ready to inject.

✘ **Do not** use the pre-filled syringe if it has been dropped on a hard surface. Use a new pre-filled syringe and call your doctor or healthcare provider.

✘ **Do not** attempt to activate the pre-filled syringe prior to injection.

✘ **Do not** attempt to remove the clear pre-filled syringe safety guard from the pre-filled syringe.

✘ **Do not** attempt to remove the peelable label on the pre-filled syringe barrel before administering your injection.

Call your doctor or healthcare provider if you have any questions.

Step 1: Prepare	
A	Remove the pre-filled syringe tray from the package and gather the supplies needed for your injection: alcohol wipes, a cotton ball or gauze pad, a plaster and a sharps disposal container (not included).

Put the original package with any unused pre-filled syringes back in the refrigerator.

For a more comfortable injection, leave the pre-filled syringe at room temperature for about 30 minutes before injecting. Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the new pre-filled syringe and the other supplies.

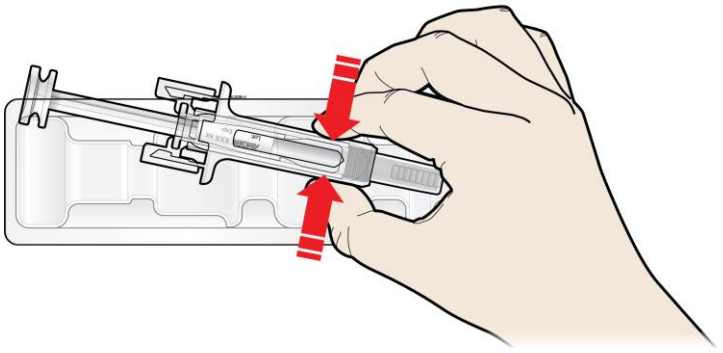
✘ **Do not** try to warm the syringe by using a heat source such as hot water or microwave

✘ **Do not** leave the pre-filled syringe exposed to direct sunlight

✘ **Do not** shake the pre-filled syringe

- **Keep pre-filled syringes out of the sight and reach of children**

B	Open the tray, peeling away the cover. Grab the pre-filled syringe safety guard to remove the pre-filled syringe from the tray.



Grab here

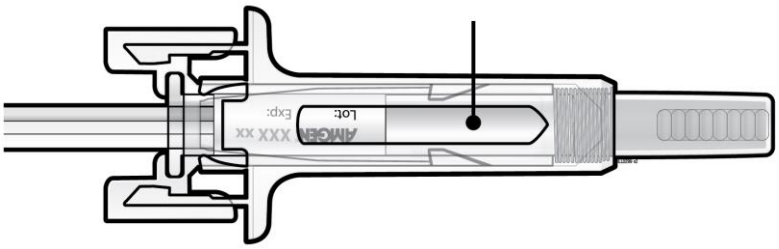
For safety reasons:

✘ **Do not** grasp the plunger

✘ **Do not** grasp the grey needle cap

C	Inspect the medicine and pre-filled syringe.

Medicine

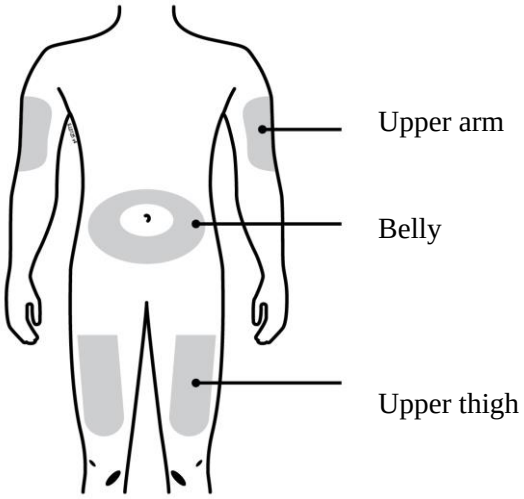


✘ **Do not** use the pre-filled syringe if:

- The medicine is cloudy or there are particles in it. It must be a clear and colourless liquid.
- Any part appears cracked or broken.
- The grey needle cap is missing or not securely attached.
- The expiry date printed on the label has passed the last day of the month shown.

In all cases, call your doctor or healthcare provider.

Step 2: Get ready	
A	Wash your hands thoroughly. Prepare and clean your injection site.



You can use:

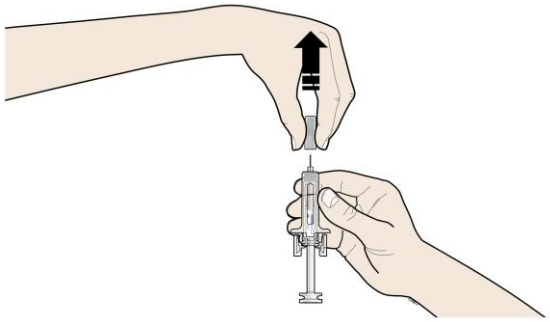
- Upper part of your thigh
- Belly, except for a 5 cm (2-inch) area right around your belly button
- Outer area of upper arm (only if someone else is giving you the injection)

Clean the injection site with an alcohol wipe. Let your skin dry.

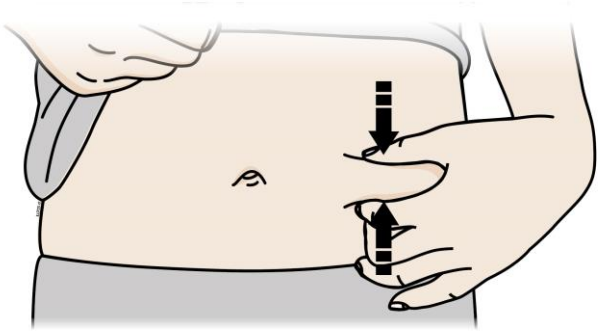
✘ **Do not** touch the injection site before injecting

Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time. **Do not** inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

B	Carefully pull the grey needle cap straight out and away from your body.

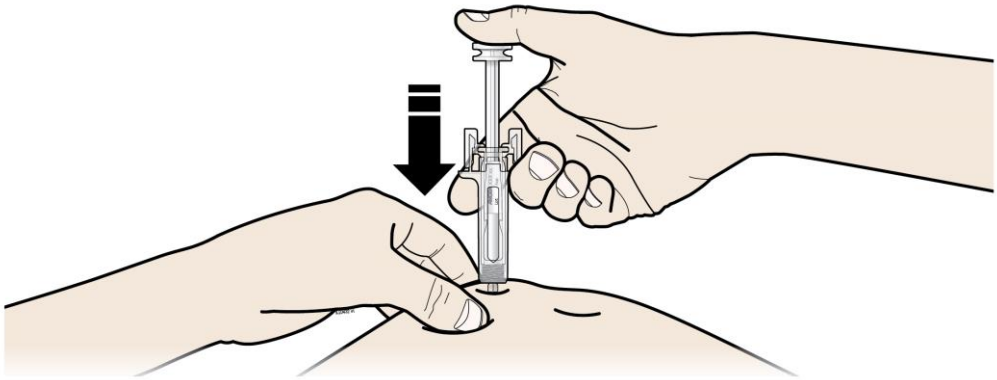


C	Pinch your injection site to create a firm surface.



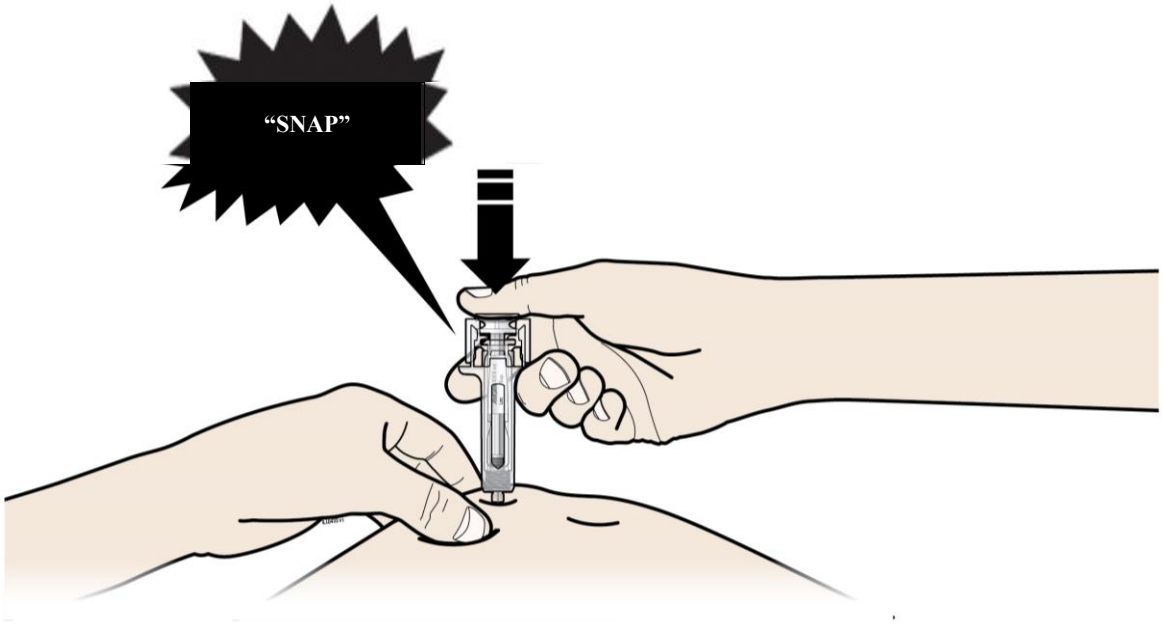
It is important to keep the skin pinched when injecting.

Step 3: Inject	
A	Hold the pinch. INSERT the needle into skin.



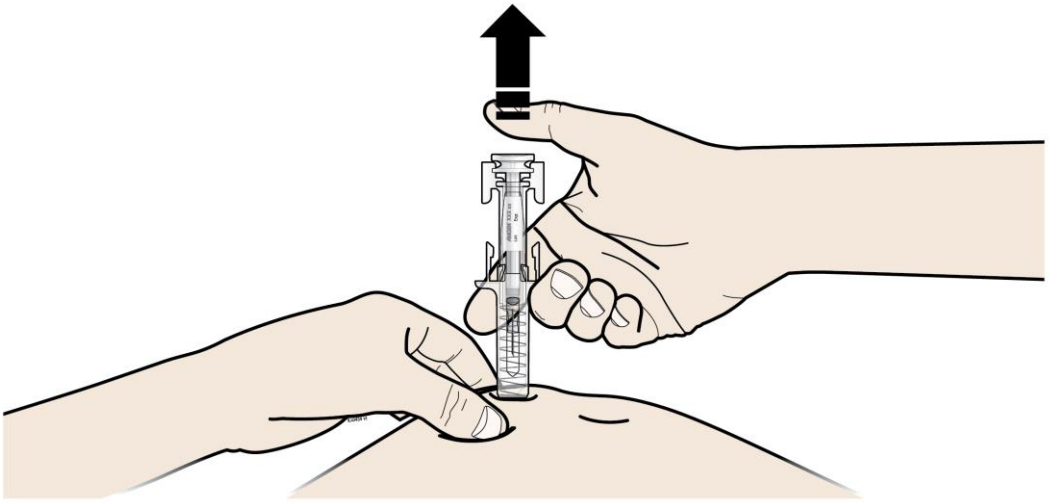
✘ **Do not** touch the cleaned area of the skin

B	PUSH the plunger with slow and constant pressure until you feel or hear a “snap”. Push all the way down through the snap.



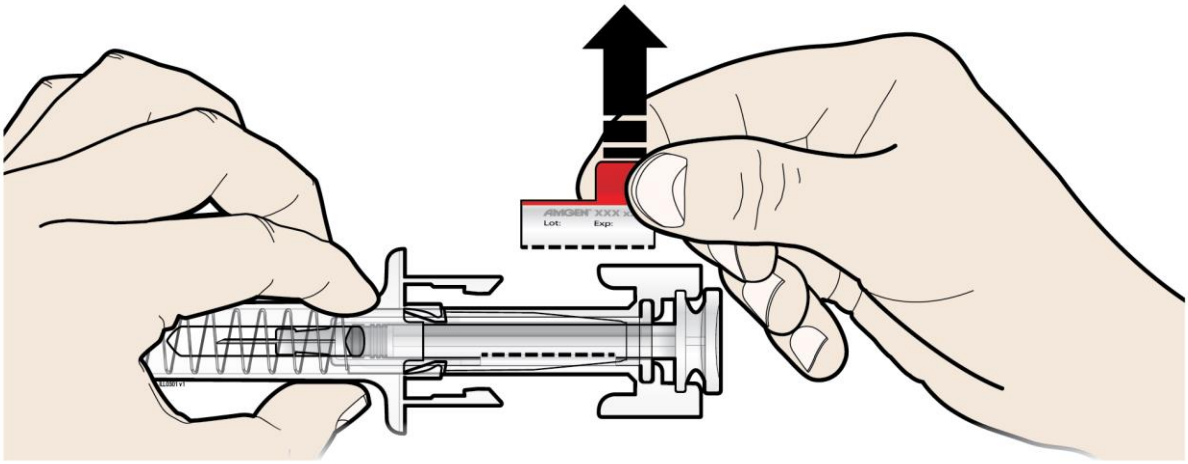
It is important to push down through the “snap” to deliver your full dose.

C	RELEASE your thumb. Then LIFT the syringe off skin.

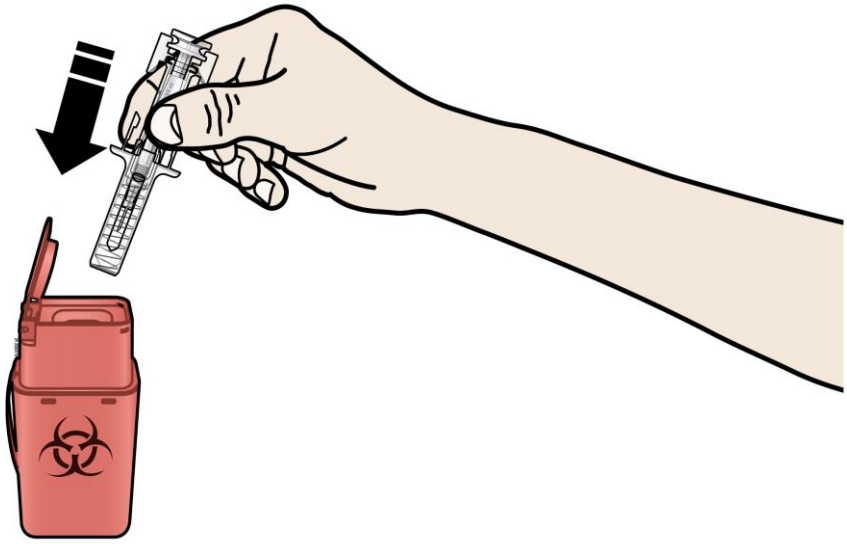


After releasing the plunger, the pre-filled syringe safety guard will safely cover the injection needle.

✘ **Do not** put the grey needle cap back on used pre-filled syringes.

Healthcare Providers only
Remove and save the pre-filled syringe label.  Turn the plunger to move the label into a position where you can remove the syringe label.

Step 4: Finish	
A	Discard the used pre-filled syringe and other supplies in a sharps disposal container.



Medicines should be disposed of in accordance with local requirements. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Keep the syringe and sharps disposal container out of sight and reach of children.

✘ **Do not** reuse the pre-filled syringe

✘ **Do not** recycle pre-filled syringes or throw them into household waste

B	Examine the injection site.
If there is blood, press a cotton ball or gauze pad on your injection site. **Do not** rub the injection site. Apply a plaster if needed.	

Package leaflet: Information for the user

Aranesp 25 micrograms solution for injection in vial
Aranesp 40 micrograms solution for injection in vial
Aranesp 60 micrograms solution for injection in vial
Aranesp 100 micrograms solution for injection in vial
Aranesp 200 micrograms solution for injection in vial
Aranesp 300 micrograms solution for injection in vial
darbepoetin alfa

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet (see section 4).

What is in this leaflet

1. What Aranesp is and what it is used for

Your doctor has given you Aranesp (an anti-anaemic) to treat your anaemia. Anaemia is when your blood does not contain enough red blood cells and the symptoms may be fatigue, weakness and shortness of breath.

Aranesp works in exactly the same way as the natural hormone erythropoietin. Erythropoietin is produced in your kidneys and encourages your bone marrow to produce more red blood cells. The active substance of Aranesp is darbepoetin alfa produced by gene-technology in Chinese Hamster Ovary Cells (CHO-K1).

If you have chronic renal failure

Aranesp is used to treat symptomatic anaemia that is associated with chronic renal failure (kidney failure) in adults and children. In kidney failure, the kidney does not produce enough of the natural hormone erythropoietin which can often cause anaemia.

Because it will take your body some time to make more red blood cells, it will be about four weeks before you notice any effect. Your normal dialysis routine will not affect the ability of Aranesp to treat your anaemia.

If you are receiving chemotherapy

Aranesp is used to treat symptomatic anaemia in adult cancer patients with non-bone marrow cancers (non-myeloid malignancies) who are receiving chemotherapy.

One of the main side effects of chemotherapy is that it stops the bone marrow producing enough blood cells. Towards the end of your chemotherapy course, particularly if you have had a lot of chemotherapy, your red blood cell count may fall making you anaemic.

2. What you need to know before you use Aranesp

Do not use Aranesp:
- if you are allergic to darbepoetin alfa or any of the other ingredients of this medicine listed in section 6.
- if you have been diagnosed with high blood pressure which is not being controlled with other medicines prescribed by your doctor.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Aranesp.

Please tell your doctor if you are **suffering** or **have suffered** from:
- high blood pressure which is being controlled with medicines prescribed by your doctor;
- sickle cell anaemia;
- epileptic fits (seizures);
- convulsions (fits or seizures);
- liver disease;
- significant lack of response to medicines used to treat anaemia; or
- hepatitis C.

Special warnings:
- If you have symptoms which include unusual tiredness and a lack of energy this could mean you have pure red cell aplasia (PRCA), which has been reported in patients. PRCA means that the body has stopped or reduced the production of red blood cells which causes severe anaemia. If you experience these symptoms you should contact your doctor who will determine the best course of action to treat your anaemia.

- Take special care with other products that stimulate red blood cell production: Aranesp is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional should always record the exact product you are using.

- If you are a patient with chronic renal failure, and particularly if you do not respond properly to Aranesp, your doctor will check your dose of Aranesp because repeatedly increasing your dose of Aranesp if you are not responding to treatment may increase the risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- Your doctor should try to keep your haemoglobin between 10 and 12 g/dL. Your doctor will check that your haemoglobin does not exceed a certain level, as high haemoglobin concentrations could put you at risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- If you have symptoms which include severe headache, drowsiness, confusion, problems with your eyesight, nausea, vomiting or fits (seizures), it could mean that you have very high blood pressure. If you experience these symptoms you should contact your doctor.

- If you are a cancer patient you should be aware that Aranesp may act as a blood cell growth factor and in some circumstances may have a negative impact on your cancer. Depending on your individual situation a blood transfusion may be preferable. Please discuss this with your doctor.

- Misuse by healthy people can cause life-threatening problems with the heart or blood vessels.

- Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.
  If you develop a serious rash or another of these skin symptoms, stop taking Aranesp and contact your doctor or seek medical attention immediately.

Other medicines and Aranesp

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Cyclosporin and tacrolimus (medicines which suppress the immune system) may be affected by the number of red cells in your blood. It is important to tell your doctor if you are taking either of these medicines.

Using Aranesp with food and drink

Food and drink do not affect Aranesp.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Aranesp has not been tested in pregnant women. It is important to tell your doctor if you:
- are pregnant;
- think you may be pregnant; or
- plan to get pregnant.

It is not known whether darbepoetin alfa is excreted in human milk. You must stop breast-feeding if you use Aranesp.

Driving and using machines

Aranesp should not affect your ability to drive or use machinery.

Aranesp contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Aranesp

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Following blood tests, your doctor has decided you need Aranesp as your haemoglobin level is 10 g/dL or less. Your doctor will tell you how much and how often you must take Aranesp in order to maintain a haemoglobin level between 10 and 12 g/dL. This may vary depending on whether you are an adult or a child.

The injections will be given by a healthcare professional.

If you have chronic renal failure

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, Aranesp is given as a single injection by a healthcare professional, either under your skin (subcutaneous) or into a vein (intravenous).

In order to correct your anaemia, your initial dose of Aranesp per kilogram of your body weight will be either:
- 0.75 micrograms once every two weeks, or
- 0.45 micrograms once weekly.

For adult patients not on dialysis, 1.5 micrograms/kg once monthly may also be used as the initial dose.

For all adult and paediatric patients ≥ 1 year of age with chronic renal failure, once your anaemia is corrected you will continue to receive Aranesp given as a single injection, either once a week or once every two weeks. For all adults and paediatric patients ≥ 11 years of age not on dialysis, Aranesp could also be given as an injection once monthly.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose once every four weeks as necessary in order to maintain long term control of your anaemia.

Your doctor will use the lowest effective dose to control the symptoms of your anaemia.

If you do not respond adequately to Aranesp, your doctor will check your dose and will inform you if you need to change doses of Aranesp.

Your blood pressure will also be checked regularly, particularly at the beginning of your treatment.

In some cases, your doctor may recommend that you take iron supplements.

Your doctor may decide to change the way that your injection is given (either under the skin or into a vein). If this changes you will start on the same dose as you have been receiving and your doctor will take blood samples to make sure that your anaemia is still being managed correctly.

If your doctor has decided to change your treatment from r-HuEPO (erythropoietin produced by gene-technology) to Aranesp, they will choose whether you should receive your Aranesp injection once weekly or once every two weeks. The route of injection is the same as with r-HuEPO but your doctor will tell you how much you should take, and when, and may adjust your dose if necessary.

If you are receiving chemotherapy

Aranesp is given as a single injection, either once a week or once every three weeks, under your skin.

In order to correct your anaemia, your initial dose will be:
- 500 micrograms once every three weeks (6.75 micrograms of Aranesp per kilogram of your body weight); or
- 2.25 micrograms (once weekly) of Aranesp per kilogram of your body weight.

Your doctor will take regular blood samples to measure how your anaemia is responding and may adjust your dose as necessary. Your treatment will continue until approximately four weeks after the end of your chemotherapy. Your doctor will tell you exactly when to stop taking Aranesp.

In some cases, your doctor may recommend that you take iron supplements.

If you use more Aranesp than you should

You could have serious problems if you receive more Aranesp than you need, such as very high blood pressure. You should contact your doctor, nurse or pharmacist if this does happen. If you feel unwell in any way you should contact your doctor, nurse or pharmacist immediately.

If you miss a dose of Aranesp

Do not use a double dose to make up for a forgotten dose.

If you miss a dose of Aranesp, you should contact your doctor to discuss when you should receive the next dose.

If you stop using Aranesp

If you want to stop using Aranesp, you should discuss it with your doctor first.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been experienced by some patients taking Aranesp:

Chronic renal failure patients

Very common: may affect more than 1 in 10 people
- High blood pressure (hypertension)
- Allergic reactions

Common: may affect up to 1 in 10 people
- Stroke
- Pain around the area injected
- Rash and/or redness of the skin

Uncommon: may affect up to 1 in 100 people
- Blood clots (thrombosis)
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection
- Blood clots in a dialysis access

Not known: frequency cannot be estimated from available data
- Pure red cell aplasia (PRCA) – (anaemia, unusual tiredness, lack of energy)

Cancer patients

Very common: may affect more than 1 in 10 people
- Allergic reactions

Common: may affect up to 1 in 10 people
- High blood pressure (hypertension)
- Blood clots (thrombosis)
- Pain around the area injected
- Rash and/or redness of the skin
- Fluid retention (oedema)

Uncommon: may affect up to 1 in 100 people
- Convulsions (fits and seizures)
- Bruising and bleeding at the site of injection

All patients

Not known: frequency cannot be estimated from available data
- Serious allergic reactions which may include:
  - Sudden life-threatening allergic reactions (anaphylaxis)
  - Swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
  - Shortness of breath (allergic bronchospasm)
  - Skin rash
  - Hives (urticaria)
- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. Stop using Aranesp if you develop these symptoms and contact your doctor or seek medical attention immediately (see section 2).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Aranesp

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the vial label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Do not use Aranesp if you think it has been frozen.

Keep the vial in the outer carton in order to protect from light.

When your vial has been removed from the refrigerator and left at room temperature for approximately 30 minutes before injection it must either be used within 7 days or disposed of.

Do not use this medicine if you notice the vial contents are cloudy or there are particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Aranesp contains

- The active substance is darbepoetin alfa, r-HuEPO (erythropoietin produced by gene-technology). The vial contains either 25, 40, 60, 100, 200 or 300 micrograms of darbepoetin alfa.

- The other ingredients are sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride, polysorbate 80 and water for injections.

What Aranesp looks like and contents of the pack

Aranesp is a clear, colourless or slightly pearly solution for injection in vial.

Aranesp is available in packs of 1 or 4 vials. Not all pack sizes may be marketed.

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4817 ZK Breda
The Netherlands

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.