ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled pen
Nordimet 10 mg solution for injection in pre-filled pen
Nordimet 12.5 mg solution for injection in pre-filled pen
Nordimet 15 mg solution for injection in pre-filled pen
Nordimet 17.5 mg solution for injection in pre-filled pen
Nordimet 20 mg solution for injection in pre-filled pen
Nordimet 22.5 mg solution for injection in pre-filled pen
Nordimet 25 mg solution for injection in pre-filled pen

Nordimet 7.5 mg solution for injection in pre-filled syringe
Nordimet 10 mg solution for injection in pre-filled syringe
Nordimet 12.5 mg solution for injection in pre-filled syringe
Nordimet 15 mg solution for injection in pre-filled syringe
Nordimet 17.5 mg solution for injection in pre-filled syringe
Nordimet 20 mg solution for injection in pre-filled syringe
Nordimet 22.5 mg solution for injection in pre-filled syringe
Nordimet 25 mg solution for injection in pre-filled syringe

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 25 mg of methotrexate.

Nordimet 7.5 mg solution for injection in pre-filled pen
Each pre-filled pen contains 7.5 mg methotrexate in 0.3 mL.

Nordimet 10 mg solution for injection in pre-filled pen
Each pre-filled pen contains 10 mg methotrexate in 0.4 mL.

Nordimet 12.5 mg solution for injection in pre-filled pen
Each pre-filled pen contains 12.5 mg methotrexate in 0.5 mL.

Nordimet 15 mg solution for injection in pre-filled pen
Each pre-filled pen contains 15 mg methotrexate in 0.6 mL.

Nordimet 17.5 mg solution for injection in pre-filled pen
Each pre-filled pen contains 17.5 mg methotrexate in 0.7 mL.

Nordimet 20 mg solution for injection in pre-filled pen
Each pre-filled pen contains 20 mg methotrexate in 0.8 mL.

Nordimet 22.5 mg solution for injection in pre-filled pen
Each pre-filled pen contains 22.5 mg methotrexate in 0.9 mL.

Nordimet 25 mg solution for injection in pre-filled pen
Each pre-filled pen contains 25 mg methotrexate in 1.0 mL.

Nordimet 7.5 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 7.5 mg methotrexate in 0.3 mL.

Nordimet 10 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 10 mg methotrexate in 0.4 mL.

Nordimet 12.5 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 12.5 mg methotrexate in 0.5 mL.

Nordimet 15 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 15 mg methotrexate in 0.6 mL.

Nordimet 17.5 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 17.5 mg methotrexate in 0.7 mL.

Nordimet 20 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 20 mg methotrexate in 0.8 mL.

Nordimet 22.5 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 22.5 mg methotrexate in 0.9 mL.

Nordimet 25 mg solution for injection in pre-filled syringe
Each pre-filled syringe contains 25 mg methotrexate in 1.0 mL.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection (injection)

Clear, yellow solution with a pH of 8.0-9.0 and an osmolality of approximately 300 mOsm/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nordimet is indicated for the treatment of:
- active rheumatoid arthritis in adult patients,
- polyarthritic forms of severe, active juvenile idiopathic arthritis (JIA), when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate,
- moderate to severe plaque psoriasis in adults who are candidates for systemic therapy, and severe psoriatic arthritis in adult patients,
- induction of remission in moderate steroid-dependent Crohn's disease in adult patients, in combination with corticosteroids and for maintenance of remission, as monotherapy, in patients who have responded to methotrexate.

4.2 Posology and method of administration

Methotrexate should only be prescribed by physicians with expertise in the use of methotrexate and a full understanding of the risks of methotrexate therapy.

Patients must be educated and trained in the proper injection technique when self-administering methotrexate. The first injection of Nordimet should be performed under direct medical supervision.

Important warning about the dosage of Nordimet

In the treatment of rheumatoid arthritis, active juvenile idiopathic arthritis, psoriasis, psoriatic arthritis and Crohn’s disease requiring dosing once a week. Nordimet **must only be used once a week.** Dosage errors in the use of Nordimet can result in serious adverse reactions, including death. Please read this section of the summary of product characteristics very carefully.

When switching from oral use to subcutaneous use, a reduction in the dose may be required, due to the variable bioavailability of methotrexate after oral administration.

Folic acid or folinic acid supplementation may be considered in accordance with current therapeutic guidelines.

The overall duration of treatment is decided by the doctor.

Posology

Dosage in adult patients with rheumatoid arthritis
The recommended initial dose is 7.5 mg of methotrexate once weekly, administered subcutaneously. Depending on the individual activity of the disease and patient tolerability, the initial dose may be increased. A weekly dose of 25 mg should in general not be exceeded. However, doses exceeding 20 mg per week can be associated with significant increase in toxicity, especially bone marrow suppression**.** Response to treatment can be expected after approximately 4-8 weeks. Once the desired therapeutic result has been achieved, the dose should be reduced gradually to the lowest possible effective maintenance dose. Symptoms may return after treatment discontinuation.

Methotrexate treatment of rheumatoid arthritis represents long-term treatment.

Dosage in patients with plaque psoriasis and psoriatic arthritis
It is recommended that a test dose of 5-10 mg be administered subcutaneously one week prior to initiation of therapy, in order to detect idiosyncratic adverse effects. The recommended initial dose is 7.5 mg methotrexate once weekly. The dose is to be increased gradually but should not, in general, exceed a weekly dose of 25 mg of methotrexate. Doses exceeding 20 mg per week can be associated with significant increase in toxicity, especially bone marrow suppression. Response to treatment can generally be expected after approximately 2-6 weeks. Depending on the clinical picture and the changes of laboratory parameters, the therapy is then continued or discontinued.

Once the desired therapeutic result has been achieved, dose should be reduced gradually to the lowest possible effective maintenance dose. In a few exceptional cases a higher dose than 25 mg might be clinically justified, but should not exceed a maximum weekly dose of 30 mg of methotrexate as toxicity will markedly increase.

Methotrexate treatment of moderate to severe plaque psoriasis and severe psoriatic arthritis represents long-term treatment.

Dosage in adult patients with Crohn's disease:

Induction treatment
25 mg/week administered subcutaneously.
Once patients have adequately responded to combination therapy, the corticosteroids should be tapered. Response to treatment can be expected after 8 to 12 weeks.

Maintenance treatment
15 mg/week administered subcutaneously, as monotherapy, if the patient has entered remission.

Special populations

Elderly
Dose reduction should be considered in elderly patients due to reduced liver and kidney function as well as lower folate reserves which occur with increased age (see sections 4.4, 4.5, 4.8 and 5.2).

Renal impairment

Methotrexate should be used with caution in patients with impaired renal function (see sections 4.3 and 4.4). The dose should be adjusted as follows:

Creatinine clearance (ml/min)	Dose
≥ 60	100 %
30-59	50 %
< 30	Nordimet must not be used

Patients with hepatic impairment
Methotrexate should be administered with great caution, if at all, to patients with significant current or previous liver disease, especially when caused by alcohol. Methotrexate is contraindicated if bilirubin values are > 5 mg/dl (85.5 µmol/L) (see section 4.3).

Use in patient with a third distribution space (pleural effusions, ascitis)
As the half-life of methotrexate can be prolonged to 4 times the normal length in patients who possess a third distribution space, dose reduction or, in some cases, discontinuation of methotrexate administration may be required (see sections 5.2 and 4.4).

Paediatric population

Dosage in children and adolescents below 16 years with polyarthritic forms of juvenile idiopathic arthritis
The recommended dose is 10-15 mg/m² body surface area (BSA) per week.
In therapy-refractory cases the weekly dose may be increased up to 20 mg/m² BSA per week. However, an increased monitoring frequency is indicated if the dose is increased. Parenteral administration is limited to subcutaneous injection. Patients with JIA should always be referred to a rheumatology unit specializing in the treatment of children/adolescents.

The safety and efficacy of Nordimet in children < 3 years of age have not been established (see section 4.4). No data available.

Method of administration
It must be explicitly pointed out to the patient that Nordimet is applied only once a week. It is recommended to specify a certain day of the week as “day for injection”.

Nordimet is for subcutaneous use (see section 6.6.).

The medicinal product is for single use only. The solution is to be visually inspected prior to use. Only clear solutions practically free from particles should be used.
Any contact of methotrexate with skin and mucosa is to be avoided. In case of contamination, the affected parts are to be rinsed immediately with plenty of water (see section 6.6).

Please refer to the package leaflet for instructions on how to use the pre-filled pen or pre-filled syringe.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Severe hepatic impairment if serum if bilirubin is > 5 mg/dl (85.5 µmol/l) (see section 4.2).
- Alcohol abuse.
- Severe renal impairment (creatinine clearance less than 30 ml/min) (see sections 4.2 and 4.4).
- Pre-existing blood dyscrasias, such as bone marrow hypoplasia, leukopenia, thrombocytopenia or significant anaemia.
- Immunodeficiency.
- Serious, acute or chronic infections such as tuberculosis and HIV.
- Stomatitis, ulcers of the oral cavity and known active gastrointestinal ulcer disease.

- Pregnancy and breast-feeding (see section 4.6).
- Concurrent vaccination with live vaccines.

4.4 Special warnings and precautions for use

Patients must be clearly advised that the therapy is to be administered once a week, and not every day. Incorrect administration of methotrexate can lead to severe, including potentially lethal adverse reactions. Healthcare professionals and patients should be clearly instructed.

Patients receiving therapy should be appropriately monitored, so that signs of possible toxic effects or adverse reactions can be recognised and assessed without delay. Hence, methotrexate should be only administered by, or under the supervision of, doctors whose knowledge and experience include the use of antimetabolite therapy.

Due to the risk of severe or even fatal toxic reactions, patients should be thoroughly informed by the doctor about the risks (including early signs and symptoms of toxicity) and recommended safety measures. They are to be informed about the necessity to immediately consult the physician if symptoms of intoxication occur, as well as about the subsequent necessary monitoring of symptoms of intoxication (including regular laboratory tests).

Doses exceeding 20 mg/week can be associated with significant increase in toxicity, especially bone marrow suppression.

Skin and mucosal contact with methotrexate is to be avoided. In the case of contamination, the parts concerned should be rinsed with plenty of water.

Fertility and reproduction

Fertility
Methotrexate has been reported to cause oligospermia, menstrual dysfunction and amenorrhoea in humans, during and for a short period after cessation of therapy, and to cause impaired fertility, affecting spermatogenesis and oogenesis during the period of its administration. These effects appear to be reversible on discontinuing therapy.

Teratogenicity – reproductive risk
Methotrexate causes embryotoxicity, abortion and foetal defects in humans. Therefore, the possible risks of effects on reproduction, pregnancy loss and congenital malformations should be discussed with female patients of childbearing potential (see section 4.6). The absence of pregnancy must be confirmed before Nordimet is used. If women of child bearing potential are treated, effective contraception must be used during treatment and for at least six months after.

For contraception advice for men, see section 4.6.

Recommended examinations and safety measures

Before initiating therapy or upon resuming therapy after a rest period
Complete blood count with differential blood count and platelets, liver enzymes, bilirubin, serum albumin, chest X-ray and renal function tests must be conducted. If clinically indicated, exclude tuberculosis and hepatitis.

During therapy
The tests below must be conducted every week during the first two weeks, then every two weeks for the next month; afterwards, depending on leukocyte count and stability of the patient, at least once monthly during the next six months and at least every three months thereafter.
Increased monitoring frequency should also be considered when increasing the dose. Particularly elderly patients should be examined for early signs of toxicity in short intervals.

Examination of the oral cavity and throat for mucosal change.

Complete blood count with differential blood count and platelets
Haematopoietic suppression induced by methotrexate may occur abruptly and at apparently safe doses. In the event of any significant drop in leukocytes or platelets, treatment must be discontinued immediately and appropriate supportive therapy instituted. Patients must be instructed to report all signs and symptoms suggestive of infection. In patients concomitantly taking haematotoxic medicinal products (e.g. leflunomide), the blood count and platelets should be closely monitored.

Liver function tests
Treatment should not be initiated or should be discontinued if there are persistent or significant abnormalities in liver function tests, other non-invasive investigations of hepatic fibrosis, or liver biopsies.

Temporary increases in transaminases to two or three times the upper limit of normal have been reported in patients at a frequency of 13-20 %. Persistent elevation of liver enzymes and/or decrease in serum albumin may be indicative for severe hepatotoxicity. In the event of a persistent increase in liver enzymes, consideration should be given to reducing the dose or discontinuing therapy.

Histological changes, fibrosis and more rarely liver cirrhosis may not be preceded by abnormal liver function tests. There are instances in cirrhosis where transaminases are normal. Therefore, non-invasive diagnostic methods for monitoring of liver condition should be considered, in addition to liver function tests. Liver biopsy should be considered on an individual basis taking into account the patient's comorbidities, medical history and the risks related to biopsy. Risk factors for hepatotoxicity include excessive prior alcohol consumption, persistent elevation of liver enzymes, history of liver disease, family history of hereditary liver disorders, diabetes mellitus, obesity and previous contact with hepatotoxic drugs or chemicals and prolonged methotrexate treatment.

Additional hepatotoxic medicinal products should not be given during treatment with methotrexate unless clearly necessary.Alcohol consumption should be avoided (see sections 4.3 and 4.5). Closer monitoring of liver enzymes should be undertaken in patients concomitantly taking other hepatotoxic medicinal products.

Increased caution should be exercised in patients with insulin-dependent diabetes mellitus, as during methotrexate therapy, liver cirrhosisdeveloped in isolated cases without any elevation of transaminases.

Renal function
Renal function should be monitored via renal function tests and urinanalysis (see sections 4.2 and 4.3). If serum creatinine is increased, the dose should be reduced. As methotrexate is predominantly excreted via the renal route, increased concentrations can be expected in cases of renal impairment, which may result in severe adverse reactions. In cases of possible renal impairment (e.g. in elderly patients), closer monitoring is required. This particularly applies to the co-administration of medicinal products which affect methotrexate excretion, cause kidney damage (e.g. NSAIDs) or can potentially lead to haematopoietic disorders. In patients with impaired renal function, concomitant administration of NSAIDs is not recommended. Dehydration may also potentiate the toxicity of methotrexate.

Assessment of respiratory system
Questioning the patient with regard to possible pulmonary dysfunctions, if necessary, lung function test. Acute or chronic interstitial pneumonitis, often associated with blood eosinophilia, may occur and deaths have been reported. Symptoms typically include dyspnoea, cough (especially a dry non-productive cough), thoracic pain and fever for which patients should be monitored at each follow-up visit. Patients should be informed of the risk of pneumonitis and advised to contact their doctor immediately should they develop persistent cough or dyspnoea.

In addition, pulmonary alveolar haemorrhage has been reported with methotrexate used in

rheumatologic and related indications. This event may also be associated with vasculitis and other comorbidities. Prompt investigations should be considered when pulmonary alveolar haemorrhage is suspected to confirm the diagnosis.

Methotrexate should be discontinued in patients with pulmonary symptoms and a thorough investigation (including chest x-ray) should be made to exclude infection and tumours. If methotrexate induced lung disease is suspected, treatment with corticosteroids should be initiated and treatment with methotrexate should not be restarted.

Pulmonary diseases induced by methotrexate were not always completely reversible.

Pulmonary symptoms require a quick diagnosis and discontinuation of methotrexate therapy. Pulmonary diseases induced by methotrexate, like pneumonitis, can occur acutely at any time of therapy, they were not always completely reversible and have been reported already at all doses (inclusive low doses of 7.5 mg/week).

During methotrexate therapy, opportunistic infection can occur including pneumocystis jiroveci pneumonia, which may take a lethal course. If a patient presents with pulmonary symptoms, the possibility of pneumocystis jiroveci pneumonia should be taken into account.

Special caution is required in patients with impaired pulmonary function.

General safety measures
Methotrexate may, due to its effect on the immune system, impair the response to vaccinations and interfere with the result of immunological tests. Concurrent vaccination using live vaccines must not be carried out.

Particular caution should be exercised in the presence of inactive, chronic infections (e.g. herpes zoster, tuberculosis, hepatitis B or C) due to possible activation.

Malignant lymphomas may occur in patients receiving low-dose methotrexate; in which case, methotrexate must be discontinued. If lymphomas should fail to regress spontaneously, initiation of cytotoxic therapy is required.

In patients with pathological accumulation of liquid in body cavities (“third space”), such as ascites or pleural effusions, the plasma elimination half-life of methotrexate is prolonged. Pleural effusions and ascites should be drained prior to initiation of methotrexate treatment.

Conditions leading to dehydration such as emesis, diarrhoea or stomatitis, can increase the toxicity of methotrexate due to elevated levels of the active substance. In these cases use of methotrexate should be interrupted until the symptoms cease.

Diarrhoea and ulcerative stomatitis can be toxic effects and require interruption of therapy, otherwise haemorrhagic enteritis and death from intestinal perforation may occur.
If haematemesis, black discoloration of the stool or blood in stool occur, therapy is to be interrupted.

Progressive multifocal leukoencephalopathy (PML)
Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients receiving methotrexate, mostly in combination with other immunosuppressive medication. PML can be fatal and should be considered in the differential diagnosis in immunosuppressed patients with new onset or worsening neurological symptoms.

Vitamin preparations or other products containing folic acid, folinic acid or their derivatives may decrease the effectiveness of methotrexate.

Use in children < 3 years of age is not recommended as insufficient data on efficacy and safety are

available for this population. (see section 4.2).

Photosensitivity
Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking methotrexate (see section 4.8). Exposure to intense sunlight or UV rays should be avoided unless medically indicated. Patients should use adequate sun-protection to protect themselves from intense sunlight.

Radiation induced dermatitis and sunburn can reappear during methotrexate therapy (recall reactions). Psoriatic lesions can worsen during UV radiation and co-administration of methotrexate. Concomitant administration of folate antagonists such as trimethoprim /sulphamethoxazole has been reported to cause an acute megaloblastic pancytopenia in rare instances.

Encephalopathy / Leukoencephalopathy have been reported in oncologic patients receiving methotrexate therapy and cannot be excluded for methotrexate therapy in non-oncologic indications.

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

4.5 Interaction with other medicinal products and other forms of interaction

NSAIDs including salicylic acid
In animal experiments NSAIDs including salicylic acid caused reduction of tubular methotrexate secretion and consequently increased its toxic effects. However, in clinical studies, where NSAIDs and salicylic acid were given as concomitant medicinal products to patients with rheumatoid arthritis, no increase of adverse reactions was observed. Treatment of rheumatoid arthritis with such medicinal products can be continued during low-dose methotrexate therapy but only under close medical supervision.

Hepatotoxicity
Regular alcohol consumption and administration of additional hepatotoxic medicinal products increase the probability of hepatotoxic effects of methotrexate. Alcohol consumption must be avoided during treatment with methotrexate.

Patients taking potentially hepatotoxic and haematoxic medicinal products during methotrexate therapy (e.g. leflunomide, azathioprine, sulphasalazine, and retinoids) should be closely monitored for possibly increased hepatotoxicity.

Haematotoxic medicinal products
Administration of additional haematotoxic medicinal products increases the likelihood of severe haematoxic adverse reactions to methotrexate. Concurrent administration of metamizole and methotrexate can increase the haematotoxic effect of methotrexate, especially in elderly patients. Therefore, coadministration should be avoided.

Pharmacokinetic interactions
One should be aware of pharmacokinetic interactions between methotrexate, anticonvulsant medicinal products (reduced methotrexate blood levels), and 5-fluorouracil (increased $t_{½}$ of 5--fluorouracil).

Alterations in bioavailability of methotrexate
Salicylates, phenylbutazone, phenytoin, barbiturates, tranquillisers, oral contraceptives, tetracyclines, amidopyrine derivatives, sulfonamides and p-aminobenzoic acid displace methotrexate from serum albumin binding and thus increase bioavailability (indirect dose increase). Probenecid and mild organic acids may also reduce tubular methotrexate secretion, and thus cause indirect dose elevations, too.

Antibiotics, like penicillin, glycopeptides, sulfonamides, ciprofloxacin and cefalotin can, in individual cases, reduce the renal clearance of methotrexate, so that increased serum concentrations of methotrexate with simultaneous haematological and gastro-intestinal toxicity may occur.
Oral antibiotics such as tetracyclines, chloramphenicol and non-absorbable broad-spectrum antibiotics may reduce intestinal methotrexate absorption or interfere with the enterohepatic circulation, due to inhibition of the intestinal flora or suppression of bacterial metabolism.

Colestyramine can increase the non-renal elimination of methotrexate by interrupting the enterohepatic circulation. Delayed methotrexate clearance should be considered in combination with other cytostatic medicinal products.

Co-administration of proton-pump inhibitors such as omeprazole or pantoprazole can lead to interactions: concomitant administration of methotrexate and omeprazole has led to a delay in the renal elimination of methotrexate. In combination with pantoprazole, inhibited renal elimination of the 7-hydroxymethotrexate metabolite, with myalgia and shivering, was reported in one case.

Substances that may have adverse effects on the bone marrow
Under (pre-)treatment with substances that may have adverse effects on the bone marrow (e.g. sulphonamides, trimethoprim-sulphamethoxazole, chloramphenicol, pyrimethamine), the possibility of marked haematopoietic disorders should be considered.

Folate metabolism
Co-administration of medicinal products which cause folate deficiency (e.g. sulphonamides, trimethoprim-sulphamethoxazole) can lead to increased methotrexate toxicity. Particular caution should therefore also be exercised in the presence of existing folic acid deficiency.
On the other hand, concomitant administration of folinic acid containing drugs or of vitamin preparations, which contain folic acid or derivatives, may impair methotrexate efficacy.

The use of nitrous oxide potentiates the effect of methotrexate on folate metabolism, yielding increased toxicity such as severe unpredictable myelosuppression and stomatitis. Whilst this effect can be reduced by administering calcium folinate, the concomitant use of nitrous oxide and methotrexate should be avoided.

Though the combination of methotrexate and sulfasalazine may enhance methotrexate efficacy by sulfasalazine related inhibition of folic acid synthesis, and thus may lead to an increased risk of adverse reactions, these were only observed in single patients within several trials.

Other antirheumatic agents
A rise in the toxicity of methotrexate is generally not anticipated when methotrexate is used concomitantly with other antirheumatic agents (e.g. gold compounds, penicillamine, hydroxychloroquine, sulfasalazine, azathioprine).

Cyclosporine
Cyclosporine may potentiate methotrexate efficacy and toxicity. There is an increased risk of renal dysfunction. In addition, there is a biological plausibility of excessive immunosuppression and its associated complications.

Theophylline and caffeine
Methotrexate may reduce theophylline clearance. Therefore, theophylline blood levels should be monitored under concomitant methotrexate administration.
Excessive consumption of beverages containing caffeine or theophylline (coffee, soft drinks containing caffeine, black tea) should be avoided during methotrexate therapy since the efficacy of methotrexate may be reduced due to possible interaction between methotrexate and methylxanthines at adenosine receptors.

Leflunomide

The combined use of methotrexate and leflunomide may increase the risk for pancytopenia. Methotrexate leads to increased plasma levels of mercaptopurines. Therefore, the combination of these may require dose adjustment.

Immune-modulating medicinal products
Particularly in the case of orthopaedic surgery where susceptibility to infection is high, a combination of methotrexate with immune-modulating medicinal products must be used with caution.

Radiotherapy
Radiotherapy during use of methotrexate can increase the risk of soft tissue or bone necrosis.

Vaccines
On account of its possible effect on the immune system, methotrexate can falsify vaccinal and test results (immunological procedures to record the immune reaction). During methotrexate therapy concurrent vaccination with live vaccines must not be carried out (see sections 4.3 and 4.4).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / contraception in females
Women must not get pregnant during methotrexate therapy, and effective contraception must be used during treatment with methotrexate and at least 6 months thereafter (see section 4.4). Prior to initiating therapy, women of childbearing potential must be informed of the risk of malformations associated with methotrexate and any existing pregnancy must be excluded with certainty by taking appropriate measures, e.g. a pregnancy test. During treatment pregnancy tests should be repeated as clinically required (e.g. after any gap of contraception). Female patients of reproductive potential must be counselled regarding pregnancy prevention and planning.

Contraception in males
It is not known if methotrexate is present in semen. Methotrexate has been shown to be genotoxic in animal studies, such that the risk of genotoxic effects on sperm cells cannot completely be excluded. Limited clinical evidence does not indicate an increased risk of malformations or miscarriage following paternal exposure to low-dose methotrexate (less than 30 mg/week). For higher doses, there is insufficient data to estimate the risks of malformations or miscarriage following paternal exposure.
As precautionary measures, sexually active male patients or their female partners are recommended to use reliable contraception during treatment of the male patient and for at least 3 months after cessation of methotrexate. Men should not donate semen during therapy or for 3 months following discontinuation of methotrexate.

Pregnancy
Methotrexate is contraindicated during pregnancy in non-oncological indications (see section 4.3). If pregnancy occurs during treatment with methotrexate and up to six months thereafter, medical advice should be given regarding the risk of harmful effects on the child associated with treatment and ultrasonography examinations should be performed to confirm normal foetal development.
In animal studies, methotrexate has shown reproductive toxicity, especially during the first trimester (see section 5.3). Methotrexate has been shown to have a teratogenic effect in humans; it has been reported to cause foetal death and/or congenital abnormalities (e.g. craniofacial, cardiovascular, central nervous system and extremity-related).

Methotrexate is a powerful human teratogen, with an increased risk of spontaneous abortions, intrauterine growth restriction and congenital malformations in case of exposure during pregnancy.

Spontaneous abortions have been reported in 42.5% of pregnant women exposed to low-dose methotrexate treatment (less than 30 mg/week), compared to a reported rate of 22.5% in disease-matched patients treated with drugs other than methotrexate.

Major birth defects occurred in 6.6% of live births in women exposed to low-dose methotrexate treatment (less than 30 mg/week) during pregnancy, compared to approximately 4% of live births in in disease-matched patients treated with drugs other than methotrexate.

Insufficient data is available for methotrexate exposure during pregnancy higher than 30 mg/week, but higher rates of spontaneous abortions and congenital malformations are expected.

When methotrexate was discontinued prior to conception, normal pregnancies have been reported.

Breast-feeding
As methotrexate is transferred into human milk and may cause toxicity in breast-feeding children, treatment is contraindicated during breast-feeding (see section 4.3). If use of methotrexate during the breast-feeding period should become necessary, breast-feeding is to be stopped prior to treatment.

Fertility
Methotrexate affects spermatogenesis and oogenesis and may decrease fertility. In humans, methotrexate has been reported to cause oligospermia, menstrual dysfunction and amenorrhoea. These effects appear to be reversible after discontinuation of therapy in most cases.

4.7 Effects on ability to drive and use machines

Nordimet has minor influence on the ability to drive and use machines. Central nervous system (CNS) symptoms, such as fatigue and confusion, can occur during treatment.

4.8 Undesirable effects

Summary of the safety profile
Most serious adverse reactions of methotrexate include bone marrow suppression, pulmonary toxicity, hepatotoxicity, renal toxicity, neurotoxicity, thromboembolic events, anaphylactic shock and Stevens-Johnson syndrome.

Most frequently (very common) observed adverse reactions of methotrexate include gastrointestinal disorders (e.g. stomatitis, dyspepsia, abdominal pain, nausea, loss of appetite) and abnormal liver function tests (e.g. increased Alanine aminotransferase (ALAT), Aspartate aminotransferase (ASAT), bilirubin, alkaline phosphatase). Other frequently (common) occurring adverse reactions are leukopenia, anaemia, thrombopenia, headache, tiredness, drowsiness, pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia, oral ulcers, diarrhoea, exanthema, erythema and pruritus.

The most relevant adverse reaction is suppression of the haematopoietic system and gastrointestinal disorders.

List of adverse reactions
Frequencies are defined using the following convention:
very common (≥ 1/10) common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Infections and infestations
Uncommon: Pharyngitis.
Rare: Infection (incl. reactivation of inactive chronic infection), sepsis, conjunctivitis.

Neoplasms benign, malignant and unspecified (including cysts and polyps)
Very rare: lymphoma (see “description” below)

Blood and lymphatic system disorders
Common: Leukopenia, anaemia, thrombopenia.
Uncommon: Pancytopenia.
Very rare: Agranulocytosis, severe courses of bone marrow depression, lymphoproliferative disorders (see "description below").
Not known: Eosinophilia

Immune system disorders
Rare: Allergic reactions, anaphylactic shock, hypogammaglobulinaemia.

Metabolism and nutrition disorders
Uncommon: Precipitation of diabetes mellitus.

Psychiatric disorders
Uncommon: Depression, confusion.
Rare: Mood alterations.

Nervous system disorders
Common: Headache, tiredness, drowsiness.
Uncommon: Dizziness.
Very rare: Pain, muscular asthenia, paraesthesia/hypoaesthesia, changes in sense of taste (metallic taste), convulsions, meningism, acute aseptic meningitis, paralysis.
Not known: Encephalopathy/ Leukoencephalopathy.

Eye disorders
Rare: Visual disturbances.
Very rare: Impaired vision, Retinopathy.

Cardiac disorders
Rare: Pericarditis, pericardial effusion, pericardial tamponade.

Vascular disorders
Rare: Hypotension, thromboembolic events

Respiratory, thoracic and mediastinal disorders
Common: Pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia. Symptoms indicating potentially severe lung injury (interstitial pneumonitis) are: dry, not productive cough, shortness of breath and fever.
Rare: Pulmonary fibrosis, *Pneumocystis jiroveci* pneumonia, shortness of breath and bronchial asthma, pleural effusion.
Not known: Epistaxis, pulmonary alveolar haemorrhage.

Gastrointestinal disorders
Very common: Stomatitis, dyspepsia, nausea, loss of appetite, abdominal pain.
Common: Oral ulcers, diarrhoea.
Uncommon: Gastrointestinal ulcers and bleeding, enteritis, vomiting, pancreatitis.
Rare: Gingivitis.
Very rare: Haematemesis, haematorrhea, toxic megacolon.

Hepatobiliary disorders (see section 4.4)
Very common: Abnormal liver function tests (increased ALAT, ASAT, alkaline phosphatase and bilirubin).
Uncommon: Cirrhosis, fibrosis and fatty degeneration of the liver, decrease in serum albumin.
Rare: Acute hepatitis.
Very rare: Hepatic failure.

Skin and subcutaneous tissue disorders

Common: Exanthema, erythema, pruritus.
Uncommon: Photosensitivity reactions , loss of hair, increase in rheumatic nodules, skin ulcer, herpes zoster, vasculitis, herpetiform eruptions of the skin, urticaria.
Rare: Increased pigmentation, acne, petechiae, ecchymosis, allergic vasculitis.
Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), increased pigmentary changes of the nails, acute paronychia, furunculosis, telangiectasia.
Not known: Skin exfoliation / dermatitis exfoliative

Musculoskeletal and connective tissue disorders
Uncommon: Arthralgia, myalgia, osteoporosis.
Rare: Stress fracture.
Not known: Osteonecrosis of jaw (secondary to lymphoproliferative disorders)

Renal and urinary disorders
Uncommon: Inflammation and ulceration of the urinary bladder, renal impairment, disturbed micturition.
Rare: Renal failure, oliguria, anuria, electrolyte disturbances.
Not known: Proteinuria.

Reproductive system and breast disorders
Uncommon: Inflammation and ulceration of the vagina.
Very rare: Loss of libido, impotence, gynaecomastia, oligospermia, impaired menstruation, vaginal discharge.

General disorders and administration site conditions
Rare: Fever, wound-healing impairment.
Not known: Asthenia, injection site necrosis, oedema.

Description of selected adverse reactions

Lymphoma/Lymphoproliferative disorders
There have been reports of individual cases of lymphoma and other lymphoproliferative disorders which subsided in a number of cases once treatment with methotrexate had been discontinued.

The appearance and degree of severity of undesirable effects depends on the dosage level and the frequency of administration. However, as severe undesirable effects can occur even at lower doses, it is indispensable that patients are monitored regularly by the doctor at short intervals.
Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, pruritus, severe itching, pain) were observed with subcutaneous use, decreasing during therapy.

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

Symptoms of overdose
The adverse toxic effects of methotrexate mainly affect the haematopoietic and gastrointestinal system. Symptoms include leukocytopenia, thrombocytopenia, anaemia, pancytopenia, neutropenia, bone marrow depression, mucositis, stomatitis, oral ulceration, nausea, vomiting, gastrointestinal ulceration and gastrointestinal bleeding. Some patients showed no signs of overdose. There are reports of death due to sepsis, septic shock, renal failure and aplastic anaemia.

Treatment of overdose

Calcium folinate is the specific antidote for neutralising the adverse toxic effects of methotrexate. In the event of accidental overdose, a dose of calcium folinate equal to or higher than the offending dose of methotrexate should be administered intravenously or intramuscularly within 1 hour, and dosing continued until serum level of methotrexate are below 10^{-7} mol/L.

In the event of a massive overdose, hydration and urinary alkalisation may be required to prevent precipitation of methotrexate and/or its metabolites within the renal tubules. Neither haemodialysis nor peritoneal dialysis has been shown to improve methotrexate elimination. Effective methotrexate clearance has been reported with acute, intermittent haemodialysis using a high-flux dialyser.
In patients with rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis or plaque psoriasis, administration of folic or folinic acid may reduce methotrexate toxicity (gastrointestinal symptoms, inflammation of oral mucosa, hair loss and increase of liver enzymes) (see section 4.5). Prior to using folic acid products, monitoring of vitamin B12 levels is recommended, since folic acid may mask an existing vitamin B12 deficiency, particularly in adults over 50 years of age.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, other immunosuppressants. ATC code: L04AX03

Mechanism of action
Methotrexate is a folic acid antagonist which belongs to the class of cytotoxic agents known as antimetabolites. It acts by the competitive inhibition of the enzyme dihydrofolate reductase and thus inhibits DNA synthesis. It has not yet been clarified, as to whether the efficacy of methotrexate, in the management of psoriasis, psoriatic arthritis, chronic polyarthritis and Crohn's disease is due to an anti-inflammatory or immunosuppressive effect and to which extent a methotrexate-induced increase in extracellular adenosine concentration at inflamed sites contributes to these effects.

Clinical efficacy and safety
A study of weekly injections of methotrexate in a group of patients with chronically active Crohn's disease (despite at least three months of prednisone therapy), showed that methotrexate was more effective than placebo in improving symptoms and reducing requirements for prednisone. A total of 141 patients were randomly assigned in a 2:1 ratio to methotrexate (25 mg weekly) or placebo. After 16 weeks, 37 patients (39.4%) were in clinical remission in the methotrexate group, as compared with 9 patients (19.4%, P=0.025;) in the placebo group. The patients in the methotrexate group received less prednisone overall and their mean score on the Crohn's Disease Activity Index was significantly lower than those in the placebo group (P=0.026 and P=0.002, respectively). [**Feagan** et al (1995)]

A study of patients, who had entered remission after 16 to 24 weeks of treatment with 25 mg of methotrexate, showed that a low dose of methotrexate maintains remission. Patients were randomly assigned to receive either methotrexate at a dose of 15 mg *I.M.* once weekly or placebo for 40 weeks. At week 40, 26 patients (65%) were in remission in the methotrexate group and fewer needed prednisone for relapse (28%), as compared with the placebo group (39%; P=0.04 and 58%, P=0.01, respectively). [**Feagan** et al (2000)]

The adverse events observed in the studies performed with methotrexate for Crohn's disease at cumulative doses have not shown a different safety profile of methotrexate than the profile that is already known. Therefore, similar cautions must be taken with the use of methotrexate for the treatment of Crohn's disease as in other rheumatic and non-rheumatic indications of methotrexate (see sections 4.4 and 4.6).

5.2 Pharmacokinetic properties

Absorption
After oral application, methotrexate is absorbed from the gastrointestinal tract. When administered in low doses (7.5 mg/m^2 to 80 mg/m^2 BSA), methotrexate has a mean bioavailability of approximately 70%, although considerable inter- and intra-subject variations are possible (25-100%). Plasma peak concentrations are attained within 1-2 hours. Subcutaneous, intravenous and intramuscular administration demonstrated similar bioavailability.

Distribution
Approximately 50% of methotrexate is bound to serum proteins. Upon being distributed into body tissues, high concentrations particularly in liver, kidneys and spleen in form of polyglutamates can be found, which can be retained for weeks or months. When administered in small doses, methotrexate passes into the body fluids in minimal amounts; under high doses (300 mg/kg body weight), concentrations between 4 and 7 µg/ml have been measured in the body fluids. Average terminal half-life is 6-7 hours and demonstrates considerable variation (3-17 hours). Half-life may be prolonged to 4 times the normal length in patients with third spaces (pleural effusion, ascites).

Biotransformation
Approximately 10% of the administered methotrexate is metabolised intrahepatically. The major metabolite is 7-hydroxymethotrexate.

Elimination
Excretion takes place, mainly in unchanged form, primarily renal via glomerular filtration and active secretion in the proximal tubulus. Approx. 5-20% of methotrexate and 1-5% of 7-hydroxymethotrexate are eliminated via the bile. Pronounced enterohepatic blood flow exists.

In case of renal insufficiency, elimination is delayed significantly. Impaired elimination in presence of hepatic insufficiency is not known.

Methotrexate passes the placental barrier in rats and monkeys.

5.3 Preclinical safety data

Chronic toxicity
Chronic toxicity studies in mice, rats and dogs showed toxic effects in the form of gastrointestinal lesions, myelosuppression and hepatotoxicity.

Mutagenic and carcinogenic potential
Long-term studies in rats, mice and hamsters did not show any evidence of a tumorigenic potential of methotrexate. Methotrexate induces gene and chromosome mutations both *in vitro* and *in vivo*. A mutagenic effect is suspected in humans.

Reproductive toxicology
Teratogenic effects have been identified in four species (rats, mice, rabbits, cats). In rhesus monkeys, no malformations comparable to humans occurred.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 25°C.
Keep the pre-filled pen orpre-filled syringe in the outer carton in order to protect from light.
Do not freeze.

6.5 Nature and contents of container

Pre-filled pen
Pre-filled pen with a 1 mL type I glass syringe with attached stainless-steel needle and a chlorobutyl rubber plunger stopper. The pre-filled pens contain 0.3 ml, 0.4 ml, 0.5 ml, 0.6 ml, 0.7 ml, 0.8 ml, 0.9 ml or 1.0 ml of solution for injection.
Each pack contains 1 pre-filled pen and one alcohol swab and multipacks containing 4 (4 packs of 1 or 1 pack of 4) and 12 (3 packs of 4) pre-filled pens and 4 and 12 alcohol swabs respectively.

Pre-filled syringe
1 mL type I glass syringe with attached stainless-steel needle, a chlorobutyl rubber plunger stopper and a needle guard to prevent needlestick injury and re-use. The pre-filled syringes contain 0.3 ml, 0.4 ml, 0.5 ml, 0.6 ml, 0.7 ml, 0.8 ml, 0.9 ml or 1.0 ml solution for injection.
Each pack contains 1 pre-filled syringe and two alcohol swabs and multipacks containing 4 (4 packs of 1) and 12 (12 packs of 1) pre-filled syringes and 8 and 24 alcohol swabs respectively.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Handling and disposal must be consistent with that of other cytotoxic preparations in accordance with local requirements. Pregnant health care personnel should not handle and/or administer methotrexate.

Methotrexate should not come into contact with the skin or mucosa. In the event of contamination, the affected area must be rinsed immediately with ample amount of water.

Nordimet is for single use only and any unused solution must be discarded.

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

7. MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

Nordimet 7.5 mg solution for injection in pre-filled pen
EU/1/16/1124/001 - 1 pre-filled pen
EU/1/16/1124/009 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/057 - 4 pre-filled pens
EU/1/16/1124/058 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 10 mg solution for injection in pre-filled pen
EU/1/16/1124/002 - 1 pre-filled pen
EU/1/16/1124/011 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/059 - 4 pre-filled pens
EU/1/16/1124/060 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 12.5 mg solution for injection in pre-filled pen
EU/1/16/1124/003 - 1 pre-filled pen
EU/1/16/1124/013 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/061 - 4 pre-filled pens
EU/1/16/1124/062 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 15 mg solution for injection in pre-filled pen
EU/1/16/1124/004 - 1 pre-filled pen
EU/1/16/1124/015 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/063 - 4 pre-filled pens
EU/1/16/1124/064 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 17.5 mg solution for injection in pre-filled pen

EU/1/16/1124/005 - 1 pre-filled pen
EU/1/16/1124/017 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/065 - 4 pre-filled pens
EU/1/16/1124/066 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 20 mg solution for injection in pre-filled pen
EU/1/16/1124/006 - 1 pre-filled pen
EU/1/16/1124/019 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/067 - 4 pre-filled pens
EU/1/16/1124/068 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 22.5 mg solution for injection in pre-filled pen
EU/1/16/1124/007 - 1 pre-filled pen
EU/1/16/1124/021 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/069 - 4 pre-filled pens
EU/1/16/1124/070 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 25 mg solution for injection in pre-filled pen
EU/1/16/1124/008 - 1 pre-filled pen
EU/1/16/1124/023 - multipack: 4 (4 packs of 1) pre-filled pens
EU/1/16/1124/071 - 4 pre-filled pens
EU/1/16/1124/072 - multipack:12 (3 packs of 4) pre-filled pens

Nordimet 7.5 mg solution for injection in pre-filled syringe
EU/1/16/1124/025 - 1 pre-filled syringe
EU/1/16/1124/026 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/049 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 10 mg solution for injection in pre-filled syringe
EU/1/16/1124/028 - 1 pre-filled syringe
EU/1/16/1124/029 - multipack: 4 (4 packs of 1) pre-filled syringes

EU/1/16/1124/050 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 12.5 mg solution for injection in pre-filled syringe
EU/1/16/1124/031 - 1 pre-filled syringe
EU/1/16/1124/032 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/051 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 15 mg solution for injection in pre-filled syringe
EU/1/16/1124/034 - 1 pre-filled syringe
EU/1/16/1124/035 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/052 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 17.5 mg solution for injection in pre-filled syringe
EU/1/16/1124/037 - 1 pre-filled syringe
EU/1/16/1124/038 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/053 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 20 mg solution for injection in pre-filled syringe
EU/1/16/1124/040 - 1 pre-filled syringe
EU/1/16/1124/041 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/054 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 22.5 mg solution for injection in pre-filled syringe
EU/1/16/1124/043 - 1 pre-filled syringe
EU/1/16/1124/044 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/055 - multipack: 12 (12 packs of 1) pre-filled syringes

Nordimet 25 mg solution for injection in pre-filled syringe
EU/1/16/1124/046 - 1 pre-filled syringe
EU/1/16/1124/047 - multipack: 4 (4 packs of 1) pre-filled syringes
EU/1/16/1124/056 - multipack: 12 (12 packs of 1) pre-filled syringes

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 August 2016
Date of latest renewal: 21 June 2021

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. 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 RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Cenexi - Laboratoires Thissen S.A.
Rue de la Papyrée 2-6
B-1420 Braine-L'Alleud
Belgium

Sever Pharma Solutions AB
Agneslundsvagen 27
P.O. Box 590
SE-201 25 Malmo
Sweden

FUJIFILM Diosynth Biotechnologies Denmark ApS
Biotek Allé 1
3400 Hillerød
Denmark

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**

The requirements for submission of periodic safety update reports 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 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.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	Due date
The MAH should implement the agreed targeted follow-up questionnaires for all medication errors resulting in overdose.	From the date of notification of the Commission Decision*

*Referral EMEA/H/A-31/1463

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.3 ml contains 7.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
7.5 mg/0.3 ml
1 pre-filled pen (0.3 ml) and 1 alcohol swab
4 pre-filled pens (0.3 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/001 1 pre-filled pen
EU/1/16/1124/057 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.3 ml contains 7.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
7.5 mg/0.3 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.3 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.3 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/009 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/058 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled pen
methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.3 ml contains 7.5 mg methotrexate (25 mg/ml).

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
7.5 mg/0.3 ml
1 pre-filled pen (0.3 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately.
4 pre-filled pens (0.3 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/009 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/058 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 7.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

7.5 mg / 0.3 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.4 ml contains 10 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
10 mg/0.4 ml
1 pre-filled pen (0.4 ml) and 1 alcohol swab
4 pre-filled pens (0.4 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/002 1 pre-filled pen
EU/1/16/1124/059 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.4 ml contains 10 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
10 mg/0.4 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.4 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.4 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/011 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/060 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.4 ml contains 10 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
10 mg/0.4 ml
1 pre-filled pen (0.4 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (0.4 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/011 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/060 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 10 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 mg / 0.4 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.5 ml contains 12.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
12.5 mg/0.5 ml
1 pre-filled pen (0.5 ml) and 1 alcohol swab
4 pre-filled pens (0.5 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/003 1 pre-filled pen
EU/1/16/1124/061 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 12.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.5 ml contains 12.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
12.5 mg/0.5 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.5 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.5 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/013 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/062 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 12.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.5 ml contains 12.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
12.5 mg/0.5 ml
1 pre-filled pen (0.5 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (0.5 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/013 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/062 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 12.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 12.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

12.5 mg / 0.5 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.6 ml contains 15 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
15 mg/0.6 ml
1 pre-filled pen (0.6 ml) and 1 alcohol swab
4 pre-filled pens (0.6 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/004 1 pre-filled pen
EU/1/16/1124/063 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.6 ml contains 15 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
15 mg/0.6 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.6 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.6 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/015 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/064 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.6 ml contains 15 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
15 mg/0.6 ml
1 pre-filled pen (0.6 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (0.6 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/015 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/064 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 15 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

15 mg / 0.6 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.7 ml contains 17.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
17.5 mg/0.7 ml
1 pre-filled pen (0.7 ml) and 1 alcohol swab
4 pre-filled pens (0.7 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/005 1 pre-filled pen
EU/1/16/1124/065 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 17.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.7 ml contains 17.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
17.5 mg/0.7 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.7 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.7 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/017 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/066 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 17.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.7 ml contains 17.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
17.5 mg/0.7 ml
1 pre-filled pen (0.7 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (0.7 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/017 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/066 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 17.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 17.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

17.5 mg / 0.7 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.8 ml contains 20 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
20 mg/0.8 ml
1 pre-filled pen (0.8 ml) and 1 alcohol swab
4 pre-filled pens (0.8 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/006 1 pre-filled pen
EU/1/16/1124/067 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.8 ml contains 20 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
20 mg/0.8 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.8 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.8 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/019 4 pre-filled pens (4 packs of 1)
U/1/16/1124/068 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.8 ml contains 20 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
20 mg/0.8 ml
1 pre-filled pen (0.8 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (0.8 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/019 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/068 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 20 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

20 mg / 0.8 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.9 ml contains 22.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
22.5 mg/0.9 ml
1 pre-filled pen (0.9 ml) and 1 alcohol swab
4 pre-filled pens (0.9 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/007 1 pre-filled pen
EU/1/16/1124/069 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 22.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.9 ml contains 22.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
22.5 mg/0.9 ml
Multipack: 4 (4 packs of 1) pre-filled pens (0.9 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (0.9 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/021 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/070 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 22.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 0.9 ml contains 22.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
22.5 mg/0.9 ml
1 pre-filled pen (0.9 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (0.9 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/021 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/070 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 22.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 22.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

22.5 mg / 0.9 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 1.0 ml contains 25 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
25 mg/1.0 ml
1 pre-filled pen (1.0 ml) and 1 alcohol swab
4 pre-filled pens (1.0 ml) and 4 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/008 1 pre-filled pen
EU/1/16/1124/071 4 pre-filled pens

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 1.0 ml contains 25 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
25 mg/1.0 ml
Multipack: 4 (4 packs of 1) pre-filled pens (1.0 ml) and 4 alcohol swabs
Multipack: 12 (3 packs of 4) pre-filled pens (1.0 ml) and 12 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before use.
Find the instructions for use here:
QR-code to be included
https://nordimetvideo.com

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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/023 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/072 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg solution for injection in pre-filled pen

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen of 1.0 ml contains 25 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
25 mg/1.0 ml
1 pre-filled pen (1.0 ml) and 1 alcohol swab. Component of a multipack, can't be sold separately
4 pre-filled pens (1.0 ml) and 4 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/023 4 pre-filled pens (4 packs of 1)
EU/1/16/1124/072 12 pre-filled pens (3 packs of 4)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

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

Nordimet 25 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

25 mg / 1.0 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.3 ml contains 7.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
7.5 mg/0.3 ml
1 pre-filled syringe (0.3 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/025 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.3 ml contains 7.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
7.5 mg/0.3 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.3 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.3 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/026 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/049 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.3 ml contains 7.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
7.5 mg/0.3 ml
1 pre-filled syringe (0.3 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/026 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/049 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 7.5 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
7.5 mg / 0.3 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 7.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

7.5 mg / 0.3 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.4 ml contains 10 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
10 mg/0.4 ml
1 pre-filled syringe (0.4 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/028 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.4 ml contains 10 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
10 mg/0.4 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.4 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.4 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/029 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/050 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.4 ml contains 10 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
10 mg/0.4 ml
1 pre-filled syringe (0.4 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/029 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/050 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 10 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
10 mg / 0.4 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 10 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 mg / 0.4 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.5 ml contains 12.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
12.5 mg/0.5 ml
1 pre-filled syringe (0.5 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/031 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 12.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.5 ml contains 12.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
12.5 mg/0.5 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.5 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.5 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/032 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/051 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 12.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.5 ml contains 12.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
12.5 mg/0.5 ml
1 pre-filled syringe (0.5 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/032 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/051 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 12.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 12.5 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
12.5 mg / 0.5 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 12.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

12.5 mg / 0.5 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.6 ml contains 15 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
15 mg/0.6 ml
1 pre-filled syringe (0.6 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/034 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.6 ml contains 15 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
15 mg/0.6 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.6 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.6 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/035 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/052 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.6 ml contains 15 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
15 mg/0.6 ml
1 pre-filled syringe (0.6 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/035 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/052 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 15 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
15 mg / 0.6 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 15 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

15 mg / 0.6 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.7 ml contains 17.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
17.5 mg/0.7 ml
1 pre-filled syringe (0.7 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/037 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 17.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.7 ml contains 17.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
17.5 mg/0.7 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.7 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.7 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/038 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/053 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 17.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.7 ml contains 17.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
17.5 mg/0.7 ml
1 pre-filled syringe (0.7 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/038 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/053 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 17.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 17.5 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
17.5 mg / 0.7 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 17.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

17.5 mg / 0.7 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.8 ml contains 20 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
20 mg/0.8 ml
1 pre-filled syringe (0.8 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/040 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.8 ml contains 20 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
20 mg/0.8 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.8 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.8 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/041 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/054 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.8 ml contains 20 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
20 mg/0.8 ml
1 pre-filled syringe (0.8 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/041 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/054 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 20 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
20 mg / 0.8 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 20 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

20 mg / 0.8 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.9 ml contains 22.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
22.5 mg/0.9 ml
1 pre-filled syringe (0.9 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/043 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 22.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.9 ml contains 22.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
22.5 mg/0.9 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (0.9 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (0.9 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/044 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/055 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 22.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 0.9 ml contains 22.5 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
22.5 mg/0.9 ml
1 pre-filled syringe (0.9 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/044 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/055 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 22.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 22.5 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
22.5 mg / 0.9 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 22.5 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

22.5 mg / 0.9 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 1.0 ml contains 25 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
25 mg/1.0 ml
1 pre-filled syringe (1.0 ml) and 2 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/046 1 pre-filled syringe

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 1.0 ml contains 25 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
25 mg/1.0 ml
Multipack: 4 (4 packs of 1) pre-filled syringes (1.0 ml) and 8 alcohol swabs
Multipack: 12 (12 packs of 1) pre-filled syringes (1.0 ml) and 24 alcohol swabs

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/047 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/056 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg solution for injection in pre-filled syringe

methotrexate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 1.0 ml contains 25 mg methotrexate (25 mg/ml)

3. LIST OF EXCIPIENTS

Sodium chloride
Sodium hydroxide
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
25 mg/1.0 ml
1 pre-filled syringe (1.0 ml) and 2 alcohol swabs. Component of a multipack, can't be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Methotrexate is injected once weekly.
Read the package leaflet before 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

Cytotoxic: handle with caution.

Use only once a week

on …….. (include weekday of use in full)

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.

Do not freeze.

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

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1124/047 4 pre-filled syringes (4 packs of 1)
EU/1/16/1124/056 12 pre-filled syringes (12 packs of 1)

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Nordimet 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister - PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Nordimet 25 mg injection
methotrexate

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nordic Group B.V.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. OTHER

SC
25 mg / 1.0 ml

Use only once a week

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

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

Nordimet 25 mg injection
methotrexate
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Batch:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

25 mg / 1.0 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Nordimet 7.5 mg solution for injection in pre-filled pen
Nordimet 10 mg solution for injection in pre-filled pen
Nordimet 12.5 mg solution for injection in pre-filled pen
Nordimet 15 mg solution for injection in pre-filled pen
Nordimet 17.5 mg solution for injection in pre-filled pen
Nordimet 20 mg solution for injection in pre-filled pen
Nordimet 22.5 mg solution for injection in pre-filled pen
Nordimet 25 mg solution for injection in pre-filled pen

methotrexate

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nordimet is and what it is used for

Nordimet contains the active substance methotrexate which works by:
- reducing inflammation or swelling, and
- reducing the activity of the immune system (the body's own defense mechanism). An overactive immune system has been linked to inflammatory diseases.

Nordimet is a medicine used to treat a range of inflammatory diseases:
- active rheumatoid arthritis in adults. Active rheumatoid arthritis is an inflammatory condition that affects the joints;
- severe, active juvenile idiopathic arthritis in five or more joints (the condition is therefore called polyarthritic), in patients who have had an inadequate response to nonsteroidal anti-inflammatory drugs (NSAIDs);
- moderate to severe plaque psoriasis in adults who are candidates for systemic therapy, as well as in severe psoriasis that also affects the joints (psoriatic arthritis) in adult patients;
- induction of remission in adults with moderate steroid-dependent Crohn's disease, in combination with corticosteroids;
- maintenance of remission of Crohn´s disease in adults who have responded to methotrexate, as monotherapy.

2. What you need to know before you use Nordimet

Do not use Nordimet if:
- you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6)

- you have severe kidney disease (your doctor will be able to tell you if you have severe kidney disease)
- you have severe liver disease (your doctor will be able to tell you if you have severe liver disease)
- you have disorders of the blood-forming system
- your alcohol consumption is high
- you have an impaired immune system
- you have a severe or existing infection, e.g. tuberculosis or HIV
- you have gastrointestinal ulcers
- you are pregnant or breast-feeding (see section “Pregnancy, breast-feeding and fertility”)
- you receive vaccinations with live vaccines at the same time.

Warnings and precautions
Acute bleeding from the lungs in patients with underlying rheumatologic disease has been reported with methotrexate. If you experience symptoms of spitting or coughing up blood you should contact your doctor immediately.

Enlarged lymph nodes (lymphoma) may occur and therapy does then have to be discontinued.

Diarrhoea can be a toxic effect of Nordimet and requires an interruption of therapy. If you suffer from diarrhoea please speak to your doctor.

Certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate is used to treat other diseases.

If you, your partner or your caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor.

Important warning about the dosing of Nordimet
Methotrexate for the therapy of rheumatic diseases, diseases of the skin and Crohn’s disease must only be used **once weekly**. Incorrect dosing of methotrexate may lead to serious adverse effects which may be fatal. Please read section 3 of this package leaflet very carefully.

Talk to your doctor before using Nordimet if:
- you have diabetes mellitus and are being treated with insulin
- you have inactive, prolonged infections (e.g. tuberculosis, hepatitis B or C, shingles [herpes zoster])
- you have/had any liver or kidney disease
- you have problems with lung function
- you are severely overweight
- you have abnormal accumulation of liquid in the abdomen or in the cavity between the lungs and chest wall (ascites, pleural effusions)
- you are dehydrated or suffer from conditions leading to dehydration (e.g. dehydration as a result of vomiting, diarrhoea or inflammation of the mouth and lips)

If you have experienced problems with your skin after radiation therapy (radiation induced dermatitis) or sun-burn, these conditions can reappear when taking Nordimet.

Children, adolescents and elderly

Dose instructions depend on the patient's body weight.

Use in children under 3 years of age is not recommended due to insufficient experience of using this medicine in this age group.

Children, adolescents and the elderly being treated with Nordimet should be kept under close medical surveillance to identify possible side effects as early as possible.

The dose for elderly patients should be lowered due to age-related reduced liver and kidney function.

Special precautionary measures for treatment with Nordimet
Methotrexate temporarily affects sperm and egg production. Methotrexate can cause miscarriage and severe birth defects. You should avoid having a baby if you are being given methotrexate at the time and for at least 6 months after the end of your treatment with methotrexate if you are a woman. If you are a man you should avoid fathering a child if you are being given methotrexate at the time and for at least 3 months after the end of your treatment. See also section "Pregnancy, breast-feeding and fertility".
Skin changes caused by psoriasis can worsen during treatment with Nordimet if exposed to ultraviolet irradiation.

Recommended follow-up examinations and precautions
Even if methotrexate is used in low doses, serious side effects can occur. In order to detect them in time, your doctor must perform monitoring examinations and laboratory tests.

Prior to the start of therapy:
Before you start treatment, your blood will be checked to see if you have enough blood cells. Your blood will also be tested to check your liver function and to find out if you have hepatitis. Furthermore, serum albumin (a protein in the blood), hepatitis (liver infection) status and kidney function will be checked. The doctor may also decide to run other liver tests, some of these may be images of your liver and others may need a small sample of tissue taken from the liver in order to examine it more closely. Your doctor may also check to see if you have tuberculosis and they may X-ray your chest or perform a lung function test.

During the treatment:
Your doctor may perform the following examinations:
- examination of the oral cavity and the pharynx for changes in the mucous membrane such as inflammation or ulceration
- blood tests/ blood count with number of blood cells and measurement of serum methotrexate levels
- blood test to monitor liver function
- Imaging tests to monitor liver condition
- small sample of tissue taken from the liver in order to examine it more closely
- blood test to monitor kidney function
- respiratory tract monitoring and, if necessary, lung function test

It is very important that you appear for these scheduled examinations.
If the results of any of these tests are conspicuous, your doctor will adjust your treatment accordingly.

Other medicines and Nordimet
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

It is especially important to tell your doctor if you are taking:

- other treatments for rheumatoid arthritis or psoriasis such as leflunomide, sulphasalazine (a medicine that besides arthritis and psoriasis is also used to treat ulcerative colitis), aspirin, phenylbutazone, or amidopyrine
- cyclosporine (for suppressing the immune system)
- azathioprine (used to prevent rejection after an organ transplant)
- retinoids (used to treat psoriasis and other skin disorders)
- anticonvulsant medicines (used to prevent fits), such as phenytoin, valproate or carbamazepine
- cancer treatments
- barbiturates (sleeping injection)
- tranquillisers
- oral contraceptives
- probenecid (used to treat gout)
- antibiotics (e.g. penicillin, glycopeptides, trimethoprim-sulphamethoxazole, sulfonamides, ciprofloxacin, cefalotin, tetracyclines, chloramphenicol)
- pyrimethamine (used to prevent and treat malaria)
- vitamin preparations containing folic acid
- proton-pump inhibitors (medicines that reduce the production of gastric acid and that are used to treat severe heartburn or ulcers), such as omeprazole or pantoprazole
- theophylline (used to treat asthma)
- colestyramine (used to treat high cholesterol, pruritus or diarrhoea)
- NSAID's, non-steroidal anti-inflammatory drugs (used to treat pain or inflammation)
- p-aminobenzoic acid (used to treat skin disorders)
- any vaccination with a live vaccine (must be avoided), such as measles, mumps or yellow fever vaccines
- metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and /or fever)
- nitrous oxide (a gas used in general anaesthesia

Nordimet with food, drink and alcohol
During treatment with Nordimet, you must not drink any alcohol and should avoid excessive consumption of coffee, soft drinks containing caffeine and black tea as this may enhance side effects or interfere with the efficacy of Nordimet. Also, make sure you drink plenty of liquids during treatment with Nordimet because dehydration (reduction in body water) can increase the toxicity of Nordimet.

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

Pregnancy
Do not use Nordimet during pregnancy or if you are trying to become pregnant. Methotrexate can cause birth defects, harm unborn babies or cause miscarriages. It is associated with malformations of the skull, face, heart and blood vessels, brain and limbs. Therefore, it is very important that methotrexate is not given to pregnant patients or patients planning to become pregnant. In women of child-bearing age any possibility of pregnancy must be excluded with appropriate measures, e.g. a pregnancy test before starting treatment. You must avoid becoming pregnant whilst taking methotrexate and for at least 6 months after treatment is stopped by using reliable contraception throughout this time (see also section "Warnings and precautions").

If you do become pregnant during treatment or suspect you might be pregnant, speak to your doctor as soon as possible. You should be offered advice regarding the risk of harmful effects on the child through treatment.
If you wish to become pregnant you should consult your doctor, who may refer you for specialist advice before the planned start of treatment.

Breast-feeding

Do not breast-feed during treatment because methotrexate passes into breast milk. If your doctor considers treatment with methotrexate absolutely necessary during the lactation period, you must stop breast-feeding.

Male fertility
The available evidence does not indicate an increased risk of malformations or miscarriage if the father takes methotrexate less than 30 mg/week. However, a risk cannot be completely excluded. Methotrexate may be genotoxic. This means that the medicine may cause genetic mutation. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen whilst taking methotrexate and for at least 3 months after treatment is stopped.

Driving and using machines
Side effects affecting the central nervous system, such as tiredness and dizziness, may occur during treatment with Nordimet. In some cases, the ability to drive vehicles and/or use machines may be impaired. If you feel tired or dizzy, you should not drive or use machines.

Nordimet 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 Nordimet

Important warning about the dose of Nordimet

Use Nordimet **only once a week** for the treatment of rheumatoid arthritis, active juvenile idiopathic arthritis, psoriasis, psoriatic arthritis and Crohn's disease requiring dosing once a week. Using too much of Nordimet may be fatal. Please read section 3 of this leaflet very carefully. If you have any questions, please talk to your doctor or pharmacist before you take this medicine.

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

Nordimet is administered **once a week only**. You and your doctor can decide on a suitable day each week to receive your injection.

Incorrect administration of Nordimet can lead to severe side effects that may be fatal.

The recommended dose is:

Dose in patients with rheumatoid arthritis
The recommended starting dose is 7.5 mg methotrexate **once a week**.

The doctor may increase the dose if the used dose is not effective but tolerated well. The average weekly dose is 15-20 mg. Generally, a weekly dose of 25 mg should not be exceeded. Once Nordimet starts working, the doctor may reduce the dose gradually to the lowest possible effective maintenance dose.

Generally, improvement of symptoms can be expected after 4-8 weeks of treatment. Symptoms may return if treatment with Nordimet is stopped.

Use in adults with moderate to severe forms of plaque psoriasis or severe psoriatic arthritis
Your doctor will give you a single test dose of 5-10 mg, in order to assess possible side effects. If the test dose is well tolerated, treatment will be continued after a week with a dose of approximately 7.5 mg.

Response to treatment can generally be expected after 2-6 weeks. Depending on the effects of treatment and results of blood and urine tests, the therapy is then continued or stopped.

Dose in adult patients with Crohn's disease:
Your doctor will start with a weekly dose of 25 mg. Response to treatment can generally be expected after 8-12 weeks. Depending on the effects of treatment in time, your doctor may decide to reduce the dose to 15 mg weekly.

Use in children and adolescents below 16 years with polyarthritic forms of juvenile idiopathic arthritis
The doctor will calculate the dose required from the child's body surface area (m^2), and the dose is expressed as mg/m^2.

Use in children under 3 years of age is not recommended due to insufficient experience in this age group.

Method and duration of administration
Nordimet is given as injection under the skin (subcutaneously). It must be injected once weekly and it is recommended to always inject Nordimet on the same day of the week.

At the start of your treatment, Nordimet may be injected by medical staff. However, your doctor may decide that you can learn how to inject Nordimet yourself. You will receive appropriate training for you to do this. Under no circumstances should you attempt to inject yourself, unless you have been trained to do so.

The duration of treatment is determined by the treating physician.

Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, plaque psoriasis, psoriatic arthritis and Crohn's disease with Nordimet is a long-term treatment.

How to give yourself an injection of Nordimet
If you have difficulty handling the pen, ask your doctor or pharmacist. Do not try to inject yourself if you have not been trained on how to do so. If you are not sure what to do, talk to your doctor or nurse immediately. Beside the below information on administration, you can find on the carton a QR code with an instruction video on how to administer yourself. This QR code can be scanned with QR reader, an application (app) on smartphone or tablet. The same information can also be found at https://nordimetvideo.com.

Before injecting yourself with Nordimet
- Check the expiry date on the medicine. Do not use if the date has passed.
- Check the pen is not damaged and the medicine in it is a clear, yellow solution. If not, use another pen.
- Check your last injection site to see if the last injection caused any redness, change in skin colour, swelling, oozing or is still painful, if so talk to your doctor or nurse.
- Decide where you are going to inject the medicine. Change the place where you inject each time.

Instructions on injecting yourself with Nordimet
1) Wash your hands thoroughly with soap and water.

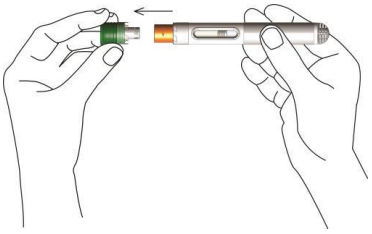
2) Sit or lie in a relaxed, comfortable position. Make sure you can see the skin area you are going to inject.

3) The pen is pre-filled and ready to use. Visually inspect the pen. You should see a yellow fluid through the viewing window. You may see a small air bubble, this does not affect the injection and will not harm you.

A droplet may appear at the tip of the needle. This is normal.

4) Choose an injection site and clean it with the enclosed alcohol swab. It requires 30-60 seconds to be effective. The skin on the front side abdominal wall and the skin at the front of the thigh are suitable as injection sites.

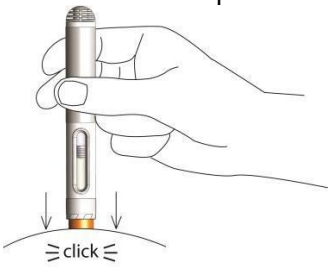
5) While holding the body of the pen, remove the green protective cap by pulling it smoothly and directly away from the unit. Do not twist or bend.
Once you have taken the cap off, keep the pen in your hand. Do not allow the pen to touch anything else. This is to make sure that the pen is not accidentally activated and that the needle stays clean.



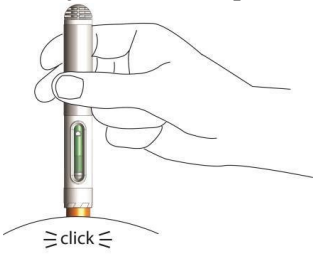
6) Make a fold in the skin by gently pinching the skin of the injection place with your forefinger and thumb. Make sure you hold the skin fold throughout the injection.

7) Move the pen towards the skin fold (site of injection) with the needle shield pointing directly at the site of injection. Place the yellow needle shield against the area of injection so that the entire rim of the needle shield is touching the skin.

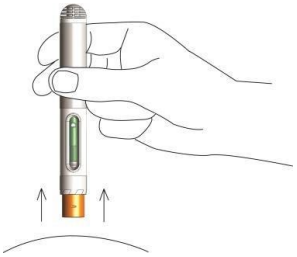
8) Apply downward pressure on the pen on to your skin until you hear and feel a “click”.
This activates the pen and the solution will inject automatically into the skin.



9) The injection lasts for a maximum of 10 seconds. You will feel and hear a second “click” once the injection is completed.



10) Wait another 2-3 seconds before removing the pen from your skin. The safety shield on the pen is now locked to prevent any needlestick injuries. You can now let go of the skin fold.



11) Visually inspect the pen through the viewing window. You should see green plastic. This means that all the fluid has been injected. Discard the used pen into the sharps bin provided. Close the container lid tightly and place the container out of reach of children. If you accidently get methotrexate on the surface of the skin or soft tissues you must rinse with plenty of water.

If you use more Nordimet than you should
Follow the dose recommendations of your treating doctor. Do not change the dose without your doctor's recommendation.

If you suspect that you have used too much Nordimet, tell your doctor or contact the nearest hospital immediately. Take your medicine package and this leaflet with you if you go to a doctor or hospital.

An overdose of methotrexate can lead to severe toxic reactions. Overdose symptoms may include easy bruising or bleeding, unusual weakness, mouth sores, nausea, vomiting, black or bloody stools, coughing up blood or vomit that looks like coffee grounds, and decreased urinating. See also section 4.

If you forget to use Nordimet
Do not take a double dose to make up for a forgotten dose, but continue taking the prescribed dose as normal. Ask your doctor for advice.

If you stop taking Nordimet
You should not interrupt or discontinue Nordimet treatment before discussing with your doctor. If you suspect that you are experiencing side effects, contact your doctor immediately for advice.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

Tell your doctor straight away if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

<u>Serious side effects</u>
If you develop any of the following side effects, contact your doctor immediately:
- inflammation of the lungs (symptoms may be general illness, dry, irritating cough, shortness of breath, breathlessness at rest, chest pain, or fever)
- spitting or coughing blood
- severe peeling or blistering of the skin
- unusual bleeding (including vomiting blood) or bruising
- severe diarrhoea
- ulcers in mouth
- black or tarry stools
- blood in the urine or stools
- tiny red spots on the skin
- fever

- yellowing of the skin (jaundice)
- pain or difficulty in passing urine
- thirst and/or frequent urination
- fits (convulsions)
- loss of consciousness
- blurred or decreased vision

The following side effects have also been reported:

Very common (may affect more than 1 in 10 people)
loss of appetite, nausea (feeling sick), tummy pain, inflammation ofthe mouth lining, abnormal digestion, and increase in liver enzymes.

Common (may affect up to 1 in 10 people)
Reduced blood cell formation with decrease in white and/or red blood cells and/or platelets (leukopenia, anaemia, thrombocytopenia), headache, tiredness, drowsiness, inflammation of the lungs (pneumonia) with dry, non-productive cough, shortness of breath and fever, mouth ulcers, diarrhoea, rash, reddening of the skin, itching.

Uncommon (may affect up to 1 in 100 people)
Decrease in the number of blood cells and platelets, throat inflammation, dizziness, confusion, depression, inflammation of blood vessels, ulcers and bleeding in the digestive tract, inflammation of the bowels, vomiting, inflammation of pancreas, liver disorders, diabetes, decreased blood protein, herpes-like skin rash, nettle rash, sunburn-like reactions due to increased sensitivity of the skin to sunlight, , hair loss, increase of rheumatic nodules, skin ulcer, shingles, joint or muscle pain, osteoporosis (reduction of bone mass), inflammation and ulcers of the bladder (possibly with blood in the urine), reduced kidney function, painful urination, inflammation and ulcers of the vagina.

Rare (may affect up to 1 in 1,000 people)
Infection (incl. reactivation of inactive chronic infection), sepsis, red eyes, allergic reactions, anaphylactic shock, decreased numbers of antibodies in the blood, inflammation of the sac around the heart, accumulation of fluid in the sac around the heart, obstruction of cardiac filling due to fluid in the sac around the heart, visual disturbance, mood fluctuations, low blood pressure, blood clots, formation of scar tissue in the lung (pulmonary fibrosis), *Pneumocystis jiroveci* pneumonia, interruption of breathing, asthma, accumulation of fluid in the sac around the lungs, inflamed gums, acute hepatitis (inflammation of the liver), brown skin, acne, red or purple spots due to vessel bleeding, allergic inflammation of blood vessels, bone fracture, kidney failure, decrease or absence of urine, electrolyte disturbances, fever, slow wound healing.

Very rare (may affect up to 1 in 10,000 people)
Reduction in certain white blood cells (agranulocytosis), severe failure of the bone marrow, liver failure, swollen glands, sleeplessness, pain, muscle weakness, sensation of numbness or tingling / having less sensitivity to stimulation than normal, changes in sense of taste (metallic taste), fits, inflammation of the lining of the brain causing paralysis or vomiting, impaired vision, damage to the retina of the eye, vomiting blood, toxic megacolon (enlargement of the large intestine associated with severe pain) , defective sperm formation (oligospermia), Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), increased pigmentation of the nails, loss of sex drive, problems having an erection, infection around a fingernail, severe complications of the gastrointestinal tract, boils, visible enlargement of small blood vessels in the skin, menstrual disorders, vaginal discharge, infertility, male breast enlargement (gynaecomastia), lymphoproliferative disorders (excessive growth of white blood cells).

Frequency not known (cannot be estimated from the available data)
Increased number of certain white blood cells (eosinophilia), certain brain disorders (encephalopathy/leukoencephalopathy), nose bleeds, bleeding from the lungs, bone damage in the jaw (secondary to excessive growth of white blood cells), protein in the urine, feeling of weakness, tissue destruction at injection site, redness and shedding of skin, swelling.

Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, severe itching, pain) were observed with Nordimet and these decreased during therapy.

Nordimet may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/sore pharynx/sore mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check for possible reduction of white blood cells (agranulocytosis). It is important to tell your doctor that you are taking Nordimet.

Methotrexate is known to cause bone disorders such as joint and muscle pain and osteoporosis. The frequency of these risks in children is not known.

Nordimet may cause serious (sometimes life-threatening) side effects. Your doctor will do tests to check for abnormalities developing in the blood (e.g. low white blood cells, low platelets, lymphoma) and changes in the kidney and the liver.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 Nordimet

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 label of the pre-filled pen and the carton after EXP. The expiry date refers to the last day of that month.

Store below 25°C.
Keep the pen in the outer carton in order to protect from light.
Do not freeze.

Do not use this medicine if you notice that the solution is not clear and contains particles.

Nordimet is for single use only. Any used pen should be discarded.
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 Nordimet contains
The active substance is methotrexate. 1.0 ml of solution contains 25 mg methotrexate.
The other ingredients are sodium chloride, sodium hydroxide and water for injections.

The following pens are available:
Pre-filled pens of 0.3 ml containing 7.5 mg methotrexate.
Pre-filled pens of 0.4 ml containing 10 mg methotrexate
Pre-filled pens of 0.5 ml containing 12.5 mg methotrexate
Pre-filled pens of 0.6 ml containing 15 mg methotrexate
Pre-filled pens of 0.7 ml containing 17.5 mg methotrexate
Pre-filled pens of 0.8 ml containing 20 mg methotrexate

Pre-filled pens of 0.9 ml containing 22.5 mg methotrexate
Pre-filled pens of 1.0 ml containing 25 mg methotrexate

What Nordimet looks like and contents of the pack
Nordimet pre-filled pens contain a clear, yellow solution for injection.

Nordimet is available in packs containing 1 or 4 pre-filled pens and 1 or 4 alcohol swabs and in multipacks comprising 4 cartons, each containing 1 pre-filled pen and one alcohol swab.
Nordimet is also available in multipacks comprising 3 cartons, each containing 4 pre-filled pens and alcohol swabs.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

Manufacturer
CENEXI - Laboratoires Thissen
Rue de la Papyrée 2-6
B-1420 Braine-l'Alleud
Belgium

Sever Pharma Solutions AB
Agneslundsvagen 27
P.O. Box 590
SE-201 25 Malmo
Sweden

FUJIFILM Diosynth Biotechnologies Denmark ApS
Biotek Allé 1
3400 Hillerød
Denmark

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http//www.ema.europa.eu.

Package leaflet: Information for the user

Nordimet 7.5 mg solution for injection in pre-filled syringe
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methotrexate

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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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nordimet is and what it is used for

Nordimet contains the active substance methotrexate which works by:
- reducing inflammation or swelling, and
- reducing the activity of the immune system (the body's own defense mechanism). An overactive immune system has been linked to inflammatory diseases.

Nordimet is a medicine used to treat a range of inflammatory diseases:
- active rheumatoid arthritis in adults. Active rheumatoid arthritis is an inflammatory condition that affects the joints;
- severe, active juvenile idiopathic arthritis in five or more joints (the condition is therefore called polyarthritic), in patients who have had an inadequate response to nonsteroidal anti-inflammatory drugs (NSAIDs);
- moderate to severe plaque psoriasis in adults who are candidates for systemic therapy, as well as in severe psoriasis that also affects the joints (psoriatic arthritis) in adult patients;
- induction of remission in adults with moderate steroid-dependent Crohn's disease, in combination with corticosteroids;
- maintenance of remission of Crohn´s disease in adults who have responded to methotrexate, as monotherapy.

2. What you need to know before you use Nordimet

Do not use Nordimet if:
- you are allergic to methotrexate or any of the other ingredients of this medicine (listed in section 6)

- you have severe kidney disease (your doctor will be able to tell you if you have severe kidney disease)
- you have severe liver disease (your doctor will be able to tell you if you have severe liver disease)
- you have disorders of the blood-forming system
- your alcohol consumption is high
- you have an impaired immune system
- you have a severe or existing infection, e.g. tuberculosis or HIV
- you have gastrointestinal ulcers
- you are pregnant or breast-feeding (see section “Pregnancy, breast-feeding and fertility”)
- you receive vaccinations with live vaccines at the same time.

Warnings and precautions
Acute bleeding from the lungs in patients with underlying rheumatologic disease has been reported with methotrexate. If you experience symptoms of spitting or coughing up blood you should contact your doctor immediately.

Enlarged lymph nodes (lymphoma) may occur and therapy does then have to be discontinued.

Diarrhoea can be a toxic effect of Nordimet and requires an interruption of therapy. If you suffer from diarrhoea please speak to your doctor.

Certain brain disorders (encephalopathy/leukoencephalopathy) have been reported in cancer patients receiving methotrexate. Such side effects cannot be excluded when methotrexate is used to treat other diseases.

If you, your partner or your caregiver notice new onset or worsening of neurological symptoms including general muscle weakness, disturbance of vision, changes in thinking, memory and orientation leading to confusion and personality changes contact your doctor immediately because these may be symptoms of a very rare, serious brain infection called progressive multifocal leukoencephalopathy (PML).

Methotrexate may make your skin more sensitive to sunlight. Avoid intense sun and do not use sun-beds or a sun-lamp without medical advice. To protect your skin from intense sun, wear adequate clothing or use a sunscreen with a high protection factor.

Important warning about the dosing of Nordimet
Methotrexate for the therapy of rheumatic diseases, diseases of the skin and Crohn’s disease must only be used **once weekly**. Incorrect dosing of methotrexate may lead to serious adverse effects which may be fatal. Please read section 3 of this package leaflet very carefully.

Talk to your doctor before using Nordimet if:
- you have diabetes mellitus and are being treated with insulin
- you have inactive, prolonged infections (e.g. tuberculosis, hepatitis B or C, shingles [herpes zoster])
- you have/had any liver or kidney disease
- you have problems with lung function
- you are severely overweight
- you have abnormal accumulation of liquid in the abdomen or in the cavity between the lungs and chest wall (ascites, pleural effusions)
- you are dehydrated or suffer from conditions leading to dehydration (e.g. dehydration as a result of vomiting, diarrhoea or inflammation of the mouth and lips)

If you have experienced problems with your skin after radiation therapy (radiation induced dermatitis) or sun-burn, these conditions can reappear when taking Nordimet.

Children, adolescents and elderly

Dose instructions depend on the patient's body weight.

Use in children under 3 years of age is not recommended due to insufficient experience of using this medicine in this age group.

Children, adolescents and the elderly being treated with Nordimet should be kept under close medical surveillance to identify possible side effects as early as possible.

The dose for elderly patients should be lowered due to age-related reduced liver and kidney function.

Special precautionary measures for treatment with Nordimet
Methotrexate temporarily affects sperm and egg production. Methotrexate can cause miscarriage and severe birth defects. You should avoid having a baby if you are being given methotrexate at the time and for at least 6 months after the end of your treatment with methotrexate if you are a woman. If you are a man you should avoid fathering a child if you are being given methotrexate at the time and for at least 3 months after the end of your treatment. See also section "Pregnancy, breast-feeding and fertility".
Skin changes caused by psoriasis can worsen during treatment with Nordimet if exposed to ultraviolet irradiation.

Recommended follow-up examinations and precautions
Even if methotrexate is used in low doses, serious side effects can occur. In order to detect them in time, your doctor must perform monitoring examinations and laboratory tests.

Prior to the start of therapy:
Before you start treatment, your blood will be checked to see if you have enough blood cells. Your blood will also be tested to check your liver function and to find out if you have hepatitis. Furthermore, serum albumin (a protein in the blood), hepatitis (liver infection) status and kidney function will be checked. The doctor may also decide to run other liver tests, some of these may be images of your liver and others may need a small sample of tissue taken from the liver in order to examine it more closely. Your doctor may also check to see if you have tuberculosis and they may X-ray your chest or perform a lung function test.

During the treatment:
Your doctor may perform the following examinations:
- examination of the oral cavity and the pharynx for changes in the mucous membrane such as inflammation or ulceration
- blood tests/ blood count with number of blood cells and measurement of serum methotrexate levels
- blood test to monitor liver function
- Imaging tests to monitor liver condition
- small sample of tissue taken from the liver in order to examine it more closely
- blood test to monitor kidney function
- respiratory tract monitoring and, if necessary, lung function test

It is very important that you appear for these scheduled examinations.
If the results of any of these tests are conspicuous, your doctor will adjust your treatment accordingly.

Other medicines and Nordimet
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

It is especially important to tell your doctor if you are taking:

- other treatments for rheumatoid arthritis or psoriasis such as leflunomide, sulphasalazine (a medicine that besides arthritis and psoriasis is also used to treat ulcerative colitis), aspirin, phenylbutazone, or amidopyrine
- cyclosporine (for suppressing the immune system)
- azathioprine (used to prevent rejection after an organ transplant)
- retinoids (used to treat psoriasis and other skin disorders)
- anticonvulsant medicines (used to prevent fits), such as phenytoin, valproate or carbamazepine
- cancer treatments
- barbiturates (sleeping injection)
- tranquillisers
- oral contraceptives
- probenecid (used to treat gout)
- antibiotics(e.g. penicillin, glycopeptides, trimethoprim-sulphamethoxazole, sulfonamides, ciprofloxacin, cefalotin, tetracyclines, chloramphenicol)
- pyrimethamine (used to prevent and treat malaria)
- vitamin preparations containing folic acid
- proton-pump inhibitors (medicines that reduce the production of gastric acid and that are used to treat severe heartburn or ulcers), such as omeprazole or pantoprazole
- theophylline (used to treat asthma)
- colestyramine (used to treat high cholesterol, pruritus or diarrhoea)
- NSAID's, non-steroidal anti-inflammatory drugs (used to treat pain or inflammation)
- p-aminobenzoic acid (used to treat skin disorders)
- any vaccination with a live vaccine (must be avoided), such as measles, mumps or yellow fever vaccines
- metamizole (synonyms novaminsulfon and dipyrone) (medicine against severe pain and /or fever)
- nitrous oxide (a gas used in general anaesthesia

Nordimet with food, drink and alcohol
During treatment with Nordimet, you must not drink any alcohol and should avoid excessive consumption of coffee, soft drinks containing caffeine and black tea as this may enhance side effects or interfere with the efficacy of Nordimet. Also, make sure you drink plenty of liquids during treatment with Nordimet because dehydration (reduction in body water) can increase the toxicity of Nordimet.

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

Pregnancy
Do not use Nordimet during pregnancy or if you are trying to become pregnant. Methotrexate can cause birth defects, harm unborn babies or cause miscarriage. It is associated with malformations of the skull, face, heart and blood vessels, brain and limbs. Therefore, it is very important that methotrexate is not given to pregnant patients or patients planning to become pregnant. In women of child-bearing age any possibility of pregnancy must be excluded with appropriate measures, e.g. a pregnancy test before starting treatment. You must avoid becoming pregnant whilst taking methotrexate and for at least 6 months after treatment is stopped by using reliable contraception throughout this time (see also section "Warnings and precautions").

If you do become pregnant during treatment or suspect you might be pregnant, speak to your doctor as soon as possible. You should be offered advice regarding the risk of harmful effects on the child through treatment.
If you wish to become pregnant you should consult your doctor, who may refer you for specialist advice before the planned start of treatment.

Breast-feeding

Do not breast-feed during treatment because methotrexate passes into breast milk. If your doctor considers treatment with methotrexate absolutely necessary during the lactation period, you must stop breast-feeding.

Male fertility
The available evidence does not indicate an increased risk of malformations or miscarriage if the father takes methotrexate less than 30 mg/week. However, a risk cannot be completely excluded. Methotrexate may be genotoxic. This means that the medicine may cause genetic mutation. Methotrexate can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen whilst taking methotrexate and for at least 3 months after treatment is stopped.

Driving and using machines
Side effects affecting the central nervous system, such as tiredness and dizziness, may occur during treatment with Nordimet. In some cases, the ability to drive vehicles and/or use machines may be impaired. If you feel tired or dizzy, you should not drive or use machines.

Nordimet 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 Nordimet

Important warning about the dose of Nordimet

Use Nordimet **only once a week** for the treatment of rheumatoid arthritis, active juvenile idiopathic arthritis, psoriasis, psoriatitic arthritis and Crohn's disease requiring dosing once a week. Using too much of Nordimet may be fatal. Please read section 3 of this leaflet very carefully. If you have any questions, please talk to your doctor or pharmacist before you take this medicine.

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

Nordimet is administered **once a week only**. You and your doctor can decide on a suitable day each week to receive your injection.

Incorrect administration of Nordimet can lead to severe side effects that may be fatal.

The recommended dose is:

Dose in patients with rheumatoid arthritis
The recommended starting dose is 7.5 mg methotrexate **once a week**.

The doctor may increase the dose if the used dose is not effective but tolerated well. The average weekly dose is 15-20 mg. Generally, a weekly dose of 25 mg should not be exceeded. Once Nordimet starts working, the doctor may reduce the dose gradually to the lowest possible effective maintenance dose.

Generally, improvement of symptoms can be expected after 4-8 weeks of treatment. Symptoms may return if treatment with Nordimet is stopped.

Use in adults with moderate to severe forms of plaque psoriasis or severe psoriatic arthritis
Your doctor will give you a single test dose of 5-10 mg, in order to assess possible side effects. If the test dose is well tolerated, treatment will be continued after a week with a dose of approximately 7.5 mg.

Response to treatment can generally be expected after 2-6 weeks. Depending on the effects of treatment and results of blood and urine tests, the therapy is then continued or stopped.

Dose in adult patients with Crohn's disease:
Your doctor will start with a weekly dose of 25 mg. Response to treatment can generally be expected after 8-12 weeks. Depending on the effects of treatment in time, your doctor may decide to reduce the dose to 15 mg weekly.

Use in children and adolescents below 16 years with polyarthritic forms of juvenile idiopathic arthritis
The doctor will calculate the dose required from the child's body surface area (m^2), and the dose is expressed as mg/m^2.

Use in children under 3 years of age is not recommended due to insufficient experience in this age group.

Method and duration of administration
Nordimet is given as injection under the skin (subcutaneously). It must be injected once weekly and it is recommended to always inject Nordimet on the same day of the week.

At the start of your treatment, Nordimet may be injected by medical staff. However, your doctor may decide that you can learn how to inject Nordimet yourself. You will receive appropriate training for you to do this. Under no circumstances should you attempt to inject yourself, unless you have been trained to do so.

The duration of treatment is determined by the treating physician.

Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, plaque psoriasis, psoriatic arthritis and Crohn's disease with Nordimet is a long-term treatment.

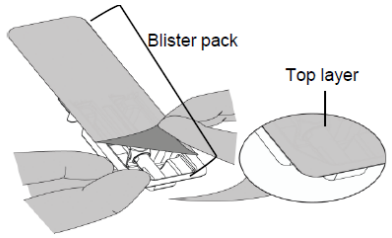
How to give yourself an injection of Nordimet
If you have difficulty handling the syringe, ask your doctor or pharmacist. Do not try to inject yourself if you have not been trained on how to do so. If you are not sure what to do, talk to your doctor or nurse immediately.

Before injecting yourself with Nordimet
- Check the expiry date on the medicine. Do not use if the date has passed.
- Check the syringe is not damaged and the medicine in it is a clear, yellow solution. If not, use another syringe.
- Check your last injection site to see if the last injection caused any redness, change in skin colour, swelling, oozing or is still painful, if so talk to your doctor or nurse.
- Decide where you are going to inject the medicine. Change the place where you inject each time.

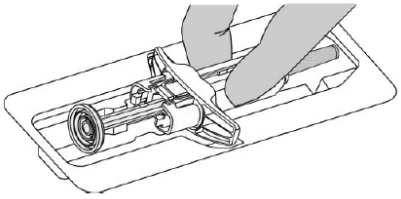
Instructions on injecting yourself with Nordimet
1) Wash your hands thoroughly with soap and water.

2) Sit or lie in a relaxed, comfortable position. Make sure you can see the skin area you are going to inject.

3) The syringe is pre-filled and ready to use. Open the blister pack by peeling back the top layer all the way off the blister pack as shown.



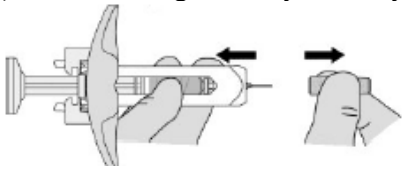
4) Precaution: DO NOT lift the product by the plunger or needle cover. Remove the syringe from the box by the body as shown in the picture below.



5) Visually inspect the syringe. You should see a yellow fluid through the viewing window. You may see a small air bubble, this does not affect the injection and will not harm you.

6) Choose an injection site and clean it with the enclosed alcohol swab. It requires 30-60 seconds to be effective. The skin on the front side abdominal wall and the skin at the front of the thigh are suitable as injection sites.

7) While holding the body of the syringe, pull the cap off.

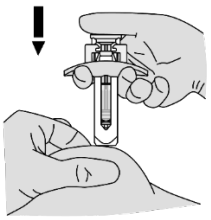


Do not press on the plunger before injecting yourself to get rid of air bubbles. This can lead to a loss of the medicine. Once you have taken the cap off, keep the syringe in your hand. Do not allow the syringe to touch anything else. This is to make sure that the needle stays clean.

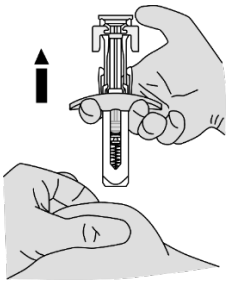
8) Hold the syringe in the hand you write with (like a pencil) and with your other hand, make a fold in the skin by gently pinching the skin of the injection place with your forefinger and thumb. Make sure you hold the skin fold throughout the injection.

9) Move the syringe towards the skin fold (site of injection) with the needle shield pointing directly at the site of injection. Insert the full length of the needle into the skin fold.

10) Press down on the plunger with your finger until the syringe is empty. This will send the medication under the skin.



11) Remove the needle by pulling it out straight. The safety shield on the syringe will automatically cover the needle to prevent any needlestick injuries. You can now let go of the skin fold.



Note: the safety system allowing release of the safety shield, can only be activated when the syringe has been emptied by pressing the plunger all the way down.

12) Discard the used syringe into the sharps bin provided. Close the container lid tightly and place the container out of reach of children. If you accidently get methotrexate on the surface of the skin or soft tissues you must rinse with plenty of water.

If you use more Nordimet than you should
Follow the dose recommendations of your treating doctor. Do not change the dose without your doctor's recommendation.

If you suspect that you have used too much Nordimet, tell your doctor or contact the nearest hospital immediately. Take your medicine package and this leaflet with you if you go to a doctor or hospital.

An overdose of methotrexate can lead to severe toxic reactions. Overdose symptoms may include easy bruising or bleeding, unusual weakness, mouth sores, nausea, vomiting, black or bloody stools, coughing up blood or vomit that looks like coffee grounds, and decreased urinating. See also section 4.

If you forget to use Nordimet
Do not take a double dose to make up for a forgotten dose, but continue taking the prescribed dose as normal. Ask your doctor for advice.

If you stop taking Nordimet
You should not interrupt or discontinue Nordimet treatment before discussing with your doctor. If you suspect that you are experiencing side effects, contact your doctor immediately for advice.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

Tell your doctor straight away if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

<u>Serious side effects</u>
If you develop any of the following side effects, contact your doctor immediately:
- inflammation of the lungs (symptoms may be general illness, dry, irritating cough, shortness of breath, breathlessness at rest, chest pain, or fever)
- spitting or coughing blood
- severe peeling or blistering of the skin
- unusual bleeding (including vomiting blood) or bruising
- severe diarrhoea
- ulcers in mouth
- black or tarry stools
- blood in the urine or stools

- tiny red spots on the skin
- fever
- yellowing of the skin (jaundice)
- pain or difficulty in passing urine
- thirst and/or frequent urination
- fits (convulsions)
- loss of consciousness
- blurred or decreased vision

The following side effects have also been reported:

Very common (may affect more than 1 in 10 people)
loss of appetite, nausea (feeling sick), tummy pain, inflammation of the mouth lining, abnormal digestion and increase in liver enzymes.

Common (may affect up to 1 in 10 people)
Reduced blood cell formation with decrease in white and/or red blood cells and/or platelets (leukopenia, anaemia, thrombocytopenia), headache, tiredness, drowsiness, inflammation of the lungs (pneumonia) with dry, non-productive cough, shortness of breath and fever, mouth ulcers, diarrhoea, rash, reddening of the skin, itching.

Uncommon (may affect up to 1 in 100 people)
Decrease in the number of blood cells and platelets, throat inflammation, dizziness, confusion, depression, inflammation of blood vessels, ulcers and bleeding in the digestive tract, inflammation of the bowels, vomiting, inflammation of pancreas, liver disorders, diabetes, decreased blood protein, herpes-like skin rash, nettle rash, sunburn-like reactions due to increased sensitivity of the skin to sunlight, hair loss, increase of rheumatic nodules, skin ulcer, shingles, joint or muscle pain, osteoporosis (reduction of bone mass), inflammation and ulcers of the bladder (possibly with blood in the urine), reduced kidney function, painful urination, inflammation and ulcers of the vagina.

Rare (may affect up to 1 in 1,000 people):
Infection (incl. reactivation of inactive chronic infection), sepsis, red eyes, allergic reactions, anaphylactic shock, decreased number of antibodies in the blood, inflammation of the sac around the heart, accumulation of fluid in the sac around the heart, obstruction of cardiac filling due to fluid in the sac around the heart, visual disturbance, mood fluctuations, low blood pressure, blood clots, formation of scar tissue in the lungs (pulmonary fibrosis), *Pneumocystis jiroveci* pneumonia, interruption of breathing, asthma, accumulation of fluid in the sac around the lungs, inflamed gums, acute hepatitis (inflammation of the liver), brown skin, acne, red or purple spots due to vessel bleeding, allergic inflammation of blood vessels, bone fracture, kidney failure, decrease or absence of urine, electrolyte disturbances, fever, slow wound healing.

Very rare (may affect up to 1 in 10,000 people):
Reduction in certain white blood cells (agranulocytosis), severe failure of the bone marrow, liver failure, swollen glands, sleeplessness, pain, muscle weakness, sensation of numbness or tingling / having less sensitivity to stimulation than normal, changes in sense of taste (metallic taste), fits, inflammation of the lining of the brain causing paralysis or vomiting, impaired vision, damage to the retina of the eye, vomiting blood, toxic megacolon (enlargement of the large intestine associated with severe pain), defective sperm formation (oligospermia), Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), increased pigmentation of the nails, loss of sex drive, problems having an erection, infection around a fingernail, severe complications of the gastrointestinal tract, boils, visible enlargement of small blood vessels in the skin, menstrual disorders, vaginal discharge, infertility, male breast enlargement (gynaecomastia), lymphoproliferative disorders (excessive growth of white blood cells).

Frequency not known (cannot be estimated from the available data):
Increased number of certain white blood cells (eosinophilia), certain brain disorders (encephalopathy/leukoencephalopathy), nose bleeds, bleeding from the lungs, bone damage in the

jaw (secondary to excessive growth of white blood cells), protein in the urine, feeling weakness, tissue destruction at injection site, redness and shedding of skin, swelling.

Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, severe itching, pain) were observed with Nordimet and these decreased during therapy.

Nordimet may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/sore pharynx/sore mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check for possible reduction of white blood cells (agranulocytosis). It is important to tell your doctor that you are taking Nordimet.

Methotrexate is known to cause bone disorders such as joint and muscle pain and osteoporosis. The frequency of these risks in children is not known.

Nordimet may cause serious (sometimes life-threatening) side effects. Your doctor will do tests to check for abnormalities developing in the blood (e.g. low white blood cells, low platelets, lymphoma) and changes in the kidney and the liver.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 Nordimet

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 label of the pre-filled syringe and the carton after EXP. The expiry date refers to the last day of that month.

Store below 25°C.
Keep the syringe in the outer carton in order to protect from light.
Do not freeze.

Do not use this medicine if you notice that the solution is not clear and contains particles.

Nordimet is for single use only. Any used syringe should be discarded.
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 Nordimet contains
The active substance is methotrexate. 1.0 ml of solution contains 25 mg methotrexate.
The other ingredients are sodium chloride, sodium hydroxide and water for injections.

The following syringes are available:
Pre-filled syringes of 0.3 ml containing 7.5 mg methotrexate.
Pre-filled syringes of 0.4 ml containing 10 mg methotrexate
Pre-filled syringes of 0.5 ml containing 12.5 mg methotrexate
Pre-filled syringes of 0.6 ml containing 15 mg methotrexate

Pre-filled syringes of 0.7 ml containing 17.5 mg methotrexate
Pre-filled syringes of 0.8 ml containing 20 mg methotrexate
Pre-filled syringes of 0.9 ml containing 22.5 mg methotrexate
Pre-filled syringes of 1.0 ml containing 25 mg methotrexate

What Nordimet looks like and contents of the pack
Nordimet pre-filled syringes contain a clear, yellow solution for injection.

Nordimet is available in packs containing 1 pre-filled syringe and two alcohol swabs and in multipacks comprising of 4 or 12 cartons, each containing 1 pre-filled syringe and two alcohol swabs.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Nordic Group B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

Manufacturer
CENEXI - Laboratoires Thissen
Rue de la Papyrée 2-6
B-1420 Braine-l'Alleud
Belgium

Sever Pharma Solutions AB
Agneslundsvagen 27
P.O. Box 590
SE-201 25 Malmo
Sweden

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http//www.ema.europa.eu.