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EPAR summary for the public

Busilvex

busulfan

This is a summary of the European public assessment report (EPAR) for Busilvex. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Busilvex.

What is Busilvex?

Busilvex is a concentrate to be made up into a solution for infusion (drip into a vein). It contains the active substance busulfan.

What is Busilvex used for?

Busilvex is used in adults and children as part of a 'conditioning' (preparative) treatment before transplantation of haematopoietic progenitor cells (the cells that make blood cells). This type of transplant is used in patients who need to replace their blood-making cells, because they have a blood disorder (such as a rare type of anaemia) or a cancer of the blood.

For a conventional conditioning treatment, Busilvex is given before treatment with a second medicine, cyclophosphamide, in adults, and either cyclophosphamide or an alternative medicine, melphalan, in children. In adult patients who are eligible for a 'reduced-intensity' conditioning regimen, Busilvex is given right after treatment with another medicine, fludarabine.

The medicine can only be obtained with a prescription.

How is Busilvex used?

Busilvex should be used by a doctor who has experience in treatments given before transplantation.

When used in combination with cyclophosphamide or melphalan the recommended dose of Busilvex in adults is 0.8 mg per kilogram body weight. In children up to 17 years of age, the recommended dose

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of Busilvex varies between 0.8 and 1.2 mg per kilogram depending on the weight of the child. Busilvex is given as a central intravenous infusion (drip into a central vein in the chest). Each infusion lasts for two hours and it is given to the patient every six hours on four consecutive days before treatment with cyclophosphamide or melphalan and the transplant.

When used in combination with fludarabine, the recommended dose of Busilvex is 3.2 mg per kilogram given once a day as a three-hour infusion immediately after fludarabine, for 2 or 3 consecutive days.

Before receiving Busilvex, patients are given anticonvulsive medicines (to prevent seizures) and anti-emetic medicines (to prevent vomiting).

How does Busilvex work?

The active substance in Busilvex, busulfan, belongs to a group of medicines called 'alkylating agents'. These substances are 'cytotoxic'. This means that they kill cells, especially cells that develop rapidly, such as cancer or progenitor (or 'stem') cells (cells that make other types of cell). Busulfan is used before transplantation to destroy abnormal cells and the patient's existing haematopoietic progenitor cells. This is called 'myeloablation'. Cyclophosphamide, melphalan or fludarabine are used to suppress the immune system, so that the body's natural defences are decreased. This helps the transplanted cells to 'engraft' (when they start to grow and produce normal blood cells).

How has Busilvex been studied?

Busilvex in combination with cyclophosphamide or melphalan has been studied in patients, mainly with blood cancer, who needed transplantation of haematopoietic progenitor cells. There were two main studies involving 103 adults and one involving 55 children. The main measures of effectiveness were the number of patients with myeloablation and 'engraftment' (the time for the transplanted stem cells to begin growing and for white blood cells to return to higher levels).

Since Busilvex in combination with fludarabine has been used in clinical practice for many years, data from 7 studies (involving 731 patients) which looked at the effectiveness of Busilvex and fludarabine as 'reduced-intensity' conditioning treatment were presented.

What benefit has Busilvex shown during the studies?

When Busilvex was given in combination with cyclophosphamide or melphalan, all adults and children achieved myeloablation. On average, engraftment was reached in 10 days in adults and 11 days in children with 'autotransplantation' (when the patient receives their own cells, harvested and stored before the transplant). Engraftment was obtained in 13 days in adults and 21 days in children with 'allotransplantation' (when the patient receives cells from a donor).

The data from the published studies showed that Busilvex in combination with fludarabine was effective as a 'reduced-intensity' conditioning treatment, with complete engraftment achieved in 80 to 100% of patients.

What is the risk associated with Busilvex?

Apart from the decrease in blood cell counts, which is the intended effect of the medicine, the most serious side effects of Busilvex are infection, liver disorders including blocking of a liver vein, graft versus host disease (when the transplanted cells attack the body) and respiratory (lung) disorders.

Busilvex must not be used in women who are pregnant. Breast-feeding should be stopped when treatment with Busilvex is started. Busilvex can affect fertility in both sexes. Because of this, female

patients should not become pregnant during treatment and for up to six months afterwards, and male patients are advised not to father a child during and for up to six months after treatment with Busilvex.

For the full list of all side effects and restrictions with Busilvex, see the package leaflet.

Why has Busilvex been approved?

The CHMP concluded that the effectiveness of Busilvex in combination with cyclophosphamide and melphalan for conventional conditioning, and with fludarabine for reduced-intensity conditioning had been shown; Busilvex also provides an alternative to busulfan tablets, which have disadvantages such as the large number of tablets that need to be taken.

The Committee decided that Busilvex's benefits are greater than its risks in these settings and recommended that Busilvex be given marketing authorisation.

Other information about Busilvex

The European Commission granted a marketing authorisation valid throughout the EU for Busilvex on 9 July 2003.

The full EPAR for Busilvex can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Busilvex, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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