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EPAR summary for the public

MabThera

rituximab

This is a summary of the European public assessment report (EPAR) for MabThera. 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 MabThera.

What is MabThera and what is it used for?

MabThera is a medicine used to treat the following blood cancers and inflammatory conditions:

- follicular lymphoma and diffuse large B cell non-Hodgkin's lymphoma (two types of non-Hodgkin's lymphoma, a blood cancer)
- chronic lymphocytic leukaemia (CLL, another blood cancer affecting white blood cells)
- severe rheumatoid arthritis (an inflammatory condition of the joints)
- two inflammatory conditions of blood vessels known as granulomatosis with polyangiitis (GPA or Wegener's granulomatosis) and microscopic polyangiitis (MPA).

Depending on the condition it is used to treat, MabThera may be given on its own, or with chemotherapy, methotrexate or a corticosteroid. MabThera contains the active substance rituximab.

How is MabThera used?

MabThera is given as an infusion (drip) into a vein. Patients with blood cancers can switch to an injection given under the skin after they have received one full dose of the infusion.

Before each infusion or injection, the patient should be given an antihistamine (to prevent allergic reactions) and an anti-pyretic (a medicine for fever). In addition, the medicine should be given under the close supervision of an experienced healthcare professional and in an environment where facilities for resuscitating patients are immediately available.

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MabThera is available as a concentrate that is made up into the solution for infusion and as a ready-made solution for the injection under the skin. It can only be obtained with a prescription.

How does MabThera work?

The active substance in MabThera, rituximab, is a monoclonal antibody designed to recognise and attach to a protein called CD20 present on the surface of B-lymphocytes. When rituximab attaches to CD20, it causes the death of B-lymphocytes, which helps in lymphoma and CLL (where B-lymphocytes have become cancerous) and in rheumatoid arthritis (where B-lymphocytes are involved in joint inflammation). In GPA and MPA, destroying the B-lymphocytes lowers the production of antibodies thought to play an important role in attacking the blood vessels and causing inflammation.

What benefits of MabThera have been shown in studies?

Studies show MabThera to be effective in treating all the conditions for which it is approved. Some results from the main studies on the benefits of MabThera are described below:

- In a follicular lymphoma study involving 322 patients, patients receiving MabThera in addition to chemotherapy lived for an average of 25.9 months without the disease coming back, compared with 6.7 months in those receiving chemotherapy alone.
- In a studies of MabThera given on its own (203 patients), 48% of the patients with follicular lymphoma who had failed previous treatment responded to MabThera.
- In a maintenance study in patients whose follicular lymphoma had come back after previous treatment, patients who received MabThera alone lived for an average of 42.2 months without the disease getting worse, compared with 14.3 months in patients who did not receive the medicine. A maintenance study in previously untreated patients showed the likelihood for the disease to get worse was reduced by 50% for patients who received MabThera.
- In a study of 399 patients with diffuse large B-cell lymphoma, patients adding MabThera to chemotherapy lived for an average of 35 months without the disease getting worse or the need for a change in treatment, compared with 13 months in those receiving chemotherapy alone.
- In a study of 817 patients with CLL, patients who had not been treated before lived for an average of 39.8 months without their disease getting worse when they received MabThera in addition to chemotherapy, compared with 32.2 months in patients receiving chemotherapy alone. In patients whose disease had come back after previous treatment, those receiving MabThera lived for 30.6 months without their disease getting worse, compared with 20.6 months in those receiving chemotherapy alone.
- In a study of 517 patients with rheumatoid arthritis, MabThera was more effective than placebo: 51% of the patients receiving MabThera had an improvement in symptoms, compared with 18% of the patients receiving placebo.
- In a study of 198 patients with GPA or MPA, 64% of patients given MabThera were in complete remission after six months, compared with 55% given cyclophosphamide, a comparator medicine.

What is the risk associated with MabThera?

The most common side effects with Mabthera intravenous infusions are reactions related to the infusion (such as fever, chills and shivering) while most common serious side effects are infusion reactions, infections and heart-related problems. Similar side effects are seen when Mabthera is

injected under the skin, with the exception of reactions around the injections site (pain, swelling and rash), which occur more frequently with the skin injections. For the full list of side effects reported with MabThera, see the package leaflet.

MabThera must not be used in people who are hypersensitive (allergic) to rituximab, mouse proteins or any of the other ingredients or in patients with a severe infection or a severely weakened immune system. The formulation injected under the skin must also not be used in patients who are allergic to a substance called hyaluronidase.

Patients with rheumatoid arthritis, GPA or MPA must not receive MabThera if they have severe heart problems.

Why has MabThera been approved?

The Committee for Medicinal Products for Human Use (CHMP) decided that MabThera's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of MabThera?

The company marketing MabThera will provide doctors and patients using the medicine for rheumatoid arthritis with educational material on the risk of infection including of a rare severe infection known as progressive multifocal leukoencephalopathy (PML). These patients are also to receive an alert card, which they are to carry at all times, instructing them to contact their doctor immediately if they experience symptoms of infection.

All doctors administering MabThera under the skin will also receive educational material to minimise the risk of improper use or errors.

In addition, the company that markets MabThera will also submit reports from studies on the long-term safety of MabThera.

Finally, recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of MabThera have been included in the summary of product characteristics and the package leaflet.

Other information about MabThera

The European Commission granted a marketing authorisation valid throughout the European Union for MabThera on 2 June 1998.

The full EPAR for MabThera 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 MabThera, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 06-2016.