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Ceplene (*histamine dihydrochloride*)

An overview of Ceplene and why it is authorised in the EU

What is Ceplene and what is it used for?

Ceplene is a medicine used in combination with interleukin-2 (a cancer medicine) as maintenance treatment in adults with acute myeloid leukaemia (AML), a type of cancer affecting the white blood cells. It is used during the patients' first 'remission' (a period without symptoms of the disease after the first course of treatment).

AML is rare, and Ceplene was designated an 'orphan medicine' (a medicine used in rare diseases) on 11 April 2005. Further information on the orphan designation can be found here: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

Ceplene contains the active substance histamine dihydrochloride.

How is Ceplene used?

Ceplene can only be obtained with a prescription and should be given under the supervision of a doctor who has experience in the treatment of AML.

It is available as a solution for injection under the skin. The recommended dose of Ceplene is one injection twice a day, one to three minutes after an interleukin-2 injection. Ceplene and interleukin-2 are given for 10 cycles. A cycle lasts 3 weeks. Between each cycle there should be a treatment-free period of 3 weeks. Each Ceplene injection must be given slowly over five to 15 minutes, in a different site from the interleukin-2 injection, and preferably in the thigh or abdomen (belly). Patients can inject themselves once they have been trained appropriately.

When Ceplene is first given, the patient's blood pressure, heart rate and lung function must be checked. Depending on the patient's response to treatment and side effects, the treatment may have to be suspended or the dose adjusted.

For more information about using Ceplene, see the package leaflet or contact your doctor or pharmacist.

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How does Ceplene work?

The active substance in Ceplene, histamine dihydrochloride, is an immune modulator. This means that it changes the activity of the immune system (the body's natural defences). Histamine is a substance occurring naturally in the body that is involved in many processes. In the treatment of AML, it is thought to work by protecting immune system cells from damage. This improves the effectiveness of interleukin-2, a medicine that stimulates the immune system to attack cancerous cells. When Ceplene is given with interleukin-2, it helps the immune system to kill the leukaemia cells that may remain in the body during remission. This can increase the length of time the patient stays in remission.

What benefit of Ceplene have been shown in studies?

The effectiveness of Ceplene has been studied in one main study involving 320 adults with AML who were in remission following leukaemia treatment. Ceplene was given in combination with interleukin-2 and compared with no treatment.

For patients who were into their first remission the combination of Ceplene and interleukin-2 was more effective than no treatment in increasing the time until AML came back or the patient died from any cause: the average time without disease increased from 291 days with no treatment to 450 days after treatment with Ceplene and interleukin-2. No effect of Ceplene and interleukin-2 was seen in patients in second or later remission.

What are the risks associated with Ceplene?

The most common side effects with Ceplene (seen in more than 1 patient in 10) are flushing (reddening), headache, tiredness, fever and inflammation or redness at the injection site. For the full list of side effects of Ceplene, see the package leaflet.

Ceplene must not be used in patients who have severe heart problems or in women who are pregnant or breastfeeding. It must also not be used in patients who have received a bone marrow transplant from a donor, or who are taking steroids (medicines used to reduce or prevent inflammation) given systemically (given by mouth or by injection), clonidine (used to reduce high blood pressure) or histamine H2 blockers (used to treat stomach ulcers, indigestion or heartburn). For the full list of restrictions, see the package leaflet.

Why has Ceplene been approved?

The European Medicines Agency decided that Ceplene's benefits are greater than its risks and it can be authorised for use in the EU.

Ceplene has been authorised under 'exceptional circumstances'. This is because it has not been possible to obtain complete information about Ceplene due to the rarity of the disease. Every year, the Agency will review any new information that may become available and this summary will be updated as necessary.

What information is still awaited for Ceplene?

The company that markets Ceplene will provide yearly updates on the safety and effectiveness of Ceplene in combination with interleukin-2 in AML patients in first remission.

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

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

As for all medicines, data on the use of Ceplene are continuously monitored. Side effects reported with Ceplene are carefully evaluated and any necessary action taken to protect patients.

Other information about Ceplene

Ceplene received a marketing authorisation valid throughout the EU on 7 October 2008.

Further information on Ceplene can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

This overview was last updated in 07-2018.