European Medicines Agency

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EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

CEPLENE

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis of the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Ceplene?
Ceplene is a solution for injection that contains the active substance histamine dihydrochloride (0.5 mg/0.5 ml).

What is Ceplene used for?
Ceplene is used in combination with interleukin-2 (an anticancer 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). The effectiveness of Ceplene has not been fully demonstrated in patients older than 60 years of age.
Because the number of people with AML is low, the disease is rare, and Ceplene was designated as an 'orphan medicine' (a medicine used in rare disease) on 11 April 2005.
The medicine can only be obtained with a prescription.

How is Ceplene used?
Ceplene should be given under the supervision of a doctor who has experience in the treatment of AML. The recommended dose of Ceplene is a 0.5-mg injection under the skin, twice a day, one to three minutes after an interleukin-2 injection. Ceplene and interleukin-2 are given for 10 cycles. The first three cycles consist of three weeks of treatment, followed by a three-week rest period. The following seven cycles consist of three weeks of treatment, followed by a six-week rest period.
When Ceplene is first given, the patient's blood pressure, heart rate and lung function must be monitored. Depending on the patient's response to treatment and side effects, the treatment may be suspended or the dose adjusted.
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 (tummy). Patients can inject themselves once they have been trained appropriately.
Ceplene should be used with caution in patients who have severe problems with their kidneys or moderate to severe problems with their liver. Ceplene is not recommended for use in patients below 18 years of age because of a lack of information on safety and effectiveness in this age group.

How does Ceplene work?
The active substance in Ceplene, histamine dihydrochloride, is an immune modulator. This means that it alters the activity of the immune system (the body's natural defences). Histamine is a naturally-occurring substance 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

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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 until AML comes back.

How has Ceplene been studied?
The effects of Ceplene were first tested in experimental models before being studied in humans. Because histamine is a known substance, the company also presented data from the published literature.
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. The main measure of effectiveness was the length of time until the disease came back or the patient died.

What benefit has Ceplene shown during the studies?
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: in the patients in their first complete remission, 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 is the risk associated with Ceplene?
The most common side effects with Ceplene (seen in more than 1 patient in 10) are eosinophilia (an increase in eosinophil levels, a type of white blood cell), thrombocytopenia (low blood platelet counts), headache, dizziness, dysgeusia (a bitter or unusual taste in the mouth), tachycardia (rapid heart beat), flushing (reddening), hypotension (low blood pressure), cough, dyspnoea (shortness of breath), nausea (feeling sick), dyspepsia (indigestion), diarrhoea, rash, arthralgia (pain in the joints), myalgia (muscle pain), pyrexia (fever), rigors (shaking chills), fatigue (tiredness), flu-like symptoms, feeling hot and injection site reaction (redness, bruising, pain and inflammation). For the full list of all side effects reported with Ceplene, see the Package Leaflet.
Ceplene should not be used in people who may be hypersensitive (allergic) to histamine dihydrochloride or any of the other ingredients. It must not be used in patients who have severe heart problems or in women who are pregnant or breast-feeding. It must also not be used in patients who have received a bone marrow transplant from a donor, or who are taking steroids (used to reduce or prevent inflammation), clonidine (used to reduce high blood pressure) or histamine H_2 blockers (used to treat stomach ulcers, indigestion or heartburn).

Why has Ceplene been approved?
The Committee for Medicinal Products for Human Use (CHMP) decided that Ceplene's benefits are greater than its risks as maintenance treatment in adults with AML when used in combination with interleukin-2. The Committee recommended that Ceplene be given marketing authorisation.
Ceplene has been authorised under 'Exceptional Circumstances', because, as the disease is rare, it has not been possible to obtain complete information on the medicine. Every year, the EMEA will review any new data that may become available and this summary will be updated as necessary.

What information is still awaited for Ceplene?
The company will carry out further studies to look in more detail at the effectiveness of the combination of Ceplene and interleukin-2 and at how the combination works.

Other information about Ceplene:
The European Commission granted a marketing authorisation valid throughout the European Union for Ceplene to EpiCept GmbH on 7 October 2008.

The summary of opinion of the Committee for Orphan Medicinal Products for Ceplene is available here.
The full EPAR for Ceplene can be found here.

This summary was last updated in 08-2008.