



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/381169/2015
EMA/H/C/000752

EPAR summary for the public

Atriance

nelarabine

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

What is Atriance?

Atriance is a cancer medicine that contains the active substance nelarabine. It is available as a solution for infusion (drip) into a vein.

What is Atriance used for?

Atriance is used to treat patients with T-cell acute lymphoblastic leukaemia (T-ALL) or T-cell lymphoblastic lymphoma (T-LBL). These are types of cancer where T-lymphoblasts (a type of immature white blood cell) multiply too quickly. In T-ALL the abnormal cells are mainly in the blood and bone marrow, and in T-LBL they are mainly in the lymphatic system (lymph nodes or thymus gland). Atriance is used when the cancer has not responded to, or has stopped responding to, at least two types of chemotherapy.

Because the number of patients with these diseases is low, the diseases are considered 'rare', and Atriance was designated an 'orphan medicine' (a medicine used in rare diseases) on 16 June 2005.

The medicine can only be obtained with a prescription.

How is Atriance used?

Atriance is given by drip into a vein under the supervision of a doctor who has experience in the use of these types of medicine. The dose and frequency of infusion depend on the patient's age and body surface area. In adults and adolescents aged 16 years and over, the recommended starting dose is 1,500 mg per square metre of body surface area (calculated using the patient's height and weight),



given over two hours on days one, three and five, repeated every 21 days. Patients aged under 16 years receive a dose of 650 mg per square metre given over one hour on five consecutive days, repeated every 21 days. This schedule can also be used in patients aged 16 to 21 years. Treatment should be stopped if the patient develops serious side effects affecting the brain or nervous system. Treatment may be delayed if other side effects occur.

Patients receiving Atriance should be monitored regularly for changes in blood cell counts and should receive adequate hydration if they are at risk of tumour lysis syndrome (a complication due to the breakdown of cancer cells).

How does Atriance work?

The active substance in Atriance, nelabarine, is a cytotoxic, a medicine that kills cells that are dividing, such as cancer cells. It belongs to the group of cancer medicines called 'antimetabolites'.

Nelarabine is converted within cells into an analogue of guanine, one of the fundamental chemicals that make up DNA. In the body, this analogue takes the place of guanine and interferes with the enzymes involved in making new DNA, DNA polymerases. This stops the production of DNA and thus slows down the growth and multiplication of cells. Because the guanine analogue accumulates in T-cells and lasts longer in these cells, Atriance slows down the growth and multiplication of the cells involved in T-ALL and T-LBL.

How has Atriance been studied?

Atriance has been studied in two main studies of patients with T-ALL and T-LBL whose cancer had stopped responding to one or more previous cancer treatments. The first study involved a total of 70 children and young adults aged below 21 years, and the second involved a total of 40 adults and adolescents aged over 16 years. Around half of the patients had failed two or more previous treatments. In both studies, the patients were treated with Atriance, but its effects were not compared with those of any other medicine. The main measure of effectiveness was the proportion of patients who responded to treatment, defined as no evidence of disease and recovery of blood cell counts, within a month of starting Atriance treatment.

What benefit has Atriance shown during the studies?

Atriance was shown to be effective in a proportion of the patients in both studies. In the first study, among the 39 children and young adults whose cancer had not responded to two or more previous treatments, five (13%) had a complete response to treatment after a month, with no evidence of disease and normal blood counts. In the second study, among the 28 adults and adolescents with cancer that had not responded to two or more previous treatments, five (18%) had a complete response to treatment. In both studies, more patients had a partial response to Atriance treatment, with blood counts returning towards normal levels.

What is the risk associated with Atriance?

The most common side effects with Atriance in adults (seen in more than 1 patient in 10) are infection, febrile neutropenia (low white blood cell counts with fever), neutropenia (low white blood cell counts), thrombocytopenia (low platelet counts), anaemia (low red blood cell counts), somnolence (sleepiness), peripheral neuropathy (damage to the nerves in the extremities), hypoaesthesia (a reduced sense of touch), paraesthesia (unusual sensations like pins and needles), dizziness, headache, dyspnoea

(breathlessness), cough, diarrhoea, vomiting, constipation, nausea (feeling sick), myalgia (muscle pain), oedema (swelling), peripheral oedema (swelling in ankles and feet), pyrexia (fever), pain, fatigue (tiredness) and asthenia (weakness). Most of these side effects were also very common in children.

Severe side effects affecting the brain and nervous system have also been reported in patients taking Atriance, including somnolence, convulsions, and peripheral neuropathy causing numbness, unusual sensations, weakness and even paralysis. Patients should be monitored closely for these side effects and treatment stopped if necessary.

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

Why has Atriance been approved?

The CHMP noted that, due to the small number of patients with these diseases, the information to support the approval of Atriance is limited, but it agreed that the medicine could allow some patients to go on to receive bone-marrow transplantation, increasing their chances of survival. Therefore, the Committee decided that Atriance's benefits are greater than its risks and recommended that it be given marketing authorisation.

Atriance has been authorised under 'exceptional circumstances'. This means that because the diseases are rare, it has not been possible to obtain complete information about Atriance. Every year, the European Medicines Agency will review any new information that may become available and this summary will be updated as necessary.

What information is still awaited for Atriance?

Since Atriance has been approved under exceptional circumstances, the company that markets Atriance will provide further information on the safety of Atriance in children and young adults from a study of Atriance taken in combination with other cancer medicines.

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

A risk management plan has been developed to ensure that Atriance is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Atriance, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Atriance

The European Commission granted a marketing authorisation valid throughout the European Union for Atriance on 22 August 2007.

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

The summary of the opinion of the Committee for Orphan Medicinal Products for Atriance can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/Rare_disease_designation.

This summary was last updated in 06-2015.