**Package leaflet: Information for the patient**

**Atriance 5 mg/ml solution for infusion**

nelarabine

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**:



## 1. What Atriance is and what it is used for

Atriance contains nelarabine which belongs to a group of medicines known as *antineoplastic agents,* used in chemotherapy to kill some types of cancer cells.

**Atriance is used to treat patients with:**
- a type of leukaemia, called T-cell acute lymphoblastic leukaemia. Leukaemia causes an abnormal increase in the number of white blood cells. The abnormal high number of white blood cells can appear in the blood and other parts of the body. The type of leukaemia relates to the type of white blood cell mainly involved. In this case, its cells are called lymphoblasts.
- a type of lymphoma, called T-cell lymphoblastic lymphoma. This lymphoma is caused by a mass of lymphoblasts, a type of white blood cell.

If you have any questions about your illness, talk to your doctor

## 2. What you need to know before you are given Atriance

**You (or your child, if he/she is being treated) must not receive Atriance**
- if you (or your child, if he/she is being treated) are allergic to nelarabine or any of the other ingredients of this medicine (listed in section 6).

**Warnings and precautions**
Severe nervous system side effects have been reported with the use of Atriance. Symptoms may be mental (e.g. tiredness) or physical (e.g. convulsions, feelings of numbness or tingling, weakness and paralysis). **Your doctor will check for these symptoms regularly during treatment (see also section 4, "Possible side effects").**

Your doctor also needs to know the following before you are given this medicine:
- **if you (or your child, if he/she is being treated) have any kidney or liver problems**. Your dose of Atriance may need to be adjusted.
- **if you (or your child, if he/she is being treated) have recently been, or plan to be vaccinated** with a live vaccine (for example polio, varicella, typhoid).
- **if you (or your child, if he/she is being treated) have any blood problems** (for example anaemia).

**Blood tests during treatment**
Your doctor should perform blood tests regularly during treatment to check for blood problems that have been associated with the use of Atriance.

**Elderly**
If you are an elderly person, you could be more sensitive to nervous system side effects (see the list above under "Warnings and precautions"). Your doctor will check for these symptoms regularly during treatment.

**Tell your doctor if any of these apply to you.**

**Other medicines and Atriance**
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines**.** This includes any herbal products or medicines you have bought without a prescription

Remember to tell your doctor if you start to take any other medicines while you are on Atriance.

**Pregnancy, breast-feeding and fertility**
Atriance is not recommended for pregnant women. It may harm a baby if conceived before, during or soon after treatment. Consideration to appropriate birth control is recommended to be discussed with your doctor. Do not try and become pregnant/father a child until your doctor advises you it is safe to do so.

Male patients, who may wish to father a child, should ask their doctor for family planning advice or treatment. If pregnancy occurs during treatment with Atriance, you must tell your doctor immediately.

It is not known whether Atriance is passed on through breast milk. Breast-feeding must be discontinued while you are taking Atriance. Ask your doctor for advice before taking any medicine.

**Driving and using machines**
Atriance can make people feel drowsy or sleepy, both during and for some days after treatment. If you feel tired or weak, do not drive, and do not use any tools or machines.

**Atriance contains sodium**
This medicine contains 88.51 mg (3.85 mmol) sodium (main component of cooking/table salt) per vial (50 ml). This is equivalent to 4.4% of the recommended maximum daily dietary intake of sodium for an adult.

## 3. How Atriance is given

The dose of Atriance you are given will be based on:
- **your/your child's (if he/she is being treated) body surface area** (which will be calculated by your doctor based on your height and weight).
- **the results of blood tests** carried out before treatment

**Adults and adolescents (aged 16 years and older)**
**The usual dose** is 1,500 mg/m$^2$ of body surface area per day.

**A doctor or nurse** will give you the dose of Atriance as an infusion (a drip). It is usually dripped into your arm over a period of about 2 hours.

**You will have an infusion (a drip) once a day on days 1, 3 and 5 of treatment**. This pattern of treatment will normally be repeated every three weeks. This treatment may vary, depending on the results of your regular blood tests. Your doctor will decide how many treatment cycles are required.

**Children and adolescents (aged 21 years and younger)**
The recommended dose is 650 mg/m$^2$ of body surface area per day.

**A doctor or nurse** will give you/your child (if he/she is being treated) a suitable dose of Atriance as an infusion (a drip). It is usually dripped into your arm over a period of about 1 hour.

**You/your child (if he/she is being treated) will have an infusion (a drip) once a day for 5 days**. This pattern of treatment will normally be repeated every three weeks. This treatment may vary, depending on the results of regular blood tests. Your doctor will decide how many treatment cycles are required.

**Stopping treatment with Atriance**
Your doctor will decide when to stop the treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The majority of side effects reported with Atriance were seen in adults, children and adolescents. Some of the side effects were reported more often in adult patients. There is no known reason for this.

If you have any concerns, discuss them with your doctor.

**Most serious side effects**

These may affect **more than 1 in 10 people** treated with Atriance.
- **Signs of infection**. Atriance may reduce the number of white blood cells and lower your resistance to infection (including pneumonia). This can even be life threatening. Signs of an infection include:
  - fever
  - serious deterioration of your general condition
  - local symptoms such as sore throat, sore mouth or urinary problems (for example, a burning sensation when urinating, which may be a urinary infection)

**Tell your doctor immediately** if you get any of these. A blood test will be taken to check possible reduction of white blood cells.

**Other very common side effects**
These may affect **more than 1 in 10 people** treated with Atriance
- Changes in the sense of feeling in hands or feet, muscle weakness appearing as difficulty getting up from a chair, or difficulty walking (*peripheral neuropathy*); reduced sensitivity to light touch, or pain; abnormal sensations such as burning and, prickling, a sensation of something crawling on the skin.
- Feeling generally weak and tired (*temporary anaemia*). In some cases you may need a blood transfusion.
- Unusual bruising or bleeding, caused by a decrease in the number of clotting cells in the blood. This can lead to severe bleeding from relatively small injuries such as a small cut. Rarely, it can lead to even more severe bleeding (*haemorrhage*). Talk to your doctor for advice on how to

minimize the risk of bleeding.
- Feeling drowsy and sleepy; headache; dizziness.
- Shortness of breath, difficult or laboured breathing; cough.
- Feeling of an upset stomach (*nausea*); being sick/throwing up (*vomiting*); diarrhoea; constipation
- Muscle pain.
- Swelling of parts of the body due to accumulation of abnormal amounts of fluid (*oedema*).
- High body temperature (*fever*); tiredness; feeling weak/loss of strength.

**Tell a doctor** if any of these becomes troublesome.

**Common side effects**

These may affect **up to 1 in 10 people** treated with Atriance:
- Violent, uncontrollable muscular contractions often accompanied by unconsciousness that can be due to an epileptic attack (*seizures*).
- Clumsiness and lack of coordination affecting balance, walking, limb or eye movements, or speech.
- Unintentional rhythmic shaking of one or more limbs (*tremors*).
- Muscle weakness (possibly associated with *peripheral neuropathy* – see above), joint pain, back pain; pains in hands and feet including a sensation of pins and needles sensation and numbness.
- Lowered blood pressure.
- Weight loss and loss of appetite (*anorexia*); stomach pains; sore mouth, mouth ulcers or inflammation.
- Problems with memory, feeling disoriented; blurred vision; altered or loss of sense of taste (*dysgeusia*).
- Build up of fluid around the lungs leading to chest pain and difficulty in breathing (*pleural effusion*); wheezing
- Increased amounts of bilirubin in your blood, which may cause yellowing of the skin and may make you feel lethargic.
- Increases in blood levels of liver enzymes.
- Increases in blood creatinine levels (a sign of kidney problems, which might lead less frequent urination).
- The release of tumour cell contents (*tumour lysis syndrome*), which may put extra stress on your body. Initial symptoms including nausea and vomiting, shortness of breath, an irregular heartbeat, clouding of urine, lethargy and/or joint discomfort. If this does occur, it is most likely to occur at the first dose. Your doctor will take appropriate precautions to minimise the risk of this.
- Low blood levels of some substances:
  - low calcium levels, which may cause muscle cramps, abdominal cramps or spasms
  - low magnesium levels, which may cause muscle weakness, confusion, "jerky" movements, high blood pressure, irregular heart rhythms and decreased reflexes with severely low blood magnesium levels.
  - low potassium levels may cause a feeling of weakness
  - low glucose levels, which may cause nausea, sweating, weakness, faintness, confusion or hallucinations.

**Tell a doctor** if any of these becomes troublesome.

**Rare side effects**

These may affect **up to 1 in 1,000 people** treated with Atriance
- Serious disease that destroys skeletal muscle characterized by the presence of myoglobin (a breakdown product of muscle cells) in the urine (*Rhabdomyolysis*), increase in blood creatine phosphokinase.

**Tell a doctor** if any of these becomes troublesome.

**Reporting of side effects**
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects

not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Atriance

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial.

This medicine does not require any special storage conditions.

Atriance is stable for up to 8 hours at up to 30°C once the vial is opened.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What Atriance contains**
- The active substance is nelarabine. Each ml of Atriance solution for infusion contains 5 mg of nelarabine. Each vial contains 250 mg of nelarabine.
- The other ingredients are sodium chloride, water for injections, hydrochloric acid, sodium hydroxide (see section 2 “Atriance contains sodium”).

**What Atriance looks like and contents of the pack**
Atriance solution for infusion is a clear, colourless solution. It is provided in clear glass vials with a rubber stopper and sealed with an aluminium cap.

Each vial contains 50 ml.

Atriance is supplied in packs of 1 vial or 6 vials.

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**This leaflet was last approved in**

This medicine has been authorised under “exceptional circumstances”. This means that because of the rarity of this disease it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on the medicine every year and this leaflet will be updated as necessary.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

The following information is intended for medical or healthcare professionals only:

INSTRUCTIONS ON HOW TO STORE AND DISPOSE OF ATRIANCE

**Storage of Atriance solution for infusion**

This medicinal product does not require any special storage conditions.

Atriance is stable for up to 8 hours at up to 30ºC once the vial is opened.

**Instructions for handling and disposal of Atriance**

The normal procedures for proper handling and disposal of anti-tumour medicinal products should be adopted, namely:

- Staff should be trained in how to handle and transfer the medicinal product.
- Pregnant staff should be excluded from working with this medicinal product.
- Personnel handling this medicinal product during handling/transfer should wear protective clothing including mask, goggles and gloves.
- All items for administration or cleaning, including gloves, should be placed in high-risk, waste disposal bags for high-temperature incineration. Any liquid waste from the preparation of the nelarabine solution for infusion may be flushed with large amounts of water.
- Accidental contact with the skin or eyes should be treated immediately with copious amounts of water.