

Package leaflet: Information for the user

Xaluprine 20 mg/ml oral suspension mercaptopurine

Read all of this leaflet carefully before you start taking 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, pharmacist or nurse.
- 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Xaluprine is and what it is used for
2. What you need to know before you take Xaluprine
3. How to take Xaluprine
4. Possible side effects
5. How to store Xaluprine
6. Contents of the pack and other information

1. What Xaluprine is and what it is used for

Xaluprine contains mercaptopurine. This belongs to a group of medicines called cytotoxics (also called chemotherapy).

Xaluprine is used for acute lymphoblastic leukaemia (also called acute lymphocytic leukaemia or ALL). This is a fast-growing disease which increases the number of new white blood cells. These new white blood cells are immature (not fully formed) and unable to grow and work properly. They therefore cannot fight infections and may cause bleeding.

Ask your doctor if you would like more explanation about this disease.

2. What you need to know before you take Xaluprine

- **Do not take Xaluprine** if you are allergic to mercaptopurine or any of the other ingredients of this medicine (listed in section 6).
- **Do not get vaccinated** with yellow fever vaccine whilst you are taking Xaluprine because it may be fatal.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Xaluprine

- if you have been vaccinated with yellow fever vaccine
- if you have kidney or liver problems, as your doctor will need to check that they are working properly.
- if you have a condition where your body produces too little of the enzyme called TPMT (thiopurine methyltransferase), as your doctor may need to adjust the dose.
- if you are planning to have a baby. This applies to both men and women. Xaluprine may harm your sperm or eggs (see 'Pregnancy, breast-feeding and fertility' below).

If you are receiving immunosuppressive therapy, taking Xaluprine could put you at greater risk of:

- tumours, including skin cancer. Therefore, when taking Xaluprine, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor
- lymphoproliferative disorders
 - o treatment with Xaluprine increases your risk of getting a type of cancer called lymphoproliferative disorder. With treatment regimen containing multiple immunosuppressants (including thiopurines), this may lead to death.
 - o A combination of multiple immunosuppressants, given concomitantly increases the risk of disorders of the lymph system due to a viral infection (Epstein-Barr virus (EBV)-associated lymphoproliferative disorders).

Taking Xaluprine could put you at greater risk of:

- developing a serious condition called Macrophage Activation Syndrome (excessive activation of white blood cells associated with inflammation), which usually occurs in people who have certain types of arthritis.

Some patients with inflammatory bowel disease who have received 6-mercaptopurine have developed a rare and aggressive type of cancer called Hepatosplenic T-cell Lymphoma (see section 4, Possible side effects).

Infections

When you are treated with Xaluprine the risk of viral, fungal and bacterial infections is increased and the infections may be more serious. See also section 4.

Tell your doctor before starting treatment whether or not you have had chickenpox, shingles or hepatitis B (a liver disease caused by a virus).

NUDT15-gene mutation

If you have an inherited mutation in the NUDT15-gene (a gene which is involved in the break-down of Xaluprine in the body), you have a higher risk of infections and hair loss and your doctor may in this case give you a lower dose.

Avoid contact of Xaluprine with your skin, eyes or nose. If you accidentally get some in your eyes or nose, flush the area with water.

If you are not sure if any of the above applies to you, talk to your doctor or pharmacist before taking Xaluprine.

Children and adolescents

Low blood sugar has sometimes been seen in children, mainly in children under the age of six or with a low body mass index. Talk to your child's doctor if this happens.

Other medicines and Xaluprine

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor, nurse or pharmacist if you are taking any of the following:

- other cytotoxic medicines (chemotherapy) - when used with Xaluprine there is a greater chance of side effects, such as anaemia
- allopurinol or febuxostat (used to treat gout)
- oral anticoagulants (used to thin the blood)
- olsalazine or mesalazine (used for a bowel disorder called ulcerative colitis)
- sulfasalazine (used for rheumatoid arthritis or ulcerative colitis).
- anti-epileptic medicines such as phenytoin, carbamazepine. Blood levels of anti-epileptic medicines may need to be monitored and doses adjusted if necessary.

Having vaccines while you are taking Xaluprine

If you are going to have a vaccination it is important to speak to your doctor or nurse before you have it. Vaccination with live vaccines (like polio, measles, mumps and rubella) is not recommended, as these vaccines may give you an infection if you have them whilst you are taking Xaluprine.

Xaluprine with food and drink

Xaluprine may be taken with food or on an empty stomach. However, the choice of method should be consistent from day to day.

Do not take Xaluprine at the same time as milk or dairy products, as they can make the medicine less effective. Xaluprine should be taken at least 1 hour before or 2 hours after milk or dairy products.

Pregnancy, breast-feeding and fertility

Do not take Xaluprine if you are planning to have a baby without first speaking to your doctor for advice. This applies to both men and women. Xaluprine may harm your sperm or eggs. Reliable contraception must be used to avoid pregnancy whilst you or your partner are taking Xaluprine. Both men and women should continue to use effective contraception for at least 3 months after stopping treatment. If you are already pregnant, you must talk to your doctor before taking Xaluprine.

Xaluprine should not be handled by women who are or planning to be pregnant or breast-feeding.

Do not breast-feed while taking Xaluprine. Ask your doctor, pharmacist or midwife for advice.

Driving and using machines

It is not expected that Xaluprine will affect your ability to drive or use machines but no studies have been done to confirm this.

Xaluprine contains aspartame, sodium methyl parahydroxybenzoate (E219), sodium ethyl parahydroxybenzoate (E215) and sucrose

This medicine contains 3 mg aspartame (E951) in each 1 ml. Aspartame is a source of phenylalanine. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

Xaluprine also contains sodium methyl parahydroxybenzoate (E219) and sodium ethyl parahydroxybenzoate (E215) which may cause allergic reactions (possibly delayed).

Xaluprine contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product. May be harmful to the teeth.

3. How to take Xaluprine

Xaluprine should only be given to you by a specialist doctor who is experienced in treating blood problems.

- When you take Xaluprine your doctor will take regular blood tests. This is to check the number and type of cells in your blood and to ensure your liver is working correctly.
- Your doctor may also ask for other blood and urine tests to monitor your uric acid levels. Uric acid is a natural body chemical, levels of which can rise while taking Xaluprine.
- Your doctor may sometimes change your dose of Xaluprine as a result of these tests.

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. The usual starting dose for adults, adolescents and children is between 25-75 mg/m² body surface area each day. Your doctor will prescribe the correct dose for you. Sometimes the doctor may change your dose of Xaluprine for example as a result of different tests. If you are not sure how much medicine to take, always ask your doctor or nurse.

It is important to take Xaluprine in the evening to make the medicine more effective.

You can take your medicine with food or on an empty stomach but the choice of method should be consistent from day to day. You should take your medicine at least 1 hour before or 2 hours after having milk or dairy products.

Your pack of Xaluprine contains a bottle of medicine, a cap, a bottle adaptor and two dosing syringes (a 1 ml syringe and a 5 ml syringe). Always use the syringes provided to take your medicine.

It is important that you use the correct dosing syringe for your medicine. Your doctor or pharmacist will advise which syringe to use depending on the dose that has been prescribed.

The **smaller** 1 ml syringe, marked from 0.1 ml to 1 ml, is for measuring doses of less than or equal to 1 ml. You should use this one if the total amount you have to take is less than or equal to 1 ml (each graduation of 0.1 ml contains 2 mg of mercaptopurine).

The **larger** 5 ml syringe, marked 1 ml to 5 ml, is for measuring doses of more than 1 ml. You should use this one if the total amount you have to take is more than 1 ml (each graduation of 0.2 ml contains 4 mg of mercaptopurine).

If you are a parent or care giver administering the medicine, wash your hands before and after administering a dose. Wipe up spillages immediately. To decrease the risk of exposure disposable gloves should be used when handling Xaluprine.

If Xaluprine comes into contact with skin, eyes or nose, it should be washed immediately and thoroughly with soap and water.

When you use the medicine follow the instructions below:



Figure 1

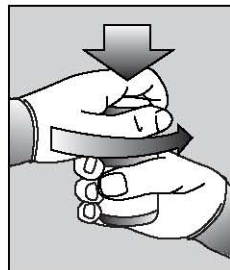


Figure 2

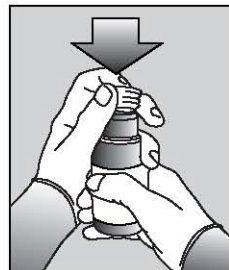


Figure 3

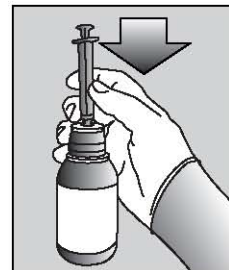


Figure 4

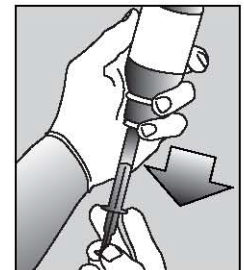


Figure 5

1. Put on disposable hand gloves before handling Xaluprine.
2. **Shake the bottle vigorously for at least 30 seconds** to ensure the medicine is well mixed (**figure 1**).
3. Remove the bottle cap (**figure 2**) and push the adaptor firmly into the top of the bottle and leave in place for future doses (**figure 3**).
4. Push the tip of the dosing syringe into the hole in the adaptor (**figure 4**). **Your doctor or pharmacist will advise you of the correct syringe to use, either the 1 ml or the 5 ml in order to give the correct dose.**
5. Turn the bottle upside down (**figure 5**).
6. Pull the plunger of the syringe back so that the medicine is drawn from the bottle into the syringe. Pull the plunger back to the point on the scale that corresponds to the dose prescribed (**figure 5**). If you are not sure about how much medicine to draw into the syringe, always ask your doctor or nurse for advice.
7. Turn the bottle back the right way up and carefully remove the syringe from the adaptor, holding it by the barrel rather than the plunger.
8. Gently put the tip of the syringe into your mouth and to the inside of your cheek.
9. Slowly and gently push the plunger down to gently squirt the medicine into the inside of your cheek and swallow it. **DO NOT** forcefully push down the plunger, or squirt the medicine to the back of your mouth or throat, as you may choke.

10. Remove the syringe from your mouth.
11. Swallow the dose of oral suspension then drink some water, making sure no medicine is left in your mouth.
12. Put the cap back on the bottle with the adaptor left in place. Ensure that the cap is tightly closed.
13. Wash the syringe with warm water and rinse well. Hold the syringe under water and move the plunger up and down several times to make sure the inside of the syringe is clean. Let the syringe air dry completely before you use that syringe again for dosing. Do not wipe dry. Store the syringe in a hygienic place with the medicine.

Repeat the above for each dose as instructed by your doctor or pharmacist.

If you take more Xaluprine than you should

If you take more Xaluprine than you should, tell your doctor or go to a hospital immediately. You may feel sick, vomit or have diarrhoea. Take the medicine pack and this leaflet with you.

If you forget to take Xaluprine

Tell your doctor. **Do not take a double dose to make up for a forgotten dose.**

If you stop taking Xaluprine

Do not stop taking your medicine unless your doctor tells you to or you may get a relapse of your condition.

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.

If you get any of the following side effects, talk to your specialist doctor or go to hospital immediately:

- Allergic reaction, the signs may include:
 - skin rashes
 - high temperature
 - joint pain
 - swollen face
 - skin nodules (erythema nodosum) (the frequency is unknown)
- Any signs of fever or infection (sore throat, sore mouth or urinary problems)
- Any **unexpected** bruising or bleeding, as this could mean that too few blood cells of a particular type are being produced
- If you **suddenly** feel unwell (even with a normal temperature) and have abdominal pain and sickness, as this could be a sign of an inflamed pancreas
- Any yellowing of the whites of the eyes or skin (jaundice)
- If you have diarrhoea

Talk to your doctor if you have any of the following side effects which may also happen with this medicine:

Very common (affects more than 1 in 10 people)

- a drop in the number of white blood cells and platelets (may show up in blood tests)

Common (affects less than 1 in 10 people)

- feeling or being sick (nausea or vomiting)
- liver damage - this may show up in blood tests
- a drop in red blood cells which may make you tired, weak or breathless (called anaemia)
- loss of appetite
- diarrhoea
- inflammation of the mouth (stomatitis)

Uncommon (affects less than 1 in 100 people)

- mouth ulcers
- inflamed pancreas
- joint pain
- skin rash
- fever
- permanent damage to the liver (hepatic necrosis)

Rare (affects less than 1 in 1,000 people)

- hair loss
- in men: temporary low sperm count
- swollen face
- various types of cancers including blood, lymph and skin cancers

Very rare (affects less than 1 in 10,000 people)

- a different type of leukaemia to that being treated
- ulcers in the intestines

Other side effects (the frequency is unknown)

- a rare type of cancer (hepatosplenic T-cell lymphoma), (see section 2, Warnings and Precautions).
- Sensitivity to sunlight causing skin reactions

Additional side effects in children and adolescents

Low blood sugar (hypoglycaemia) - the frequency is unknown.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Xaluprine

- Keep this medicine out of the sight and reach of children, preferably in a locked cupboard. Accidental ingestion can be lethal for children.
- Do not use this medicine after the expiry date which is stated on the carton and the bottle after 'EXP'. The expiry date refers to the last day of that month.
- Do not store above 25°C.

- Keep the bottle tightly closed to prevent spoilage of the medicine and reduce the risk of accidental spillage.
- After first opening of the bottle, discard any unused contents after 56 days.

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 Xaluprine contains

The active substance is mercaptopurine (as monohydrate). One ml of suspension contains 20 mg of mercaptopurine monohydrate.

The other ingredients are xanthan gum, aspartame (E951), concentrated raspberry juice, sucrose, sodium methyl parahydroxybenzoate (E219), sodium ethyl parahydroxybenzoate (E215), potassium sorbate (E202), sodium hydroxide and purified water (see section 2 Xaluprine contains aspartame, sodium methyl parahydroxybenzoate (E219), sodium ethyl parahydroxybenzoate (E215) and sucrose).

What Xaluprine looks like and contents of the pack

Xaluprine is a pink to brown oral suspension. It comes in glass bottles of 100 ml capped with a child-resistant closure. Each pack contains one bottle, a bottle adaptor and two dosing syringes (a syringe graduated to 1 ml and a syringe graduated to 5 ml). Your doctor or pharmacist will advise which syringe to use depending on the dose that has been prescribed.

Marketing Authorisation Holder

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Manufacturer

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>