Package leaflet: Information for the user

Oncaspar 750 U/ml powder for solution for injection/infusion
pegaspargase

▼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 are given 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.
- 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 Oncaspar is and what it is used for

Oncaspar contains pegaspargase, which is an enzyme (asparaginase) that breaks down asparagine, an important building block of proteins without which cells cannot survive. Normal cells can make asparagine for themselves, while some cancer cells cannot. Oncaspar lowers asparagine level in blood cancer cells and stops the cancer cells growing.

Oncaspar is used to treat acute lymphoblastic leukaemia (ALL) in children from birth to 18 years and adults. ALL is a white blood cell cancer type in which certain immature white cells (named lymphoblasts) start growing out of control thus preventing the production of functional blood cells. Oncaspar is used together with other medicines.

2. What you need to know before you are given Oncaspar

Do not use Oncaspar
- if you are allergic to pegaspargase or to any of the other ingredients of this medicine (listed in section 6).
- if you have severe hepatic disease.
- if you ever had pancreatitis.
- if you ever had severe bleeding following asparaginase therapy.
- if you ever had blood clots following asparaginase therapy.

Tell your doctor if any of these conditions apply to you. If you are the parent of a child who is being treated with Oncaspar, please tell the doctor if any of them apply to your child.

Warnings and precautions
Talk to your doctor before you are given Oncaspar. This medicine may not be suitable for you:
- if you have had serious allergic reactions to other forms of asparaginase, for example itching, flushing or swelling of the airways, because major allergic reactions to Oncaspar can occur.
- if you suffer from a bleeding disorder or had serious blood clots.

- if you get a fever. This medicine may make you more susceptible to infections.
- if you have had poor liver function or are using other medicines which may harm the liver. When Oncaspar is used in combination with other cancer treatments, liver and central nervous system damage can occur.
- if you suffer abdominal pain. Inflammation of the pancreas, that in some cases caused death, can occur with Oncaspar treatment.

This medicine can lead to fluctuations in clotting factors and may increase the risk of bleeding and/or clotting.

If you are the parent of a child being treated with Oncaspar, tell the doctor if any of the above conditions apply to your child.

During treatment with Oncaspar
During Oncaspar administration you will be closely watched for an hour after the start of treatment for any signs of serious allergic reactions. Medical equipment to treat allergic reactions will be available nearby.

Additional monitoring tests
Blood and urine sugar levels, liver and pancreas function and other tests will be carried out regularly to monitor your health during and after treatment because this medicine can affect your blood and other organs.

Other medicines and Oncaspar
Tell your doctor if you are using, have recently used or might use any other medicines. This is important as Oncaspar may increase the side effects of other medicines through its effect on the liver which plays an important role in removing medicines from the body. In addition, it is especially important to tell your doctor if you are also using any of the following medicines:
- immunisation with live vaccines within three months of completing your leukaemia treatment. This will increase the risk of severe infections.
- vincristine, another cancer medicine. If used at the same time as Oncaspar there is an increased risk of side effects or allergic reactions.
- medicines which reduce the blood´s ability to clot such as anticoagulants (e.g., coumarin/warfarin and heparin), dipyridamole, acetylsalicylic acid or non-steroidal anti-inflammatory medicines (such as ibuprofen or naproxen). If used at the same time as Oncaspar, there is a higher risk of bleeding disorders.
- medicines which require cell division for their effect, for example, methotrexate (a medicine used for cancer as well as arthritis treatment) may have a decrease in its effect.
- prednisone, a steroid medicine. If used at the same time as Oncaspar, the effects on the clotting ability of your blood are increased.
- cytarabine, a medicine which can be used in cancer treatment, and could interfere with the effects of Oncaspar.

Oncaspar can also cause changes in liver function which can affect the way other medicines work.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

You should not use Oncaspar if you are pregnant because its effects during pregnancy have not been studied. Your physician will decide whether your disease requires treatment. Women who are able to get pregnant must use reliable contraception during treatment, and for at least 6 months after Oncaspar treatment has been discontinued. Oral contraception is not an effective method of contraception while on treatment with Oncaspar. Ask your doctor for advice on the best contraceptive method that you can use. Men must also use effective contraception while they or their partners are treated with Oncaspar.

It is not known whether pegaspargase is excreted into the breast milk. As a precautionary measure, breast-feeding should be discontinued during treatment with Oncaspar and should not be re-started until after treatment with Oncaspar has been discontinued.

Driving and using machines
Do not drive or use machines when using this medicine because it may make you feel drowsy, tired or confused.

Oncaspar contains sodium
This medicine contains less than 1 mmol sodium per dose, i.e., it is essentially ´sodium-free´.

3. How Oncaspar is given

Your treatment with Oncaspar has been prescribed by a doctor experienced in medicines used to treat cancer. Your doctor will decide what dose of the medicine is needed and how often, based on your age and body surface area which is calculated from your height and weight.

The medicine is given as a solution by injection into a muscle or, if more suitable, into a vein.

If you are given too much Oncaspar
As your doctor will administer the medicine, it is very unlikely you will be given more than you need.

In the unlikely event of accidental overdose, you will be monitored carefully by medical staff and treated appropriately.

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

4. Possible side effects

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

Serious side effects
Tell your doctor **immediately** if you get any of the following side effects:

Very common (may affect more than 1 in 10 people)
- Inflammation or other disorders of the pancreas (pancreatitis) causing severe stomach pain which may spread to your back, vomiting, increase in blood sugar levels;
- Serious allergic reactions with symptoms such as rash, itching, swelling, hives, shortness of breath, fast heart beat and drop in blood pressure;
- Severe infection with very high fever;
- Blood clots.

Common (may affect up to 1 in 10 people)
- Severe bleeding or bruising;
- Violent shaking (seizures) and loss of consciousness;
- Problems with your liver (e.g., change in colour of your skin or urine or stool and laboratory results of elevated liver enzymes or bilirubin).

Rare (may affect up to 1 in 1,000 people)
- Liver failure.

Not known (frequency cannot be estimated from the available data)
- Severe skin reaction called toxic epidermal necrolysis;
- Loss of kidney function (e.g., change in urine output, swelling of feet and ankles);
- Stroke;

- Severe allergic reaction that may cause loss of consciousness and could be life-threatening (anaphylactic shock).

Other side effects
Talk to your doctor if you get any of the following:

Very common (may affect more than 1 in 10 people)
- Changes in the function of the pancreas;
- Weight loss;
- Leg pain (which could be a symptom of thrombosis), chest pain or shortness of breath (which may be a symptom of blood clots in the lungs, called pulmonary embolism);
- Loss of appetite, general weakness, vomiting, diarrhoea, nausea;
- Increased blood sugar levels.

Common (may affect up to 1 in 10 people)
- Decreased number of red blood cells;
- Build-up of fluid in the stomach (ascites);
- Fever and flu-like symptoms;
- Mouth sores;
- Back, joint or abdominal pain;
- High levels of fat and cholesterol in your blood; low potassium in your blood.

Rare (may affect up to 1 in 1,000 people)
- Reversible posterior leukoencephalopathy syndrome (RPLS), a syndrome characterised by headache, confusion, seizures and visual loss which resolves after some time.

Not known (frequency cannot be estimated from the available data)
- Decreased number of white blood cells and platelets;
- Palpitations;
- Cysts in your pancreas, swelling of the salivary glands;
- High levels of urea in your blood; antibodies against Oncaspar; high levels of ammonia in your blood; decreased blood sugar levels;
- Sleepiness, confusion, mild twitching of the fingers.

Reporting of side effects
If you get any side effects you think might be related to your chemotherapy, talk to your doctor. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the Yellow Card Scheme at: 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 Oncaspar

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 label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C-8°C).
Do not freeze.

After the medicinal product has been reconstituted and diluted, the solution should be used immediately. If immediate use is not possible, the diluted solution can be stored at 2°C-8°C for up to 48 hours.

Do not use this medicine if you notice the reconstituted solution is cloudy or has visible particles.

Do not throw away any medicines via wastewater. Ask the pharmacist how to dispose of unused medicines. These measures will help protect the environment.

6. Contents of the pack and other information

What Oncaspar contains
The active substance is pegaspargase. Each vial contains 3,750 U of pegaspargase.

After reconstitution, 1 ml of solution contains 750 U pegaspargase (750 U/ml).

The other ingredients are: disodium phosphate heptahydrate, sodium dihydrogen phosphate monohydrate, sodium chloride, sucrose, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment) (see section 2 "Oncaspar contains sodium").

What Oncaspar looks like and contents of the pack
Oncaspar is a white to off-white powder. After reconstitution, the solution is clear, colourless and free from visible foreign particles.
Each pack contains 1 glass vial with 3,750 U pegaspargase.

Marketing Authorisation Holder
Les Laboratoires Servier
50 rue Carnot
92284 Suresnes Cedex
France

Manufacturer
Les Laboratoires Servier Industrie
905 Route de Saran
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Servier Laboratories Ltd
Tel: +44 (0)1753 666409

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

The following information is intended for healthcare professionals only:

It is strongly recommended that every time Oncaspar is administered to a patient, the name and lot number of the product are recorded in order to link the patient and the lot of the product.

In view of the unpredictability of adverse reactions, Oncaspar should be administered only by health care personnel experienced in the use of cancer chemotherapeutic medicinal products.

Particularly in patients with known hypersensitivity to the other forms of L-asparaginase, hypersensitivity reactions to Oncaspar can occur during the therapy, e.g., anaphylaxis. A routine precaution is to observe the patients for an hour with resuscitation equipment and other items required for the treatment of anaphylaxis in readiness (epinephrine, oxygen, intravenous steroids etc.).

Patients should be informed about possible hypersensitivity reactions to Oncaspar, including immediate anaphylaxis. Patients who receive Oncaspar are at increased risk of bleeding and thrombotic disorders. It should be explained to patients that Oncaspar should not be used at the same time as other medicines associated with an increased risk of bleeding (see section 2 "Other medicines and Oncaspar").

This medicinal product can cause irritation on contact. The powder must therefore be handled and administered with particular care. Inhalation of the vapour and contact with the skin and mucosa, particularly that of the eyes, must be avoided; if the product comes in contact with eyes, skin, or mucous membranes, rinse immediately with plenty of water for at least 15 minutes.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Instructions on how to prepare, store and dispose of Oncaspar

Instructions for handling

1. Staff should be trained in how to handle and transfer the medicinal product (pregnant staff should be excluded from working with this medicinal product).
2. Aseptic technique must be used.
3. Procedures for proper handling of antineoplastic agents should be observed.
4. The use of disposable gloves and protective garments is recommended when handling Oncaspar.
5. All items for administration or cleaning, including gloves, should be placed in high-risk waste disposal bags for high-temperature incineration.

Reconstitution

1. 5.2 ml water for injections are injected into the vial using a syringe and 21 gauge needle.
2. The vial should be gently swirled until the powder is reconstituted.
3. After reconstitution, the solution should be clear, colourless and free from visible foreign particles. Do not use if the reconstituted solution is cloudy or if a precipitate has formed. Do not shake.
4. The solution should be used within 24 hours after reconstitution, when stored below 25°C.

Administration

1. Parenteral medicinal products should be inspected for particulate matter prior to administration, only a clear, colourless solution free from visible foreign particles should be used.
2. The medicinal product should be administered intravenously or intramuscularly. The solution should be administered slowly.
   For intramuscular injection, the volume should not exceed 2 ml in children and adolescents and 3 ml in adults.
   For intravenous administration, the reconstituted solution should be diluted in 100 ml sodium chloride 9 mg/ml (0.9%) solution for injection or 5% glucose solution.
   The diluted solution can be given over 1 to 2 hours together with an already-running infusion of either sodium chloride 9 mg/ml (0.9%) solution or 5% glucose. Do not infuse other medicinal products through the same intravenous line during administration of Oncaspar.
   After dilution, the solution should be used immediately. If immediate use is not possible, the diluted solution can be stored at 2°C-8°C for up to 48 hours.

Disposal

Oncaspar is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Further detailed information can be found in the SmPC.