

Zarzio® 30 MU/0.5 ml

solution for injection or infusion in pre-filled syringe

Zarzio® 48 MU/0.5 ml

solution for injection or infusion in pre-filled syringe

Filgrastim



Read all of this leaflet carefully before you start using this medicine.

- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- 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.

In this leaflet:

1. What Zarzio is and what it is used for
2. Before you use Zarzio
3. How to use Zarzio
4. Possible side effects
5. How to store Zarzio
6. Further information

1 What Zarzio is and what it is used for

Zarzio contains the active substance filgrastim. It belongs to a group of proteins called cytokines, and is very similar to the granulocyte-colony stimulating factor (G-CSF) produced by the human body. Filgrastim stimulates the bone marrow to produce more white blood cells that help fight infection. If the number of white blood cells is too low (neutropenia), the risk of infection increases.

Anticancer chemotherapy

Zarzio is used to reduce the duration of neutropenia and the occurrence of febrile neutropenia (with fever) which can be caused by the use of cytotoxic anticancer chemotherapy in children and adults. It is not used in patients with chronic myeloid leukaemia (CML) and myelodysplastic syndromes (MDS).

Bone marrow transplantation

Zarzio is used to reduce the duration of neutropenia after high-dose chemotherapy and total body irradiation (radiotherapy) followed by bone marrow transplantation, in children and adults at increased risk of prolonged severe neutropenia.

Peripheral blood stem cell mobilisation

Zarzio is used to stimulate the bone marrow to release (mobilisation) peripheral blood progenitor cells (PBPC, a type of stem cells) into the blood, so that they eventually grow and develop into all types of blood cells: white blood cells, red blood cells and platelets.

If you are a patient with cancer these PBPCs will be removed from your blood and returned after your chemotherapy and/or radiotherapy. As chemotherapy and/or radiotherapy can depress the activity of your bone marrow, this will help to speed up its recovery.

If you donate stem cells for another person, the PBPCs will be removed from your blood and given to the recipient after he/she has received their chemotherapy and/or radiotherapy.

Severe chronic neutropenia

Zarzio is used in children and adults to

increase the number of white blood cells and reduce the occurrence and duration of infections related to specific forms of severe chronic neutropenia: congenital (inborn), cyclic (recurring), or idiopathic (without known cause).

HIV infection neutropenia

Zarzio is used to treat persistent neutropenia in patients with advanced HIV infection, in order to reduce the risk of bacterial infections, when other treatments are not appropriate.

2 Before you use Zarzio

Do not use Zarzio

- if you are allergic (hypersensitive) to filgrastim or to any of the other ingredients of Zarzio (listed in section 6. 'What Zarzio contains').

Take special care with Zarzio

Please tell your doctor:

- if you have osteoporosis.
- if you have sickle cell anaemia (disorder of the red blood cells leading to a sickle-shaped form of the red blood cells).
- if you have specific blood disorders, such as myelodysplastic syndromes (MDS) or chronic myeloid leukaemia (CML).
- if you act as a donor for another person and are treated with anticoagulants (blood thinning medicines) or you have bleeding problems.

Take special care with other products that stimulate white blood cell production

Zarzio is one of a group of products that stimulate the production of white blood cells. Your healthcare professional should always record the exact product you are using.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

It is important to tell your doctor if you are pregnant, think you may be pregnant or plan to get pregnant, as the doctor may decide that you should not use this medicine.

Filgrastim could affect your ability to become or stay pregnant.

Your doctor may decide that you should not use filgrastim if you are breast-feeding, as it is not known whether it passes into milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Zarzio has no influence on the ability to drive and use machines.

Important information about some of the ingredients of Zarzio

This medicine contains sorbitol (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3 How to use Zarzio

The amount of Zarzio you need depends on your bodyweight and the condition you are treated for.

Anticancer chemotherapy

The usual dose is 0.5 million units (MU) per kg bodyweight each day. For example, if you weigh 60 kg, your daily dose will be 30 MU. The first dose should not be administered less than 24 hours following cytotoxic chemotherapy. Your treatment can last up to 14 days. In some disease types, however, longer treatment of up to about 1 month may be required.

Bone marrow transplantation

The usual starting dose is 1 MU per kg bodyweight each day. For example, if you weigh 60 kg, your daily dose will be 60 MU. You will normally receive your first dose at least 24 hours after your chemotherapy, but within 24 hours of receiving your bone marrow transfusion. Your doctor will then test your blood to tell how well your treatment is working and how long it should last.

Peripheral blood stem cell mobilisation

– If you are donating stem cells for yourself, the usual dose is 1 MU per kg bodyweight each day. Zarzio will be given for 5 - 7 consecutive days. Treatment with Zarzio should be maintained until the last stem cell collection.

- If you are donating stem cells for yourself after chemotherapy, the usual dose is 0.5 MU per kg bodyweight each day. Zarzio will be given until the expected lowest level of white blood cells is passed and has recovered to the normal range.
- If you are acting as a stem cell donor for another person, the usual dose is 1 MU per kg bodyweight each day. Zarzio treatment will last for 4 - 5 consecutive days.

Your doctor will perform regular blood tests to determine the best time to collect the stem cells.

Severe chronic neutropenia

The usual starting dose is between 0.5 and 1.2 MU per kg bodyweight each day in a single or divided dose. Your doctor will then test your blood to see how well your treatment is working and to find the dose that is best for you. Long-term treatment with Zarzio is required for neutropenia.

HIV infection neutropenia

The usual starting dose is between 0.1 and 0.4 MU per kg bodyweight each day. Your doctor will test your blood at regular intervals to see how well the treatment is working. Once the number of white cells in your blood have returned to normal it may be possible to reduce the dose frequency to less than once per day. Your doctor will continue to test your blood regularly and will recommend the best dose for you. Long-term treatment with Zarzio may be required to maintain a normal number of white cells in your blood.

Children and adolescents

The dose recommendations are the same as those for adults receiving chemotherapy.

How Zarzio is used

Always use Zarzio exactly as your doctor has told you. You should check with your doctor, nurse or pharmacist if you are not sure. This medicine is given by injection into the tissue just under the skin (subcutaneous injection), or through an intravenous infusion ("a drip").

Your doctor may decide that it would be more convenient for you to inject Zarzio yourself. Your doctor or nurse will show you how to inject yourself. **Do not try to inject yourself if you have not been trained.**

Instructions on how to inject yourself with Zarzio can be found at the end of this leaflet.

If you use more Zarzio than you should
If you have used more Zarzio than you should, contact your nurse, doctor or pharmacist immediately.

If you forget to use Zarzio

If you have forgotten a dose of Zarzio, you should contact your doctor to discuss when you should inject the next dose.

If you stop using Zarzio

Your doctor will tell you when you can stop using Zarzio. It is quite normal to have several courses of treatment with Zarzio.

4 Possible side effects

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

Tell your doctor immediately

- if you experience a cough, fever and difficulty breathing since you may develop severe pulmonary side effects like pneumonia and respiratory distress;
- if you get pain in the upper left side of your stomach or pain at the tip of your shoulder since this may relate to a problem with your spleen;
- if you have sudden difficulty breathing or dizziness, swelling of your face or throat, skin weals or rash. As this may be a serious allergic reaction, stop your injection and get medical help immediately.

Side effects may occur with certain frequencies, which are defined as follows:

- very common: affects more than 1 user in 10
- common: affects 1 to 10 users in 100
- uncommon: affects 1 to 10 users in 1,000
- rare: affects 1 to 10 users in 10,000
- very rare: affects less than 1 user in 10,000
- not known: frequency cannot be estimated from the available data.

Very common side effects

- bone, joint and muscle pain
- elevations in blood levels of uric acid and certain enzymes

- decreases in blood glucose
- leukocytosis (an abnormally high number of white blood cells in the blood)
- low level of blood platelets (which increases risk of bleeding or bruising)
- low level of red blood cells (which can make the skin pale and cause weakness and breathlessness)
- headache
- nose bleed
- enlarged spleen

Common side effects

- diarrhoea
- injection site pain
- hair loss
- rash
- enlarged liver
- inflammation of blood vessels of the skin
- loss of calcium from the bones (osteoporosis)
- spleen disorder

Uncommon side effects

- decrease in blood pressure
- allergic-type reactions, including anaphylaxis (dizziness, severe drop in blood pressure, difficulty in breathing), angioedema (painful swelling of the face or throat), difficulty in breathing, low blood pressure, skin rash, nettle rash; these reactions can occur at the start of the treatment or throughout the treatment
- worsening of rheumatoid arthritis or arthritic symptoms
- blood or protein in the urine

Rare side effects

- vascular disorders, including venoocclusive disease (a disease which affects the liver) and water retention, which can cause swelling in the limbs

Very rare side effects

- difficulties in passing urine
- Sweet's syndrome (plum-coloured, raised, painful lesions on the limbs, sometimes the face and neck, with fever)
- water retention in the lungs, bleeding in the lungs, coughing up of blood, lack of oxygen, inflammation of the lungs (which can cause breathlessness, cough, raised temperature); in some cases, this could lead to respiratory failure or adult respiratory

distress syndrome (ARDS, a condition causing increased shortness of breath, in very ill patients), which may be fatal

- sickle cell crises (acute collapse of red blood cells) in patients with sickle cell disease
- rupture of the spleen

Frequency unknown

- rejection of transplanted bone marrow
- pain and swelling of the joints, similar to gout (pseudogout)

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.

5 How to store Zarzio

Keep out of the reach and sight of children.

Do not use Zarzio after the expiry date which is stated on the carton and on the syringe label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).

The syringe can be removed from the refrigerator and left at room temperature for a single period of maximum 72 hours (but not above 25°C). At the end of this period, the product should not be put back in the refrigerator and should be disposed of.

Keep the pre-filled syringe in the outer carton in order to protect from light.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6 Further information

What Zarzio contains

- The active substance is filgrastim. Zarzio 30 MU/0.5 ml solution for injection or infusion in pre-filled syringe: Each pre-filled syringe contains 30 MU filgrastim in 0.5 ml, corresponding to 60 MU/ml. Zarzio 48 MU/0.5 ml solution for injection or infusion in pre-filled syringe: Each pre-filled syringe contains 48 MU filgrastim in 0.5 ml, corresponding to 96 MU/ml

- The other ingredients are glutamic acid, sorbitol (E420), polysorbate 80 and water for injections.

What Zarzio looks like and contents of the pack

Zarzio is a clear, colourless to slightly yellowish solution for injection or infusion in a pre-filled syringe.

Zarzio is available in packs containing 1, 3, 5 or 10 pre-filled syringes with injection needle and with or without a needle safety guard.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Sandoz GmbH
Biochemiestrasse 10
A-6250 Kundl
Austria

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Sandoz nv/sa
Tel/Tel: +32 2 722 97 97

България
Представителство Сандоз д.д.
Тел.: +359 2 970 47 47

Česká republika
Sandoz s.r.o.
Tel: +420 221 421 611

**Danmark/Norge/Island/
Sverige**
Sandoz A/S
Tlf: +45 63 95 10 00

Deutschland
NeoCorp AG
Tel: +49 881 909 5960
oder

Sandoz Pharmaceuticals GmbH
Tel: +49 8024 902 40 00

Eesti
Sandoz d.d. Eesti filiaal
Tel: +372 665 2400

Ελλάδα
Novartis (Hellas) A.E.B.E.
Τηλ: +30 210 281 17 12
†

DEMO Ανώνυμος Βιοφάρμακική και Εμπορική Εταιρεία
Τηλ.: +210 8161802

España
Sandoz Farmacéutica, SA
Tel: +34 90 211 87 61

France
Sandoz SAS
Tel: +33 1 49 64 48 00

Ireland
Rowex Ltd
Tel: +353 27 50077

Italia
Sandoz S.p.A.
Tel: +39 02 96541

Κύπρος
Διαγονίας Κύπρου
Τηλέφωνο: +357 25372425

Latvija
Sandoz d.d. Parstāvniecība
Latvijā
Tel: +371 67 892 006

Lietuva
Sandoz Pharmaceuticals d.d. filialas
Tel: +370 5 2636 038

Luxembourg/Luxemburg
Sandoz GmbH
Tel: +43 5338 200

Magyarország
Sandoz Hungária Kft.
Tel: +36 1 430 2890

Malta
Sandoz GmbH
Tel: +43 5338 200

Niederland
Sandoz B.V.
Tel: +31 36 52 41 600

Österreich
Sandoz GmbH
Tel: +43 5338 200

Polska
Sandoz Polska Sp. z o.o.
Tel: +48 22 549 15 00

Portugal
Sandoz Farmacêutica Lda.
Tel: +351 21 924 19 11

This leaflet was last approved in 06/2011.

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

Instructions on how to inject yourself

This section contains information on how to give yourself an injection of Zarzio. It is important that you do not try to give yourself the injection unless you have received special training from your doctor or nurse. Zarzio is provided with or without a needle safety guard and you will be shown how to use this by your doctor or nurse. If you are not sure about giving the injection or you have any questions, please ask your doctor or nurse for help.

How do I inject myself?

You will need to give yourself an injection into the tissue under the skin, known as a subcutaneous injection. Your doctor or nurse will tell you how frequently it should be injected.

What do I need?

To give yourself a subcutaneous injection you will need:

1. A new pre-filled syringe of Zarzio with or without a needle safety guard

România
S.C. Sandoz SRL
Tel: +40 265 208 120

Slovenija
Lek farmacevtska družba d.d.
Tel: +386 1 580 21 11

Slovenská republika
Sandoz d.d. - organizačná zložka
Tel: +421 2 48 200 600

Suomi/Finland
Sandoz A/S
Puh/Tel: +358 9 85 20 20 30

United Kingdom
Sandoz Limited
Tel: +44 1276 69 8020

2. Alcohol wipes or similar
3. A puncture-proof container for disposing of used syringes safely if you use the Zarzio pre-filled syringe without a needle safety guard.

What should I do before I give myself a subcutaneous injection of Zarzio?

1. Take your Zarzio pack out of the refrigerator. Accidental exposure to freezing temperatures does not adversely affect the stability of Zarzio.
2. Do not shake the packing containing the pre-filled syringe.
3. Check that it is the correct strength you need for the dose that your doctor has prescribed.
4. Check the expiry date which is stated on the carton and syringe label (EXP). Do not use it if the date has passed the last day of the month shown.
5. Check the appearance of Zarzio. It must be clear. If it is cloudy or there are particles in it, you must not use it.
6. For a more comfortable injection, let the pre-filled syringe stand for 30 minutes to reach room temperature or hold the pre-filled syringe gently in your hand for a few minutes. **Do not warm Zarzio in any other way** (for example, do not warm it in a microwave or in hot water).
7. **Do not** remove the plastic cover from the needle until you are ready to inject.
8. **Wash your hands thoroughly.**
9. Find a comfortable, well-lit place and put the syringe, the alcohol wipes and if necessary the puncture-proof container where you can reach them.

How do I prepare the injection?

Before you inject Zarzio you must do the following:

1. Gently remove the plastic cover from the needle without twisting it. Do not touch the needle or push the plunger.
2. Hold the syringe with the needle pointing upwards to check if there are air bubbles in the syringe. If there are air bubbles in it expel all air from the syringe by cautiously pushing the plunger upwards (avoid expelling liquid from the syringe).
3. The syringe has a scale on the syringe

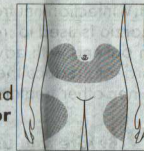
barrel. Push the plunger up to the number (ml) that matches the dose of Zarzio that your doctor prescribed.

4. Check again to make sure the correct dose of Zarzio is in the syringe.
5. You can now use the pre-filled syringe.

Where should I give my injection?

The most suitable places to inject yourself are:

- The top of your thighs; and
- The abdomen, **except for the area around the navel.**



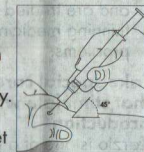
Change the place that you inject each time so you don't become sore in one area. If someone is injecting for you, they can also use the back of your arms.

How do I give my injection?

1. Disinfect your skin by using an alcohol wipe and pinch the skin between your thumb and forefinger, without squeezing it.
2. Insert the needle under the skin at an angle of approximately 45° as shown by your nurse or doctor.
3. Pull slightly on the plunger to check that a blood vessel has not been punctured. If you see blood in the syringe, remove the needle and put it in another place.

Pre-filled syringe without needle safety guard

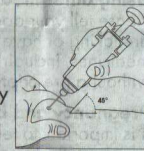
4. Always keeping your skin pinched, depress the plunger slowly and evenly.
5. After injecting the liquid, remove the needle and let go of your skin.



6. Put the used syringe in the disposal container. Use each syringe only for one injection.

Pre-filled syringe with needle safety guard

4. Always keeping your skin pinched, depress the plunger slowly and evenly until the entire dose has been given and the plunger cannot be depressed any further. Do not release the pressure on the plunger!



5. After injecting the liquid, remove the needle while maintaining pressure on the plunger and then let go of your skin.
6. Let go of the plunger. The needle safety guard will rapidly move to cover the needle.
7. Use each syringe only for one injection.

Remember

If you have any problems, please do not be afraid to ask your doctor or nurse for help and advice.

Disposal of used syringes

The used syringes should be disposed of in accordance with local requirements.

Pre-filled syringe without needle safety guard

- Do not put the cover back on used syringes.
- Put used syringes into the puncture-proof disposal container and keep it out of the reach and sight of children.
- Dispose of the full container as instructed by your doctor, nurse or pharmacist.
- **NEVER** put used syringes into your normal household waste bin.

Pre-filled syringe with needle safety guard

- The needle safety guard prevents needle stick injuries after use, so no special disposal precautions are required. Dispose of the syringe as instructed by your doctor, nurse or pharmacist.

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

The solution should be visually inspected prior to use. Only clear solutions without particles should be used. Accidental exposure to freezing temperatures does not adversely affect the stability of Zarzio.

Zarzio contains no preservative: In view of the possible risk of microbial contamination, Zarzio syringes are for single use only.

Dilution prior to administration (optional)
If required, Zarzio may be diluted in glucose 50 mg/ml (5%) solution. Zarzio must not be diluted with sodium chloride solutions.

Dilution to a final concentration < 0.2 MU/ml (2 µg/ml) is not recommended at any time.

For patients treated with filgrastim diluted to concentrations < 1.5 MU/ml (15 µg/ml),

human serum albumin (HSA) should be added to a final concentration of 2 mg/ml.

Example: In a final volume of 20 ml, total doses of filgrastim less than 30 MU (300 µg) should be given with 0.2 ml of human serum albumin 200 mg/ml (20%) solution Ph. Eur. added.

When diluted in glucose 50 mg/ml (5%) solution, filgrastim is compatible with glass and a variety of plastics including polyvinylchloride, polyolefin (a copolymer of polypropylene and polyethylene) and polypropylene.

After dilution: Chemical and physical in-use stability of the diluted solution for infusion has been demonstrated for 24 hours at 2°C to 8°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Using the pre-filled syringe with a needle safety guard

The needle safety guard covers the needle after injection to prevent needle stick injury. This does not affect normal operation of the syringe. Depress the plunger slowly and evenly until the entire dose has been given and the plunger cannot be depressed any further. While maintaining pressure on the plunger, remove the syringe from the patient. The needle safety guard will cover the needle when releasing the plunger.

Using the pre-filled syringe without a needle safety guard

Administer the dose as per standard protocol.

Disposal

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