Package leaflet: Information for the user

Exembol Multidose 100 mg/ml concentrate for solution for infusion

argatroban monohydrate

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.
• If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Exembol Multidose is and what it is used for

Exembol Multidose is an anticoagulant (a drug that helps to prevent blood clots from forming in your blood circulation). It works by blocking the action of thrombin, a substance in your blood that is important in blood clotting.
Exembol Multidose is used if you are suffering from a disorder known as heparin-induced thrombocytopenia type II (HIT type II). If you have HIT type II, you are at risk of developing blood clots in your blood circulation that can cause heart attacks, stroke, breathing problems and problems with the blood supply to your limbs. Exembol Multidose can prevent these problems or prevent them from becoming worse.

2. What you need to know before you use Exembol Multidose

Do not use Exembol Multidose:
• If you have uncontrolled bleeding
• If you are allergic (hypersensitive) to argatroban or to any of the other ingredients of Exembol Multidose
• If you have severely impaired liver function

Warnings and precautions
Exembol Multidose will be given to you with special care:
• If there is an increased risk of bleeding
• If you have recently had injections or infusions of other anticoagulants such as heparin
• If you have liver disease

Children and Adolescents
It is not advised to give this medicine to children or adolescents as the safe or effective dose of Exembol Multidose has not been clearly established.

Other medicines and Exembol Multidose
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

Combined use with other blood thinning or blood clot dissolving medicines can increase the risk of bleeding.

Because Exembol Multidose contains ethanol, this can influence the effect of other medicines containing metronidazole (for infections) or disulfiram (for alcoholism).

Pregnancy, breast-feeding and fertility
If you are pregnant, or breast-feeding, think you may be pregnant or are planning to have a baby, you should ask your doctor for advice before Exembol Multidose is given to you.

As a precautionary measure, it is preferable to avoid the use of Exembol Multidose during pregnancy.

Avoid breast-feeding while you are being given Exembol Multidose. See also "Exembol Multidose contains alcohol".

Driving and using machines

Since Exembol Multidose contains alcohol you should not drive a car or use machines in connection with the treatment. See also "Exembol Multidose contains alcohol".

Exembol Multidose contains alcohol

This product contains 400 mg/ml or 50% by volume of alcohol (ethanol) before dilution, which corresponds to 0.5% by volume after dilution in accordance with the instructions. The daily dose may therefore contain up to 5 ml (4 g) of alcohol, corresponding to 100 ml beer or 40 ml wine. This may be harmful for persons suffering from liver disease, alcoholism or epilepsy as well as for pregnant and nursing women and their children. See also "Pregnancy, breast-feeding and fertility".

If you are addicted to alcohol, talk to your doctor or pharmacist before taking this medicine.

The amount of alcohol in this medicine is not likely to have an effect in adults and adolescents. The alcohol in this medicine may alter the effect of other medicines. Talk to your doctor or pharmacist if you are taking other medicines.

Because this medicine is usually given slowly over several hours, the effects of alcohol may be reduced.

Exembol Multidose contains sorbitol

This medicine contains 750 mg sorbitol in each vial (2.5 ml) which is equivalent to 300 mg/ml.

Sorbitol is a source of fructose. If you have hereditary fructose intolerance (HFI), a rare genetic disorder, you must not receive this medicine. Patients with HFI cannot break down fructose, which may cause serious side effects.

You must tell your doctor before receiving this medicine if you have HFI.

3. How to use Exembol Multidose

Exembol Multidose will always be given to you by medical personnel. Exembol Multidose will

be given to you intravenously (into a vein) by continuous infusion. The doctor will decide the dose and how long you will be treated.

4. Possible side effects

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

The most common side-effects are bleeding. Major bleeding can occur in about 5% of patients and minor bleeding in about 39% of patients. **You must tell your doctor immediately** if you experience any of the following symptoms:
● bleeding or bruising
● blood in urine or stools
● vomiting or coughing up blood
● black stools
● difficulty in breathing
● cold sweaty skin
● dry mouth
● dilated pupils and/or weak rapid pulse.

These symptoms could indicate that you are experiencing bleeding problems.

Common side effects *(may affect up to 1 in 10 people):*

● anaemia
● blood clotting
● bleeding, including numerous small bleedings in skin and mucus membranes (purpura)
● nausea

Uncommon side effects *(may affect up to 1 in 100 people):*

● infections such as urinary tract infection
● changes in blood values
● blood clotting
● lack of appetite
● low blood sugar levels
● low sodium levels in the blood
● confusion
● dizziness
● fainting
● headache
● stroke
● muscle disorders
● speech disorder
● vision problems
● deafness
● heart attack
● fluid in the heart sac
● abnormal heart rhythm
● fast heartbeat
● low blood pressure

- high blood pressure
- inflammation of veins
- shock
- reduced oxygen supply to the tissues
- breathing difficulties
- fluid around the lungs
- hiccup
- blood in cough, vomit or stools
- constipation
- diarrhoea
- stomach inflammation
- difficulty in swallowing
- tongue disorder
- abnormal liver function
- jaundice (yellowing of the skin and eyes)
- changes in blood tests for liver function
- rash including nettle rash
- itching
- increased sweating
- hair loss
- muscle weakness
- muscle pain
- kidney failure
- fever
- pain
- tiredness
- injection site reactions
- swelling of the legs
- increased wound drainage
- abnormal laboratory results.

Not known *(frequency cannot be estimated from the available data).*
- Cases of bleeding into the brain have been reported.

Reporting of side effects
If you experience 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 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 Exembol Multidose

Keep out of the sight and reach of children.
Keep vial in the outer carton in order to protect from light.
Do not refrigerate or freeze.
Diluted solutions should not be exposed to direct sunlight.
Solutions should not be used if they are cloudy or contain any particles.

After opening, before dilution:

Chemical and physical stability has been demonstrated in use following multiple needle entries and product withdrawal for 28 days at both 25ºC and at 2 to 8ºC.

Diluted solution:
Chemical and physical in-use stability has been demonstrated for up to 14 days at 25ºC and 2 to 8ºC in sodium chloride 9 mg/ml (0.9%) solution for infusion, glucose 50 mg/ml (5%) solution for infusion, or sodium lactate intravenous infusion compound.

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 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Do not use Exembol Multidose after the expiry date which is stated on the carton/vial after "EXP". The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What Exembol Multidose contains
The active substance is argatroban monohydrate 100 mg/ml.

1 ml concentrate for solution for infusion contains 100 mg argatroban monohydrate.

1 Vial with 2.5 ml concentrate for solution for infusion contains 250 mg argatroban monohydrate.

The other ingredients are anhydrous ethanol, sorbitol and water for injections

What Exembol Multidose looks like and contents of the pack
This medicinal product is a clear colourless to pale yellow concentrate for solution for infusion. Each vial contains 2.5ml of solution and the vials are packed in cardboard boxes of 1 or 6 vials.

Not all pack sizes may be marketed.

Marketing authorisation holder
Ethypharm, 194, Bureaux de la Colline, Bâtiment D, 92213 Saint-Cloud cedex, France.

Manufacturer
Central Pharma (Contract Packing) Limited, Caxton Road, Bedford, MK41 0XZ, UK.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:
United Kingdom : Macarthys Laboratories Ltd
email: medinfo@ethypharm.com

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Argatra Multidose
Finland	Novastan
France	Arganova
Germany	Argatra Multidose

Italy	Novastan Multidose
Netherlands	Arganova Multidose
Sweden	Novastan Multidos
United Kingdom	Exembol Multidose

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The following information is intended for healthcare professionals only.

Instructions for use, handling and disposal

Exembol Multidose should be diluted in sodium chloride 9 mg/ml (0.9%) solution for infusion, glucose 50 mg/ml (5%) solution for infusion, or Sodium Lactate Intravenous Infusion Compound to a final concentration of 1 mg/ml. If the solution is cloudy, or if an insoluble precipitate is noted, the vial should be discarded.

Following multiple needle entries and product withdrawals, the vials maintain microbial, chemical and physical stability for up to 28 days at 25ºC and at 2 to 8ºC. Other in-use storage times and conditions are the responsibility of the user.

The 100 mg/ml concentrate for solution for infusion should be diluted 100-fold by mixing with diluent. For a starting infusion rate of 0.5 microgram/kg/min, use 50 mg (0.5 ml) concentrate for solution for infusion per 50 ml of diluent.

The constituted solution must be mixed by repeated inversion of the diluent bag or bottle for one minute. The diluted solution should be clear and practically free from visible particles. Upon preparation, the solution may show slight but brief haziness due to the formation of microprecipitates that rapidly dissolve upon mixing. The pH of the intravenous solution prepared as recommended is 3.2-7.5.

Multiple use of Exembol Multidose applies to the 100 mg/ml concentrate for solution for infusion in its original container. The diluted solution should be used immediately. Any unused solution should be discarded.

Light resistant measures such as foil protection for intravenous lines are not necessary. No significant potency losses have been noted following simulated delivery of the solution through intravenous tubing.

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