

Fragmin® 2,500 IU/0.2 ml Solution for Injection (dalteparin sodium)

Your medicine is available using the above name but will be referred to as Fragmin throughout the following leaflet. Fragmin is also available in other strengths.

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, pharmacist or nurse.
- This medicine has been prescribed for you only. If your doctor has given you this medicine to use at home 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What Fragmin is and what it is used for

Fragmin is a solution for injection. Its active ingredient is dalteparin sodium.

Fragmin belongs to a group of medicines called low molecular weight heparins or antithrombotics, which help prevent the formation of blood clots by thinning the blood.

Venous thromboembolism is a condition where blood clots develop in the legs (deep vein thrombosis) or the lungs (pulmonary embolism), e.g. after surgery, prolonged bed rest or in patients with certain types of cancer.

- Fragmin is used to prevent blood clots (venous thromboembolism) forming before and after an operation or if you are bedridden due to illness and to prevent their recurrence.

The 5000 IU product can also be used for:

- Prevention of deep vein thrombosis in patients bedridden due to a medical condition but not limited to, for example heart failure and respiratory failure.
- Treatment of patients with solid tumours who suffer from low platelet counts.

Ask your doctor if you are unsure why you have been given Fragmin.

2. What you need to know before you are given or use Fragmin You should not be given Fragmin:

- if you are allergic (hypersensitive) to the active ingredient dalteparin sodium or a similar product or any of the other ingredients of this medicine (listed in section 6).
- if you have an active stomach ulcer or ulcer of the duodenum (small intestine).
- if you have suffered from a brain haemorrhage (bleeding in your brain).
- if you have fluid mixed with blood that appears around heart and lungs.
- if you suffer from any condition which may cause you to bleed more easily (e.g. haemophilia, liver failure). Ask your doctor if you are unsure.
- if you have a condition called septic endocarditis (an infection and inflammation of the lining of the heart and heart valves). Your doctor will have told you if you have this.
- if you have had a condition called “heparin-induced thrombocytopenia” (a decrease in the number of clotting cells (platelets) in your blood caused by heparin, which may cause you to bruise and bleed more easily). Your doctor will have told you if you have this.
- if you have an injury to, or have had an operation involving your spine, head, eyes or ears.

If you are receiving Fragmin to treat blood clots, you should not have a local, spinal or epidural anaesthetic.

If you are given this medicine as part of your cancer treatment your doctor will check that you weigh more than 40 kg, and that you have not had a stroke within the last 3 months.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given or use Fragmin:

- if you have conditions which make you more susceptible to bleeding e.g:
 - after an operation or trauma
 - a stroke caused by a bleed
 - a brain tumour
 - severe liver or kidney failure
 - abnormal or low numbers of platelets (clotting cells)
 - eye disease caused by blood pressure or diabetes
 - taking other medicines that thin the blood (e.g. aspirin, warfarin, dipyridamole)

- uncontrolled high blood pressure.
- if you have been told by your doctor that you have a lot of potassium in your blood or have a low blood pH. Your doctor will monitor your blood regularly before and during treatment.
- if you have ever had an operation to insert an artificial heart valve.
- if you need to have any other injections.

You may need to have blood tests to monitor the effects of Fragmin:

- if you have kidney failure or liver problems
- if you are very thin or morbidly obese
- if you are pregnant
- if you are at increased risk of bleeding or rethrombosis (more blood clots)
- if you are a child
- if you have blood problems due to cancer treatment.

Children and adolescents

Dosing recommendations in children are based on clinical experience; there are limited data from clinical trials, which will help your doctor calculate the dose of Fragmin.

Other medicines and Fragmin

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or are planning to take or use any other medicines. This includes medicines that you have bought for yourself.

Some medicines can affect the way Fragmin works, or Fragmin itself can reduce the effectiveness of other medicines taken at the same time.

Medicines that **increase** the effect of Fragmin include:

- Those used to thin your blood (e.g. aspirin, dipyridamole, glycoprotein receptor antagonists and warfarin).
- Medicines called non-steroidal anti-inflammatory drugs (NSAIDs) used to reduce pain and inflammation (e.g. indometacin).
- Some medicines for gout (e.g. sulfipyrazone and probenecid).
- Etacrynic acid (a water retention tablet (diuretic)).
- Solutions given to increase the blood volume (e.g. dextrans).
- Medicines known as cytostatics (used in cancer treatment).
- Thrombolytic medications for treating transmural heart attack (e.g. TPA-tissue plasminogen activator).

Medicines that can **reduce** the effect of Fragmin include:

- Those for allergy and hay fever (e.g. antihistamines).
- Those used for heart or circulation problems (e.g. digoxin or digitoxin).
- Antibiotics known as tetracyclines which are used to treat bacterial infections.
- Vitamin C (e.g. some vitamin supplements).

Other medicines that may interfere with Fragmin include:

- Those used to treat angina (intravenous nitroglycerine)
- Antibiotics such as high dose penicillin which are used to treat bacterial infections.
- Anti-malarials (e.g. quinine)
- Tobacco smoking

Please note that if you are being treated with Fragmin for unstable coronary artery disease your doctor may adjust your dose of aspirin accordingly.

Please tell your doctor or pharmacist if you are taking or have recently taken any other low molecular weight heparins or anti-thrombotics.

Pregnancy and breast-feeding

Fragmin has not been found to cause harmful effects during pregnancy. The possibility of harm to the baby appears remote. Tell your doctor if you are pregnant and they will advise you.

Fragmin is not recommended for the prevention of blood clots on artificial heart valves during pregnancy.

If you are receiving Fragmin to treat blood clots, you should not have a local, spinal or epidural anaesthetic.

Ask your doctor or pharmacist for advice before being given or using this medicine whilst breast-feeding.

Driving and using machines

Fragmin does not affect the ability to drive and operate machinery.

3. How Fragmin is given to you

Your medicine will usually be administered by a doctor or nurse or you may be shown how to give the injection yourself at home (See Section on How to Inject Fragmin). The amount of Fragmin you receive will depend on your body weight.

Fragmin is given as a single, once daily, subcutaneous injection, which means it is injected beneath the skin. It is usually injected into a skin fold in your abdomen (stomach), or the outer aspects of your thigh. It should not be injected into your muscles.

Use in adults and the elderly

To prevent blood clots (venous thromboprophylaxis)

- **Patients with a moderate risk of developing a clot:** The recommended dose is 2,500 IU one to two hours before the operation, then 2,500 IU each morning. This is continued for five to seven days, or until you are fully able to move about.

- **Patients with a greater risk of developing a clot e.g. those who have had clots in the past:**

For this type of patient, the recommended dose is 2,500 IU one to two hours before the operation, the same dose 8 to 12 hours later, then 5,000 IU each morning. As an alternative, 5,000 IU may be given the evening before the operation, then 5,000 IU on following evenings. The first dose (2500 IU) may also be given as soon as possible after your operation and is to be continued for five to seven days, or until you are able to move about.

- **Hip Replacement Surgery**

After a hip operation, your doctor may decide to continue treating you with Fragmin for five weeks using a dose of 5,000 IU every evening. If you have an artificial heart valve, the normal dose for prevention of blood clots is not sufficient. Your doctor will discuss this with you.

- The maximum dose you will be given in a 12 hour period is 10,000 IU.
- If you are bedridden due to illness, the dose of Fragmin given will be 5,000 IU daily. The length of treatment will be up to 14 days, depending on your illness.

These are typical doses for adults, including elderly patients. Your doctor will work out the right dose for you. Some of the liquid in the syringe may have to be expelled before the injection is given.

To treat blood clots (venous thromboembolism) in certain types of cancer and prevent recurrence

The usual dose used to treat venous thromboembolism in cancer is 200 IU (international units) for every kilogram you weigh (see table below) once daily during the first month after a thromboembolic event (blood clot), followed by 150 IU for every kilogram you weigh (during months 2-6).

Dose of Fragmin during month 1

Body weight (kg)	Dose (IU)
< 46	7,500
46-56	10,000
57-68	12,500
69-82	15,000
≥83	18,000

Dose of Fragmin during months 2-6

Body Weight (kg)	Dose (IU)
<56	7,500
57 to 68	10,000
69 to 82	12,500
83 to 98	15,000
≥99	18,000

This treatment course is not recommended for patients weighing less than 40 kg.

The maximum daily dose is 18,000 IU. The recommended duration of treatment is 6 months. If you are suffering from severe kidney disease or a decreased platelet count (clotting cells) caused by chemotherapy or another condition with an elevated bleeding risk, your doctor will adjust this dose accordingly.

In some cases of decreased platelet count (clotting cells), your doctor may interrupt your treatment with Fragmin for a short period.

Medical staff may take blood samples during your treatment to monitor the effects of Fragmin.

How to Inject Fragmin

This section of the leaflet explains how you should go about injecting Fragmin yourself, but you should only do so if you have been given permission by your doctor. It is a simple process and one that you can do at home.

Fragmin is given by a small injection under the skin. You should inject (or give) the dose of Fragmin at the time recommended by your doctor.

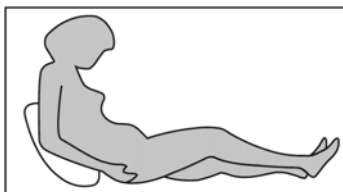
Please follow the steps explained below.

- Gather the single dose Fragmin syringe and the yellow sharps bin.
- Wash and dry your hands. The injection site should be cleaned.

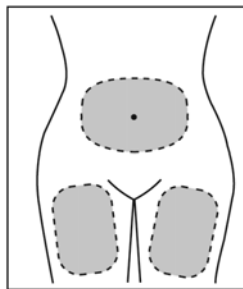
Please note that if a carer is doing the injecting, it is recommended that they wear gloves to perform the injection.

Step 1:

Get yourself in a comfortable sitting down position where you can see your stomach.

**Step 2:**

Choose an injection site either on your stomach or outer aspects of your left or right thigh (see shaded areas). Your stomach is usually best as the injection site and it is important that you change the site each time

**Step 3:**

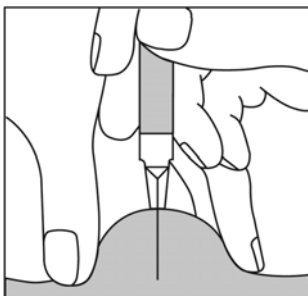
Pick up the syringe and remove the grey rubber cover by pulling it straight off. You will notice an air bubble in the syringe. It is supposed to be there and you can just ignore it. It is important not to press the plunger just yet as some of the medicine may be lost.

Step 4:

Hold the syringe in one hand and with the other hand, gently pinch a fold of skin with its fatty tissue (see the shaded areas above) between your thumb and index finger. This will be the injection site.

Step 5:

Hold the syringe above the folded skin keeping it at a right angle (ie vertically as in the diagram and not at an angle). Insert the needle into the skin until the needle is fully inserted

**Step 6:**

Now press the plunger and inject the Fragmin slowly until all of the medicine has been injected. Keep pinching the fold of skin while you are injecting and then release the fold of skin and pull the needle out.

If there is any oozing of blood at the injection site, apply gentle pressure. Do not rub the injection site as this may encourage bruising.

Dispose of the syringe in the yellow sharps bin provided. Keep your sharps bin out of reach of other people. When the sharps bin is almost full please speak to your doctor or nurse.

Children and adolescents

The dose will be based on both the child's age and weight. Younger children may need slightly more Fragmin per kg than adults. Your doctor will work out the right dose for you. Medical staff may take blood samples during your treatment to monitor the effects of Fragmin.

If you are given more Fragmin than you should

If you feel that you have been given more Fragmin than you should, inform your doctor or nursing staff immediately. Your doctor may initiate measures to decrease the risk of bleeding.

If you forget to use Fragmin

Tell your doctor or pharmacist if you think that a dose has been forgotten. A double dose should not be given to make up for a forgotten dose.

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

4. Possible side effects

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

Stop using Fragmin and talk to a doctor or nurse at once if you get any signs of a severe allergic reaction (such as difficulty breathing, swelling of the lips, mouth, throat or eyes)

- Common side effects (may affect up to 1 in 10 people):
 - A reversible decrease in the number of clotting cells (platelets) in your blood (Type I thrombocytopenia). This may make you bruise more easily.
 - Bleeding at any site
 - Certain substances produced by your liver may increase
 - Pain and reactions at the injection site
 - Haematoma – you may notice blood collecting under the skin

- Uncommon side effects (may affect up to 1 in 100 people):
 - Increased levels of potassium in your blood (symptoms may include temporary muscle weakness, loss of feeling and changes in your heartbeat)
 - Red skin rash and itchiness
 - Itching
 - Allergic reactions
- Rare side effects (may affect up to 1 in 1,000 people):
 - An immune system problem resulting in a severe decrease in the number of clotting cells (platelets) in your blood (Type II thrombocytopenia)
 - Alopecia (hair loss)
 - Painful skin lesions
- Not known (frequency cannot be estimated from the available data):
 - Bleeding inside or around your brain, symptoms may include sudden severe headache
 - Bleeding behind your abdomen (stomach), symptoms may include a feeling of tenderness and swelling around your stomach
 - Bruising of the spine which may lead to back pain, tingling, numbness or weakness in your legs, bowel or bladder problems

If you have an artificial heart valve, treatment with Fragmin might not be sufficient to prevent a blood clot, and you might develop a clot in the heart valve.

The adverse reactions in children are expected to be the same as in adults, however there is only a little information about the possible side effects of long term use in children.

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

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fragmin

Keep out of the sight and reach of children.
Fragmin should not be used after the expiry date, which is on the pack. The expiry date refers to the last day of that month.
Do not store above 25°C. Store in the original package.
Your doctor or nurse will store Fragmin in a safe place under the above conditions.
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. Contents of the pack and other information

The active ingredient in Fragmin is dalteparin sodium.
Each single dose pre-filled syringe contains dalteparin sodium 2,500 IU (anti-factor Xa) in 0.2 ml isotonic solution.
Excipients: water for injection, sodium chloride and sodium hydroxide or hydrochloric acid (for pH adjustments).

What Fragmin looks like and contents of the pack

Fragmin is available as a clear, colourless or straw-coloured solution in pre-filled single dose syringes with a rubber stopper.
Each pack contains 10 x 0.2 ml single dose pre-filled syringes.

Manufacturer and Product Licence holder

Manufactured by
Pfizer Manufacturing Belgium NV., Rijksweg 12, 2870 Puurs, Belgium.
Catalent France Limoges S.A.S., Z.I. Nord, 87 rue de Dion Bouton, 87000 Limoges, France.
Procured from the EU by Product Licence holder
Star Pharmaceuticals Ltd, 5 Sandridge Close, Harrow, Middlesex HA1 1XD.
Repackaged by Servipharm Ltd.

POM

Fragmin® 2,500 IU/0.2 ml Solution for Injection
PL 20636/2517

Leaflet issue and Revision date (Ref): 07.10.14[4]

Fragmin is trademark of Pfizer Health AB