Package leaflet: Information for the user

Tirofiban-Tchaikapharma 0,25 mg/ml concentrate for solution for infusion

Tirofiban

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 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 or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Tirofiban-Tchaikapharma is and what it is used for

Tirofiban-Tchaikapharma is used to help assist the blood flow to your heart and to help prevent chest pain and heart attacks. It works by preventing platelets, cells found in the blood, from forming blood clots. This medicine may also be used in patients whose heart vessels are dilated with a balloon - angioplasty (percutaneous coronary intervention or PCI). This is a procedure, possibly with implantation of a small tube-stent in the coronary artery, to improve the blood flow to the heart. Tirofiban-Tchaikapharma is intended for use with acetylsalicylic acid and unfractionated heparin.

2. What you need to know before you are given Tirofiban-Tchaikapharma

Do not use Tirofiban-Tchaikapharma
- if you are allergic (hypersensitive) to tirofiban or any of the other ingredients of Tirofiban-Tchaikapharma;
- if you are bleeding internally or have a history of bleeding internally within the last 30 days;
- if you have a history of bleeding in the brain, brain tumor or abnormal blood vessels in the brain;
- if you have severe uncontrolled high blood pressure (malignant hypertension);
- if you developed thrombocytopenia if you had received treatment with Tirofiban-Tchaikapharma or another medicine in the same group of drugs previously;
- if you have a history of stroke within the last 30 days or any history of stroke with bleeding;
- if you have been seriously injured or had a major operation within the last 6 weeks;
- if you have severe liver disease.

Your doctor will review your medical history to see if you are at an increased risk of any side effects associated with being given this medicine.

Warnings and precautions
Talk to your doctor before using Tirofiban-Tchaikapharma, if you have or have had:

- any medical problems;
- any allergies;
- cardiopulmonary resuscitation (CPR), a biopsy, or a procedure to break up kidney stones within the last 2 weeks;
- been seriously injured or had a major operation within the last 3 months;
- an ulcer in the stomach or intestine (duodenum) within the last 3 months;
- a recent bleeding disorder (within 1 year) such as bleeding in the stomach or intestine, or blood in your urine or stool;
- recent spinal procedure;
- A a history or symptoms of splitting of the aorta (aortic dissection);
- uncontrolled high blood pressure (hypertension);
- an inflammation of the lining around your heart (pericarditis);
- an inflammation of the blood vessels (vasculitis);
- problems with the blood vessels in the back of your eye (retina);
- treatment with medications that help to prevent or dissolve blood clots;
- kidney problems;
- a special intravenous line inserted under your collar bone within the last 24 hours;
- heart failure;
- very low blood pressure due to a failing heart (cardiogenic shock);
- a liver disorder;
- low blood count or anemia.

Other medicines and Tirofiban-Tchaikapharma

Tirofiban-Tchaikapharma can be used with other medicines. However, you need to tell your doctor about other medicines you are taking, including medicines obtained without a prescription, as some drugs may affect each other's action. It is especially important to tell your doctor if you are taking other medicines that help prevent your blood from clotting such as warfarin.

Tirofiban-Tchaikapharma with food, drink and alcohol
Food and drink have no effect on the treatment with this medicine.

Pregnancy, breastfeeding and fertility
You should tell your doctor if you are pregnant or suspect you may be pregnant. He/she must decide whether to use Tirofiban-Tchaikapharma. You should consult your doctor if you are breastfeeding or intend to breastfeed. Ask your doctor for advice before taking any medicine.

Driving and using machines
Due to your disease state, you will not be able to drive or operate machinery while Tirofiban-Tchaikapharma is being used.

3. How to use Tirofiban-Tchaikapharma

Tirofiban-Tchaikapharma should be prescribed by a qualified doctor who is experienced in the management of heart attacks.
Tirofiban-Tchaikapharma is administered intravenously by a medical person. Your doctor will decide on the appropriate dose, depending on your condition and your weight.

Use in children
Safety and efficacy in children have not been studied.

If you use more Tirofiban-Tchaikapharma than you should

Your individual dose of Tirofiban-Tchaikapharma has been carefully calculated by your doctor or pharmacist.

The most frequently reported symptom of overdose is bleeding. If you notice bleeding, you should notify your doctor immediately.

If you forget to use Tirofiban-Tchaikapharma
Your doctor will decide when to take the next dose of the medicine.

If you stop using Tirofiban-Tchaikapharma
Your doctor will decide when treatment should be stopped. However, if you wish to stop your treatment earlier, you should discuss other options with your doctor.

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

4. Possible side effects

Like all medicines, Tirofiban-Tchaikapharma can cause side effects, although not everybody gets them.

The most common side effect of treatment with Tirofiban-Tchaikapharma is bleeding which could occur anywhere in the body. This can become serious and may, rarely, be fatal.

If side effects occur, their treatment may be necessary. While using Tirofiban-Tchaikapharma, if you develop any of the following symptoms, you should contact your doctor immediately:
- signs of bleeding in the skull such as pain in the head, sensory impairments (visual or hearing), difficulties in speech, numbness or problems with movement or balance;
- signs of internal bleeding such as coughing up blood or blood in your urine or stool;
- signs of serious allergic reactions such as difficulties in breathing and dizziness.

Below is a list of side effects that have occurred in some people following treatment with Tirofiban-Tchaikapharma. The side effects are listed in decreasing order of frequency.

Very common side effects (affects 1 to 10 in 100 patients)
- Blood in urine;
- Coughing up of blood;
- Nose bleeds;
- Bleeding in the gums and mouth;
- Bleeding from vessel puncture site;
- Reduction in red blood cells (reduced haematocrit and haemoglobin);
- Decreases in platelet count below 90 000/mm^3
- Fever.

Rare side effects (affects 1 to 10 in 1000 patients)
- Bleeding in the stomach or intestines;
- Vomiting of blood;
- Decreases in platelet count below 50 000/mm^3.

Side effects with unknown frequency (cannot be calculated from available data):
- Bleeding in the skull;
- Haematoma in the spinal region;
- Bleeding in the abdomen of the internal organs;
- Accumulation of blood around the heart;
- Bleeding in the lung;
- Acute and/or severe decreases in platelet counts below 20 000/mm^3

- Severe allergic reactions with tightness of chest, hives or nettle rash, including reactions that cause difficulty in breathing and dizziness.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system to the Bulgarian Drug Agency. By reporting side effects you can help provide more information on the safety of this medicine.

Contacts:
Bulgarian Drug Agency
8 Damyan Gruev Str,
1303 Sofia, Bulgaria
Tel .: +359 2 8903417
website: www.bda.bg

5. How to store Tirofiban-Tchaikapharma

Your doctor or pharmacist will know how to store and dispose of this medicine.

Keep this medicine out of the sight and reach of children.

Store below 25°C. Do not freeze.

Do not use Tirofiban-Tchaikapharma after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

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 to protect the environment.

6. Contents of the pack and other information

What Tirofiban-Tchaikapharma contains:
The active substance is: tirofiban hydrochloride monohydrate

One milliliter of Tirofiban-Tchaikapharma concentrate for solution for infusion contains 0.281 mg tirofiban hydrochloride monohydrate equivalent to 0.25 mg tirofiban.

The other ingredients are: sodium dihydrogenphosphate dihydrate, mannitol, sodium hydroxide, hydrochloric acid, nitrogen, water for injections.

What Tirofiban-Tchaikapharma looks like and contents of pack
Tirofiban-Tchaikapharma is available as a concentrate for solution for infusion (vials of 50 ml).

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Tchaikapharma High Quality Medicines Inc.
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The following information is intended for healthcare professionals only:
This product is for hospital use only, by specialist physicians experienced in the management of acute coronary syndromes.

Posology and method of administration
In patients who are managed with an early invasive strategy for Non-ST-Segment Elevation Acute Coronary Syndrome (NSTE-ACS) but not planned to undergo angiography for at least 4 hours and up to 48 hours after diagnosis, Tirofiban-Tchaikapharma is given intravenously at an initial infusion rate of 0.4 microgram/kg/min for 30 minutes. At the end of the initial infusion, Tirofiban-Tchaikapharma should be continued at a maintenance infusion rate of 0.1 microgram/kg/min. Tirofiban-Tchaikapharma should be given with unfractionated heparin (usually an intravenous bolus of 5000 Units (U) simultaneously with the start of Tirofiban-Tchaikapharma therapy, then approx. 1000 U per hour, titrated on the basis of the activated partial thromboplastin time (APTT), which should be about twice the normal value) and oral antiplatelet therapy, including but not limited to acetylsalicylic acid, unless contraindicated.

In patients in the acute coronary syndrome group without ST elevation (NSTE-ACS), patients planned to undergo PCI within the first 4 hours of diagnosis or in patients with acute myocardial infarction intended for primary PCI, Tirofiban-Tchaikapharma should be administered utilizing an initial bolus of 25 microgram/kg given over a 3 minute period, followed by a continuous infusion at a rate of 0.15 microgram/kg/min for 12-24, and up to 48 hours. Tirofiban-Tchaikapharma should be administered with unfractionated heparin (dosage as above) and oral antiplatelet therapy, including but not limited to acetylsalicylic acid, unless contraindicated.

No dosage adjustment is necessary for the elderly.

Patients with severe kidney failure
In severe kidney failure (creatinine clearance < 30 ml/min) the dosage of Tirofiban-Tchaikapharma should be reduced by 50%.

Paediatric population
The safety and efficacy of Tirofiban-Tchaikapharma in children have not been established. There is insufficient clinical data on this.

Start and duration of treatment with Tirofiban-Tchaikapharma
In patients who are managed with an early invasive strategy for NSTE-ACS but not planned to undergo angiography for at least 4 hours and up to 48 hours after diagnosis, the Tirofiban-Tchaikapharma 0.4 microgram/kg/min loading dose regimen should be initiated upon diagnosis.

The recommended duration of the maintenance infusion should be at least 48 hours. Infusion of Tirofiban-Tchaikapharma and unfractionated heparin may be continued during coronary angiography and should be maintained for at least 12 hours and not more than 24 hours after angioplasty/atherectomy. Once a patient is clinically stable and no coronary intervention is planned by the treating physician, the infusion should be discontinued. The entire duration of treatment should not exceed 108 hours.

If the patient diagnosed with NSTE-ACS and managed with an invasive strategy undergoes angiography within 4 hours after the diagnosis, the Tirofiban-Tchaikapharma 25 microgram/kg dose bolus regimen should be initiated at the start of PCI with the infusion continued for 12-24 hours and up to 48 hours.
In patients with acute myocardial infarction intended for primary PCI, the bolus infusion regimen should be initiated as soon as possible after diagnosis.

Concurrent therapy (unfractionated heparin, oral antiplatelet therapy)
Treatment with unfractionated heparin is initiated with an intravenous bolus of 5000 units (U) and then continued with a maintenance infusion of 1000 units per hour. The heparin dosage is titrated to maintain an APTT of approximately twice the normal value. Unless contraindicated, all patients should receive oral antiplatelet agents, including but not limited to acetylsalicylic acid, before the start of Tirofiban-Tchaikapharma. This medication should be continued at least for the duration of the infusion of Tirofiban-Tchaikapharma. Most studies investigating the administration of Tirofiban-Tchaikapharma as an adjunct to PCI have used acetylsalicylic acid in combination with clopidogrel as oral antiplatelet therapy. The efficacy of Tirofiban-Tchaikapharma in combination with prasugrel or ticagrelor has not been established in randomized controlled trials after PCI and the sheaths should be withdrawn once coagulation has returned to normal, e.g. when the activated clotting time (ACT) is less than 180 seconds (usually 2-6 hours after discontinuation of heparin).

Incompatibilities
Incompatibility has been found with diazepam. Therefore, Tirofiban-Tchaikapharma and diazepam should not be administered in the same intravenous line. No incompatibilities have been found with Tirofiban-Tchaikapharma and the following intravenous formulations: atropine sulfate, dobutamine, dopamine, epinephrine HCl, furosemide, heparin, lidocaine, midazolam HCl, morphine sulfate, nitroglycerin, potassium chloride, propranolol HCl, and famotidine injection.

Instructions for use
Tirofiban-Tchaikapharma concentrated solution should be diluted before use:

1. Withdraw 250 ml sterile 0.9% physiological serum or 5% glucose solution, withdraw 50 ml and replace with 50 ml Tirofiban-Tchaikapharma (one vial of 50 ml) to obtain a solution of 50 µg/ml. Shake well before infusion.
2. Use the dosages listed in the table below.

The table below provides instructions for adjusting the dose according to the patient's weight.
Tirofiban-Tchaikapharma concentrate for intravenous administration should first be diluted to the required concentration, as explained in the Instructions for use.

Patient weight (kg)	0.4 microgram/kg/min Loading dose regimen Most patients		0.4 microgram/kg/min Loading dose regimen Severe kidney failure		25 microgram/kg Dose bolus regimen Most patients		25 microgram/kg Dose bolus regimen Severe kidney failure	
	30 min Loading infusion rate (ml/hr)	Maintenance infusion rate (ml/hr)	30 min Loading infusion rate (ml/hr)	Maintenance infusion rate (ml/hr)	Bolus (ml)	Maintenance infusion rate (ml/hr)	Bolus (ml)	Maintenance infusion rate (ml/hr))
30-37	16	4	8	2	17	6	8	3
38-45	20	5	10	3	21	7	10	4

46-54	24	6	12	3	25	9	13	5
55-62	28	7	14	4	29	11	15	5
63-70	32	8	16	4	33	12	17	6
71-79	36	9	18	5	38	14	19	7
80-87	40	10	20	5	42	15	21	8
88-95	44	11	22	6	46	16	23	8
96-104	48	12	24	6	50	18	25	9
105-112	52	13	26	7	54	20	27	10
113-120	56	14	28	7	58	21	29	10
121-128	60	15	30	8	62	22	31	11
129-137	64	16	32	8	67	24	33	12
138-145	68	17	34	9	71	25	35	13
146-153	72	18	36	9	75	27	37	13

Where the solution and the vial permit, parenteral preparations should be inspected for visible particles or discolouration before use.
Tirofiban-Tchaikapharma should only be given intravenously and may be administered with unfractionated heparin through the same infusion tube.
It is recommended that Tirofiban-Tchaikapharma be administered with a calibrated infusion set using sterile equipment.
Care should be taken to ensure that no prolongation of the infusion of the initial dose occurs and that miscalculation of the infusion rates for the maintenance dose on the basis of the patient’s weight is avoided.