PATIENT INFORMATION LEAFLET

AGREDUR READY 50 mcg/mL Solution for I.v. Infusion
Administered intravenously
Sterile

- ***Active Substance:*** Each ml contains 0,0562 mg tirofiban hydrochloride equivalent to 0,05 mg tirofiban.
- ***Excipients:*** Sodium chloride, soium citrate dihydrate, citric acid anhidr, water for injection, hydrochloric acid and/or sodium hydroxide.

Before using this medicine, read all of this PATIENT INFORMATION LEAFLET carefully. Because, this leaflet includes important information for you.

- *Keep this PATIENT INFORMATION 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.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow the written instructions exactly. Do not use **higher or lower** dose than the recommended dose.*

What is in this leaflet

1. ***What AGREDUR READY is and what it is used for?***

AGREDUR READY is a dilute, sterile, colorless solution, presented as ready-to-use, and is available in PP (Polypropylene) bags of 100 and 250 ml. AGREDUR READY is a medicine that should only be prepared and administered by your doctor.
AGREDUR READY is used to help blood flow to your heart and to help prevent chest pain and heart attacks.

It acts by preventing platelets, which are cells in the blood, from forming clots.
This drug is also used in patients whose heart vessels are dilated with a balloon (percutaneous coronary intervention or PCI). This is a procedure usually done by inserting a small tube (stent) to increase the flow of blood to the heart.

AGREDUR READY is designed to be used with other blood thinning medicines.

2. ***What you need to know before use AGREDUR READY?***
DO NOT use AGREDUR READY in the following situations:
If;

- you are hypersensitive to the active substance of the drug (tirofiban) or any of its ingredients,
- you have internal bleeding or have experienced internal bleeding in the last 30 days.

- you have experienced bleeding in the skull (intracranial), a tumor, a malformation in the blood vessels in the skull or an aneurysm,
- you have severe high blood pressure that cannot be controlled (malignant hypertension),
- you have low blood platelet count (thrombocytopenia) or have problems with your blood clotting,
- you have had a decrease in the number of thrombocytes (thrombocytopenia) while taking AGREDUR READY or another drug in the same group,
- you have had a stroke in the last 30 days or have a history of any bleeding (haemorrhagic) stroke.
- you have had a serious injury or major surgery within the last 6 weeks,
- you have severe liver failure,

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

USE AGREDUR READY CAREFULLY in the following cases
If;

- you have an existing chronic disease
- you are hypersensitive to anything,
- you have had heart massage (cardiopulmonary resuscitation), breaking kidney stones or taking a biopsy in the last 2 weeks,
- you have had a serious injury or major surgery within the last 3 months.
- you have had a stomach or small intestine (duodenal) ulcer in the last 3 months,
- recent bleeding disorder (last 1 year); for example (gastrointestinal) gastrointestinal bleeding or blood in the urine or feces
- you have recently had a procedure in your spine or coccyx (spinal / epidural procedures)
- you have a history or symptoms of opening (dissection) of the aorta, the main vein to the heart,
- you have uncontrolled high blood pressure (hypertension),
- you have inflammation in the tissue surrounding your heart (pericarditis)
- you have inflammation of the blood vessels (vasculitis)
- you have problems with the blood vessels in the retina of the eye (retinopathy).
- you are being treated with medicines that help prevent or dissolve blood clots,
- you have kidney problems
- a special intravenous catheter was placed under your collarbone in the last 24 hours,
- you have heart failure
- you have very low blood pressure due to heart failure (cardiogenic shock),
- you have liver problems
- you have low blood cell counts or anemia.

If these warnings are valid for you, even at any time in the past, please consult your doctor.

Using AGREDUR READY with food and drink
With AGREDUR READY, it can be applied on an empty or full stomach. Food and drink have no effect on this medicine.

Pregnancy
Consult your doctor or pharmacist before using this medication.
AGREDUR READY should not be used during pregnancy unless absolutely necessary.
If you are pregnant or suspect of pregnancy, your doctor will decide whether to take AGREDUR READY.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Lactation
Consult your doctor or pharmacist before using this medication.
Please inform your doctor if you are breastfeeding your child. Your doctor will tell you whether it is appropriate for you to use this medicine.

Ability to drive and use machines
While using AGREDUR READY, depending on the condition of your illness, you may not be able to drive or use machinery.

Important information about some of the excipients contained in AGREDUR READY
This medicinal product contains less than 1 mmol (23 mg) of sodium per each 100 ml; that is, it does not contain sodium.

Use in combination with other drugs
Generally AGREDUR READY can be used with other medicines. However, it is important to tell your doctor about any other drug you are taking, including over-the-counter drugs, as some drug can affect each other. It is especially important to tell your doctor if you are taking other medicines that prevent your blood from clotting (such as warfarin).

If you are currently taking or recently took any prescribed or over-the-counter drugs, please inform your physician or pharmacist.

3. *How to use AGREDUR READY?*

- **Instructions regarding correct use and dosage/administration frequency:**

You have been or are planned to be given AGREDUR READY by a specialist in heart health.
Your doctor will determine the dose of your medicine and apply it to you, depending on the condition of your disease and your weight.

- **Method of administration:**

AGREDUR READY will be administered to you by slow injection (intravenous administration).

- **Different age groups:**

Usage in children:
It is not recommended for use in children.

Usage in elderly
Dosage adjustment is not required in the elderly.

- **Conditions of special use:**

Renal failure
If you have severe renal impairment (creatinine clearance <30 ml/min) your dose of AGREDUR READY will be reduced by 50% by your doctor.

Liver failure
Do not use AGREDUR READY in severe liver failure.

Talk to your doctor or pharmacist if you have the impression that the effect of AGREDUR READY is too strong or too weak.

If you use more AGREDUR READY than you should:
The dosage schedule will be adjusted by your doctor according to your condition and response to treatment. In the event of overdose, the most commonly reported symptom is bleeding. If you notice bleeding, you should inform your healthcare provider immediately.

If you use more AGREDUR READY than you should, talk to a doctor or pharmacist.

If you forget to use AGREDUR READY:
The dosage schedule will be adjusted by your doctor according to your condition and response to treatment.

Do not take a double dose to make up for forgotten doses.

If AGREDUR READY treatment stopped, effects may occur:
Do not end your treatment without consulting your doctor. Your doctor will decide when your treatment will end. However, if you want to end your treatment early, you should discuss other possibilities with your doctor.

4. Possible side effects
Like all other medicines, AGREDUR READY may cause side effects in patients with hypersensitivity to any component of the drug.
The most common side effect of AGREDUR READY treatment is bleeding that can occur anywhere in the body. This condition can become serious and rarely fatal.

You may need medical help if side effects occur.

If one of following occurs tell your doctor immediately:
Symptoms that indicate bleeding in the skull, such as headache, sensory disturbances (visual or auditory), difficulty speaking, numbness, or problems with movement or balance,

- Signs of internal bleeding, such as coughing up blood or blood in your urine or stools
- Signs of a serious allergic reaction such as difficulty breathing or dizziness.

A list of side effects that occur in some people after treatment with AGREDUR READY are listed as shown in the following categories. This list is sorted in descending order of frequency of side effects:

Very common	: can be seen in at least 1 in 10 patients
Common	: less than 1 in 10 patients, but more than 1 in 100 patients.
Uncommon	: less than 1 in 100 patients, but more than 1 in 1,000 patients.
Rare	: less than 1 in 1,000 patients, but more than 1 in 10,000 patients.
Very rare	: less than 1 in 10,000 patients can be seen.
Unknown	: it cannot be estimated from the available data.

Very common:

- Post-operative bleeding
- Subcutaneous bleeding causing swelling at the injection site or muscles
- Small red bruises on the skin
- Occult blood in urine or stool
- Nausea
- Headache

Common:

- Blood in urine
- Coughing up blood
- Nosebleeds
- Bleeding gums and bleeding in the mouth
- Bleeding from the puncture sites
- Reduction in red blood cells (decreased hematocrit and hemoglobin)
- Platelet count falling below 90,000 / mm3
- Fever

Uncommon:

- Bleeding in the stomach or intestines
- Vomiting blood
- Platelet count falling below 50,000/mm^3

Unknown:

- Bleeding inside the skull
- Hematoma in the spine area (collection of blood in the tissue)
- Bleeding of internal organs in the abdominal cavity
- Blood collecting around the heart
- Bleeding in the lungs
- Sudden and/or severe decrease in thrombocyte count of less than 20,000/mm^3
- Severe allergic reactions in the form of urticaria, hives, chest tightness, including difficulty in breathing and dizziness

Inform your doctor or pharmacist if you encounter any side effects not mentioned in these instructions for use.

5. How to store AGREDUR READY?
Keep AGREDUR READY out of the reach and sight of children and store in its original package.

Store at room temperature below 25°C.

Use in accordance with expiration dates.
Do not use AGREDUR READY after the expiry date on the packaging.

If you notice any damage to the product and/or packaging, do not use AGREDUR-READY. Do not freeze. Store in the original packaging to protect from light.

Do not throw away expired or unused medicines! Give to the collection system determined by the Ministry of Environment and Urbanization.

Marketing Authorization Holder:
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This patient leaflet was approved on 03.10.2019.

THE FOLLOWING INFORMATION IS FOR THE HEALTH PERSONNEL WHO WILL APPLY THIS MEDICINE.

Administration instructions:

AGREDUR READY is a medicine that should only be prepared and administered by a doctor.

Incompatibilities:

Incompatibility has been reported with diazepam. Therefore AGREDUR READY should not be used through the same intravenous route as diazepam.

This product should only be administered in a hospital by specialist physicians experienced in the treatment of acute coronary syndromes. AGREDUR READY is ready to use. It should not be diluted.

	0,4 mcg/kg/minute Loading Dose In Most Patients		**0,4 mcg/kg/minute Loading Dose Severe Renal Failure**		**25 mcg/kg Bolus Dose In Most Patients**		**25 mcg/kg Bolus Dose Severe Renal Failure**	
Patient Weight (kg)	30 minutes Loading Infusion Rate (ml/hour)	Maintanence Infusion Rate (ml/hour)	30 minutes Loading Infusion Rate (ml/hour)	Maintanence Infusion Rate (ml/hour)	Bolus (ml)	Maintanence Infusion Rate (ml/hour)	Bolus (ml)	Maintanence Infusion Rate (ml/hour)
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

Frequency and Duration of administration:

In patients who are treated for NSTE-ACS by an early invasive route and are not scheduled to have angiography for at least 4 to 48 hours after diagnosis, AGREDUR READY is administered intravenously for 30 minutes at an initial infusion rate of 0.4 micrograms (mcg)/kg/min. At the end of the initial infusion, AGREDUR READY should be continued at a maintenance infusion rate of 0.1 microgram (mcg)/kg/min. AGREDUR READY, unfractionated heparin (usually 50-60 units [U]/kg intravenously with the initiation of AGREDUR READY therapy, then titrated to keep the activated thromboplastin time (APTT) at approximately twice the normal value, approximately 1000 U/hour and should be given together with oral antiplatelet therapy, including, but not limited to, ASA, unless contraindicated.

In NSTE-ACS patients planned to undergo Percutaneous Coronary Intervention (PCI) in the first 4 hours of diagnosis or in patients who have had acute myocardial infarction and who are required to perform primary PCI; It should be administered as an initial bolus dose of 25 micrograms/kg

over a 3-minute period followed by a continuous infusion of up to 48 hours at a rate of 0.15 micrograms/kg per minute for 12-24 hours. AGREDUR READY should be given in conjunction with unfractionated heparin (at the doses specified above) and oral antiplatelet therapy, including but not limited to ASA, unless contraindicated (see section 5.1).

Starting AGREDUR READY treatment and duration of treatment
In patients treated for NSTE-ACS by an early invasive route and for whom angiography is not planned for at least 4 to 48 hours after diagnosis, a loading dose of 0.4 micrograms/kg/min of AGREDUR READY should be initiated at the time of diagnosis. The 0.4 microgram/kg/min loading dose regimen should be initiated according to the diagnosis. The recommended time is at least 48 hours. The infusion of AGREDUR READY and unfractionated heparin can be continued during coronary angiography and should be maintained for a minimum of 12 hours and a maximum of 24 hours after angioplasty/atherectomy. The infusion should be discontinued when the patient is clinically stabilized and no coronary intervention procedure is planned by the treating physician. The whole treatment period should not exceed 108 hours.

If angiography is performed within 4 hours after diagnosis in a patient diagnosed with NSTE-ACS and treated by an invasive way, a bolus dose of 25 micrograms/kg AGREDUR READY should be initiated at the beginning of PCI for 12-24 hours and up to 48 hours. In patients with acute myocardial infarction undergoing primary PCI, a bolus dose of 25 micrograms/kg should be initiated as soon as the diagnosis is made.

Concomitant therapy (unfractionated heparin, oral antiplatelet therapy)
Unfractionated heparin treatment is started with 50-60 U/kg I.V. bolus and then continued with a 1000 U maintenance infusion per hour. The dose of heparin is titrated to maintain APTT approximately twice the normal value.

Unless contraindicated, all patients should take oral antiplatelet medications, including but not limited to ASA, before starting AGREDUR READY (see Section 5.1). These drugs should be continued for at least the duration of the AGREDUR READY infusion. Clopidegrel has been used as oral antiplatelet therapy with ASA in many studies investigating the use of AGREDUR READY as an adjunct to PCI treatment. The effectiveness of the combination of AGREDUR READY with prasurgel or ticagrelor has not been proven in randomized controlled studies.

If angioplasty (PTCA) is required, heparin should be discontinued after PTCA, and the sheaths should be removed as soon as clotting returns to normal, that is active clotting time (ACT) falls below 180 seconds (usually 2-6 hours after heparin discontinuation).

- There is no need for dose adjustment for the elderly.
- In case of severe renal impairment (creatinine clearance <30 ml/min) the dose should be reduced by 50%.

Method of Administration:
AGREDUR READY is ready to use. It should not be diluted.
Use according to the dosage table above.

Before parenteral drugs are used, the solution and bag, if appropriate, should be checked for visible particles or discoloration.

AGREDUR READY should only be administered intravenously and can be administered with unfractionated heparin from the same infusion tube.

It is recommended that AGREDUR READY be administered with a calibrated infusion set using sterile equipment.

Care should be taken not to prolong the initial dose infusion time and not to make mistakes in calculating maintenance dose infusion rates based on the patient's body weight.

Special precautions for storage
Do not use AGREDUR READY after the expiry date on the label and box. The expiry date refers to the last day of the relevant month.
Do not freeze. Store in the original packaging to protect from light.