

AGREDUR READY 50 mcg/ml I.V. solution for infusion

For intravenous infusion. · Sterile

Prescription only

Platelet Aggregation Inhibitor

Active substance:
Tirofiban

COMPOSITION

Active substance: Each mL contains 50 micrograms of tirofiban equivalent to 56.2 micrograms of tirofiban hydrochloride monohydrate.

Excipient(s): Sodium chloride, sodium citrate dihydrate, anhydrous citric acid, water for injection, hydrochloric acid and/or sodium hydroxide (for pH adjustment).

Packaging: Available in 100 and 250 mL PP (Polypropylene) bags.

IMPORTANT

Before you start using this medicine, read this USER MANUAL carefully, because it contains important information for you. Keep this user manual. You may need to read it again later. If you have any further questions, please ask your doctor or pharmacist.

This medicine has been prescribed for you personally, do not give it to others. When you visit a doctor or hospital during the use of this medicine, tell your doctor that you are using this medicine. Follow the instructions in this manual exactly. Do not use a **higher or lower** dose than the dose recommended for you.

IN THIS USER MANUAL:

- [1.What is AGREDUR READY and what is it used for?](#)
- [2.Things to consider before using AGREDUR READY](#)
- [3.How to use AGREDUR READY?](#)
- [4.What are the possible side effects?](#)
- [5.Storage of AGREDUR READY](#)

What is AGREDUR READY and what is it used for?

AGREDUR READY is a member of a group of medicines called platelet aggregation inhibitors (which prevent platelets from clumping together).

AGREDUR READY is a ready-to-use, sterile, colorless solution supplied in 100 and 250 mL PP (Polypropylene) bags. AGREDUR READY is a medicine that must only be administered by your doctor.

A decrease in blood flow to the heart can cause unstable angina and chest pain. AGREDUR READY has been prescribed to support blood flow to the heart, to prevent chest pain and associated heart attack.

AGREDUR READY is also used in patients undergoing balloon-type procedures (percutaneous coronary angioplasty) on the coronary arteries to improve blood flow to the heart. These procedures include the placement of a stent in the coronary arteries to improve blood flow to the heart.

AGREDUR READY works by preventing platelets (platelets are blood cells that form clusters during blood clotting) in the bloodstream from clotting. By blocking a receptor on the platelet, it prevents platelets from sticking together to form blood clots

and thereby reduces blood flow to the heart, which can cause chest pain and heart attacks.

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

Things to consider before using AGREDUR READY

DO NOT USE AGREDUR READY in the following conditions

If you have hypersensitivity to the active substance (tirofiban) or any of the excipients,

If you have internal bleeding or have had internal bleeding in the last 30 days,

If you have had intracranial hemorrhage, intracranial tumor, vascular malformation, or aneurysm,

If you have uncontrolled severe high blood pressure (malignant hypertension),

If your platelet count is low (thrombocytopenia) or if you have problems with blood clotting,

If you have previously developed a decrease in platelet count (thrombocytopenia) while taking AGREDUR READY or another medicine from the same group,

If you have had a stroke in the last 30 days or have a history of hemorrhagic stroke,

If you have had a serious injury or major surgery in the last 6 weeks,

If you have severe liver failure,

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

USE AGREDUR READY with CAUTION in the following conditions

If you have an existing chronic illness,

If you have an allergic constitution,

If you have undergone cardiopulmonary resuscitation, lithotripsy for kidney stones, or biopsy procedures in the last 2 weeks,

If you have had a serious injury or major surgery in the last 3 months,

If you have had a stomach or small intestine (duodenal) ulcer in the last 3 months,

If you have had a recent bleeding disorder (within the last 1 year); for example, gastrointestinal bleeding or blood in urine or stool,

If you have recently had a procedure on your spine or tailbone (spinal/epidural procedure),

If you have a history or symptoms of dissection of the aorta (the main vessel going to the heart),

If you have uncontrolled high blood pressure (hypertension),

If you have inflammation of the tissue surrounding the heart (pericarditis),

If you have inflammation of blood vessels (vasculitis),

If you have problems with the blood vessels in the retina of the eye (retinopathy),

If you are being treated with medicines that help prevent or dissolve blood clots,

If you have kidney problems,

If a special intravenous catheter has been placed under your collarbone in the last 24 hours,

If you have heart failure,

If you have very low blood pressure due to heart failure (cardiogenic shock),

If you have liver impairment,

If you have low blood cell count or anemia.

If any of these warnings apply to you, even if they applied in the past, please consult your doctor.

Use of AGREDUR READY with food and beverages

AGREDUR READY can be administered with or without food. Food and beverages have no effect on this medicine.

Pregnancy

Consult your doctor or pharmacist before using the medicine.

AGREDUR READY should not be used during pregnancy unless absolutely necessary.

If you are pregnant or suspect you may be pregnant, your doctor will decide whether you should take AGREDUR READY.

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

Breast-feeding

Consult your doctor or pharmacist before using the medicine.

If you are breast-feeding, please inform your doctor. Your doctor will tell you if it is appropriate for you to use this medicine.

Driving and using machines

Depending on the state of your illness, you may not be able to drive or use machines while using AGREDUR READY.

Important information about some excipients in AGREDUR READY

This medicinal product contains less than 1 mmol (23 mg) sodium per 100 mL; i.e., it is essentially "sodium-free".

Use with other medicines

In general, AGREDUR READY can be used with other medicines. However, since some medicines can alter each other's effects, it is important that you tell your doctor about any other medicines you are taking, including over-the-counter medicines. It is particularly important that you inform your doctor if you are taking other medicines that prevent blood clotting (such as warfarin).

If you are currently using or have recently used any prescribed or over-the-counter medicines, please inform your doctor or pharmacist about them.

How to use AGREDUR READY?

Instructions for correct use and dose/administration frequency:

AGREDUR READY has been given to you or is planned to be given to you by a physician specialized in heart health.

Your doctor will determine the dose of your medicine based on the state of your illness and your weight, and will administer it to you.

Route and method of administration:

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

Different age groups:**Use in children:**

Safety and efficacy have not been established in children. Use is not recommended.

Use in the elderly:

No dosage adjustment is required in the elderly.

Special use conditions:**Renal impairment:**

If you have severe renal impairment (creatinine clearance <30 mL/min), inform your doctor. Your doctor will reduce your AGREDUR READY dose.

Hepatic impairment:

Do not use AGREDUR READY in severe hepatic impairment.

If you have the impression that the effect of AGREDUR READY is too strong or too weak, talk to your doctor or pharmacist.

If you have used more AGREDUR READY than you should:

The dose of AGREDUR READY will be carefully adjusted by your doctor according to your condition and your response to treatment. In case of overdose, the most frequently reported symptom is bleeding. Accordingly, if you notice bleeding or think you have been given too high a dose of AGREDUR READY, contact your doctor or other healthcare professional immediately.

If you have used 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 your response to treatment. *Do not take a double dose to make up for a missed dose.*

Effects that may occur when treatment with AGREDUR READY is discontinued

Do not stop your treatment without consulting your doctor. Your doctor will decide when to stop your treatment. However, if you wish to end your treatment early, you should discuss other options with your doctor.

What are the possible side effects?

Like all medicines, AGREDUR READY may cause side effects in people who are sensitive to the substances in its composition.

The most common side effect seen with AGREDUR READY treatment is bleeding that may occur anywhere in the body. This may become serious and rarely may be fatal.

If side effects occur, they may require medical intervention.

Inform your doctor immediately if you notice any of the following:

Symptoms indicating intracranial bleeding such as headache, sensory disturbances (visual or auditory), difficulty speaking, numbness, and problems with movement or balance,

Symptoms indicating internal bleeding such as coughing up blood, blood in urine or stool,
Symptoms of serious allergic reactions such as difficulty breathing and dizziness.

The side effects that occurred in some people after AGREDUR READY treatment are listed below, categorized as shown. This list is classified from most to least frequent:

Very common: May occur in at least 1 in 10 patients

Common: May occur in less than 1 in 10 patients, but more than 1 in 100 patients.

Uncommon: May occur in less than 1 in 100 patients, but more than 1 in 1,000 patients.

Rare: May occur in less than 1 in 1,000 patients, but more than 1 in 10,000 patients.

Very rare: May occur in less than 1 in 10,000 patients.

Unknown: Cannot be estimated from available data.

Very common:

Bleeding after surgery

Bleeding at the injection site, under the skin, or in the muscle causing swelling

Small red bruises on the skin

Hidden (occult) blood in urine or stool

Nausea

Headache

Common:

Blood in urine

Coughing up blood

Nosebleeds

Bleeding gums and oral bleeding

Bleeding from vascular puncture sites

Decrease in red blood cells (low hematocrit and hemoglobin)

Platelet count dropping below 90,000/mm³

Fever

Uncommon:

Bleeding in the stomach or intestines

Vomiting blood

Platelet count dropping below 50,000/mm³

Unknown:

Intracranial bleeding

Blood accumulation in the spinal cord area (hematoma)

Internal organs bleeding into the abdominal cavity

Blood accumulation around the heart

Bleeding in the lungs

Sudden and/or severe drop in platelet count below 20,000/mm³

Severe allergic reactions including urticaria (hives), rash, or chest tightness with reactions causing difficulty breathing and dizziness.

If you experience any side effect not mentioned in this user manual, please inform your doctor or pharmacist.

Reporting of side effects

If you experience any side effect, whether or not listed in the User Manual, talk to your doctor, pharmacist, or nurse. Additionally, report the side effects you experience to the Turkish Pharmacovigilance Center (TÜFAM) by clicking on the "Drug Side Effect Reporting" icon on the website www.titck.gov.tr or by calling the side effect reporting line at 0 800 314 00 08. By reporting side effects, you can contribute to obtaining more information about the safety of the medicine you are using.

Storage of AGREDUR READY

Store AGREDUR READY out of the sight and reach of children, in its packaging.

Store at room temperature below 25°C.

Use in accordance with the expiration date.

Do not use AGREDUR READY after the expiration date on the packaging.

If you notice any defects in the product and/or packaging, do not use AGREDUR READY.

Do not throw away medicines that have expired or are no longer used!

Dispose of them through the collection system determined by the Ministry of Environment, Urbanisation and Climate Change.

THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ADMINISTERING THIS MEDICINE.

This product should only be administered in hospitals, by specialist physicians experienced in the treatment of acute coronary syndromes. AGREDUR READY should be administered in combination with fractional heparin and oral antiplatelet therapy including acetylsalicylic acid (ASA).

Administration frequency and duration

In non-ST elevation unstable angina patients managed with an early invasive strategy in whom angiography is not planned for at least 4 hours and up to 48 hours after diagnosis, AGREDUR READY is administered intravenously at an initial infusion rate of 0.4 micrograms/kg/min for 30 minutes. At the end of the initial infusion, AGREDUR READY should be continued at a maintenance infusion rate of 0.1 micrograms/kg/min. AGREDUR READY is administered with unfractionated heparin (generally given as an intravenous bolus dose of 5000 U (units) at the start of AGREDUR READY treatment, then titrated to approximately 1000 U/hour based on activated partial thromboplastin time which should be maintained at approximately twice normal) and antiplatelet therapy including but not limited to ASA, unless contraindicated.

Patients undergoing Percutaneous Coronary Intervention

In patients with non-ST elevation acute coronary syndrome in whom percutaneous coronary intervention is planned within the first 4 hours after diagnosis, or in patients with acute myocardial infarction primarily intended for percutaneous coronary

intervention, it should be administered following an initial bolus of 25 micrograms/kg tirofiban over 3 minutes, with a continuous infusion at 0.15 micrograms/kg/minute for 12-24 hours and up to 48 hours. Tirofiban is administered with unfractionated heparin (at the dose given above) and antiplatelet therapy including but not limited to ASA, unless contraindicated.

Initiation of AGREDUR READY treatment and treatment duration

In non-ST elevation acute coronary syndrome patients managed with an early invasive strategy in whom angiography is not planned for at least 4 hours and up to 48 hours after diagnosis, the 0.4 micrograms/kg/min loading dose regimen should be initiated upon diagnosis. The 0.4 micrograms/kg/min loading dose regimen should be initiated. The recommended duration of maintenance infusion should be at least 48 hours. AGREDUR READY and unfractionated heparin infusion may be continued during coronary angiography and should be maintained for at least 12 hours and up to 24 hours after angioplasty/atherectomy. Infusion should be discontinued when the patient is clinically stabilized and no coronary intervention procedure is planned by the treating physician. The total treatment duration should not exceed 108 hours.

In patients diagnosed with non-ST elevation acute coronary syndrome (NSTEMI-ACS) who are treated with an invasive strategy and undergo angiography within 4 hours after diagnosis, a 25 micrograms/kg tirofiban bolus dose should be initiated at the start of percutaneous coronary intervention (PCI), and continued with infusion for 18-24 hours and up to 48 hours.

In patients with acute myocardial infarction primarily directed to percutaneous intervention (PCI), the bolus dose regimen should be initiated as soon as possible after diagnosis.

Concurrent treatment (unfractionated heparin, oral antiplatelet therapy including ASA)

Treatment with unfractionated heparin is initiated with 5000 U, I.V. bolus and then continued with a maintenance infusion of 1000 U per hour. Heparin dose is titrated to maintain aPTT at approximately twice the normal value.

Unless contraindicated, all patients should receive oral antiplatelet agents including but not limited to ASA before starting AGREDUR READY (see Summary of Product Characteristics). This medicine should be continued at least during the duration of AGREDUR READY infusion.

In most studies investigating the use of tirofiban as an adjunct to percutaneous intervention, clopidogrel has been used as oral antiplatelet therapy together with ASA. The efficacy of the combination of tirofiban with prasugrel or ticagrelor has not been established in randomized controlled studies.

If angioplasty (PTCA) is required, heparin should be discontinued after PTCA, and sheaths should be removed as soon as coagulation returns to normal, i.e., when activated clotting time (ACT) falls below 180 seconds (usually 2-6 hours after heparin is discontinued).

No dosage adjustment is required for the elderly.

In severe renal impairment (creatinine clearance < 30 mL/min), the dose should be reduced by 50%.

There is no experience with tirofiban treatment in the pediatric population; therefore, use is not recommended.

Incompatibilities

Incompatibility with diazepam has been identified. Therefore, tirofiban and diazepam should not be administered in the same intravenous line.

Method of administration

Using the container

To open: Tear the packaging from the top and remove the bag containing the solution. Some opacity may be seen on the plastic due to moisture absorption during sterilization. This is normal and does not affect the quality and safety of the solution. The opacity will disappear over time. Check the inner bag by squeezing for leakage. If leakage is found, discard the solution as sterility may be compromised. Do not use if the solution is not clear or if the packaging is damaged.

Do not add supplementary medication or withdraw solution directly from the bag with a syringe.

WARNING: Do not use plastic containers in series connections. This type of use can cause air embolism due to residual air being withdrawn from the first container before fluid delivery from the secondary container is complete.

Preparation for administration

1. Hang the medicine bag on an IV pole.
2. Twist the plastic twist-off at the outlet at the bottom of the container.
3. Attach the administration set. Refer to the accompanying set for instructions to complete.
4. Use according to the dosage table.

Parenteral products should be inspected visually for particulate matter and discoloration prior to use, as permitted.

AGREDUR READY should only be given by the intravenous route and can be administered through the same infusion line with unfractionated heparin.

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

Care should be taken to avoid errors when calculating the initial dose infusion duration and maintenance dose infusion rates based on patient body weight.

A guide for dose adjustment based on body weight is provided.

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

Marketing Authorization Holder

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