

PATIENT INFORMATION

THROMBOREDUCTIN 0.5 MG CAPSULES

For oral use.

Active ingredient: One capsule contains 0.57 mg anagrelide hydrochloride (equivalent to 0.5 mg anagrelide).

Excipients: Lactose monohydrate (derived from rennet obtained from calf stomach), povidone, crospovidone, microcrystalline cellulose, magnesium stearate, titanium dioxide, indigo carmine, gelatin (bovine gelatin)

Read these PATIENT INFORMATION carefully before you start using this medicine, because it contains important information for you.

- **Keep these instructions for use. You may need to read them again later.**
- **If you have any additional questions, please consult your doctor or pharmacist.**
- **This medicine has been prescribed for you personally, do not give it to others.**
- **When you go to a doctor or hospital during the use of this medicine, tell your doctor that you are using this medicine.**
- **Follow the instructions written in this leaflet exactly. Do not use high or low doses other than the dose recommended for you for this medicine.**

In These Instructions for Use;

1. What is THROMBOREDUCTIN and what is it used for?

2. Things to consider before using THROMBOREDUCTIN

3. How to use THROMBOREDUCTIN?

4. What are the possible side effects?

5. How to store THROMBOREDUCTIN?

are included.

1. What is THROMBOREDUCTIN and what is it used for?

- THROMBOREDUCTIN is a medicine used in the treatment of hereditary thrombocythemia (excessive proliferation of platelets in the blood) by reducing the number of platelets, which play an important role in blood clotting.
- THROMBOREDUCTIN is in plastic bottles containing 100 capsules.
- THROMBOREDUCTIN is in the form of blue capsules containing 0.5 mg anagrelide.
- THROMBOREDUCTIN is indicated for the treatment of essential thrombocythemia with high vascular risk (an excessive increase in blood platelets without a known cause, with a high risk of vascular disease) in patients who are unresponsive to hydroxyurea and aspirin treatment, or who develop anemia and/or leukopenia (decrease in white blood cell count) to an intolerable degree after hydroxyurea use, and/or venous thrombosis (formation of blood clots in veins).

[Page: 1]

- Additionally, THROMBOREDUCTIN may be used in the treatment of thrombocytosis (increase in platelet count in the blood) developing during the course of myeloproliferative diseases (bone marrow diseases), if a response cannot be achieved with hydroxyurea under the above conditions.
- Lactose monohydrate, one of the excipients, is derived from rennet obtained from calf stomach, and gelatin is derived from bovine.

2. Things to consider before using THROMBOREDUCTIN

DO NOT USE THROMBOREDUCTIN in the following situations

If;

- You have hypersensitivity to anagrelide or to lactose or other excipients in the medicine,

- You have heart disease,
- You have severe renal failure,
- You have moderate to severe hepatic impairment.

USE THROMBOREDUCTIN CAREFULLY in the following situations

If;

- You are intolerant to certain sugars,
- You have known or suspected heart disease (heart attack, heart failure, irregular heartbeat, etc.),
- You have a history of congenital QT syndrome or known QT prolongation (a disease that can be congenital or caused by medical interventions, characterized by sudden death and fainting),
- You have used a medicine that can cause low electrolyte levels (low potassium, magnesium, or calcium) and abnormal ECG changes,
- You are being treated for cardiovascular disease,
- You have mild hepatic impairment,
- You have insufficient kidney function,
- You have a lung condition,
- You are going to have any surgery/operation,
- You are pregnant or planning to become pregnant,
- You are breastfeeding.

[Page: 2]

Severe cardiovascular diseases may develop as a side effect.

Your doctor should monitor you for cardiovascular disease risk during treatment. Your doctor may want to monitor some of your blood values during treatment.

If these warnings apply to you, even at any time in the past, please consult your doctor.

Using THROMBOREDUCTIN with food and drink

Consumption of grapefruit juice is not recommended during treatment. It can be taken with or without food.

Pregnancy

Consult your doctor or pharmacist before using the medicine.

THROMBOREDUCTIN interacts with oral contraceptives. Therefore, an alternative, effective, and reliable method of contraception should be used during treatment.

THROMBOREDUCTIN is not recommended during pregnancy. Before starting THROMBOREDUCTIN, tell your doctor if you are pregnant or suspect you are pregnant.

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

Breastfeeding

Consult your doctor or pharmacist before using the medicine.

Do not use THROMBOREDUCTIN during breastfeeding. If you are using this medicine, you should stop breastfeeding.

Driving and using machines

Those who experience dizziness during the use of THROMBOREDUCTIN should not drive or use machines.

Important information about some excipients contained in THROMBOREDUCTIN

THROMBOREDUCTIN contains lactose. If your doctor has previously told you that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Use with other medicines

Tell your doctor if you are using any of the following medicines:

[Page: 3]

- Medicines that alter your heart rhythm (caution should be exercised when using THROMBOREDUCTIN),

- Certain types of antibiotics used to treat infections; e.g., enoxacin (may decrease the elimination rate of THROMBOREDUCTIN from the body),
- Fluvoxamine used to treat depression (may decrease the elimination rate of THROMBOREDUCTIN from the body),
- Certain types of medicines used to reduce stomach acid, e.g., omeprazole (may decrease the elimination rate of THROMBOREDUCTIN from the body),
- Theophylline used to treat lung diseases such as asthma (THROMBOREDUCTIN may decrease the elimination rate of theophylline from the body),
- Medicines used to treat heart diseases, e.g., milrinone, enoximone, amrinone, olprinone, and cilostazol (THROMBOREDUCTIN may increase the effect of these medicines),
- Medicines that affect your platelets, e.g., acetylsalicylic acid (co-administration of acetylsalicylic acid, also known as aspirin, and THROMBOREDUCTIN may lead to an increased tendency to bleed).

In some patients, the use of this medicine may cause indigestion (e.g., diarrhea) and may reduce the effectiveness of oral contraceptives.

There is insufficient information on the interaction of THROMBOREDUCTIN with other medicines. If other medicines need to be used, a doctor should be consulted.

If you have recently been treated with heparin, your doctor should be informed before starting THROMBOREDUCTIN.

Grapefruit juice may prolong the elimination time of this medicine from your body. It is recommended not to drink grapefruit juice while using THROMBOREDUCTIN.

If you are currently using or have recently used any prescribed or non-prescribed medicine, please inform your doctor or pharmacist.

3. How to use THROMBOREDUCTIN?

- **Instructions for proper use and dose/frequency of administration:**

Your THROMBOREDUCTIN dose will be adjusted by your doctor.

In normal use, one capsule is initially taken daily, and the dose is gradually increased over time. The maintenance dose is usually 1-3 mg (2-6 capsules) per day.

The dose level is adjusted in increments of 0.5 mg per week. After the maintenance dose is adjusted, the total daily dose is administered divided into 2-3 doses. The total daily dose should not exceed 5 mg.

- **Route and method of administration:**

[Page: 4]

Capsules should be swallowed whole with a small amount of water. Do not break the capsules or dilute their contents in a liquid. You can take the capsules with food, after food, or on an empty stomach. It is recommended to take the capsules at the same time each day.

- **Different age groups:**

Use in children: Experience with THROMBOREDUCTIN in children is limited, and there is no significant difference compared to the dose given to adults.

Use in the elderly: There are no specific studies conducted on the elderly.

- **Specific use cases:**

Renal/hepatic impairment: There are no specific studies conducted on this patient group.

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

If you have used more THROMBOREDUCTIN than you should:

Taking higher doses than recommended may cause dizziness, vomiting, and a drop in blood pressure associated with heart rhythm problems.

If you have used more THROMBOREDUCTIN than you should, talk to a doctor or pharmacist.

If you forget to use THROMBOREDUCTIN:

Your doctor will decide when to take the missed dose.

It is important to follow your doctor's instructions for the timing of the next dose.

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

Effects that may occur when treatment with THROMBOREDUCTIN is stopped:

Do not stop treatment with THROMBOREDUCTIN until your doctor decides.

THROMBOREDUCTIN is effective when used continuously. The use of the medicine should not be interrupted in any way without consulting your doctor.

4. What are the possible side effects?

Like all medicines, THROMBOREDUCTIN may cause side effects in people sensitive to the substances contained in it.

The following side effects may occur as a result of using THROMBOREDUCTIN:

Side effects are listed in the following categories:

Very common: May be seen in at least 1 in 10 patients.

[Page: 5]

Common: May be seen in less than 1 in 10 patients, but more than 1 in 100 patients. Uncommon: May be seen in less than 1 in 100 patients, but more than 1 in 1,000 patients. Rare: May be seen in less than 1 in 1,000 patients, but in 1 or more in 10,000 patients.

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

Frequency unknown: May be seen in too few patients to be determined from available data.

If any of the following occur, stop using THROMBOREDUCTIN and IMMEDIATELY notify your doctor or go to the emergency department of the nearest hospital:

Uncommon:

- Symptoms including severe chest pain and shortness of breath (heart failure)
- Symptoms including severe chest pain associated with very rapid heartbeat and shortness of breath (ventricular tachycardia)
- Symptoms including shortness of breath, swelling in the legs and ankles, bluish discoloration of the skin and lips (pulmonary hypertension)

Rare:

- Symptoms including severe chest pain and shortness of breath (heart attack)
- Symptoms including severe chest pain associated with very rapid heartbeat and shortness of breath (atrial fibrillation)
- Symptoms of severe chest pain caused by insufficient blood flow to the heart (angina pectoris)

These are all very serious side effects.

If you have any of these, it means you have a serious allergy to THROMBOREDUCTIN. You may need urgent medical attention or hospitalization.

If you have any of these, you may need urgent medical attention or hospitalization.

Other side effects:

Very common:

- Headache

Common:

- Anemia
- Local skin bleeding
- Edema
- Dizziness (vertigo)
- Tingling, numbness
- Insomnia
- Irregular heartbeat
- Excessive increase in heart rate (tachycardia)
- Nosebleed
- Nausea, diarrhea

- Indigestion
- Eczema

[Page: 6]

- Back pain
- Fatigue
- High blood pressure

Uncommon:

- Excessive decrease in platelet (one of the elements in blood composition) count in the blood
- Bleeding
- Accumulation of blood in tissue leaking from a damaged vessel (hematoma)
- Weight gain
- Depression, irritability
- Dry mouth
- Migraine
- Decreased sense of touch or sensation (hypoesthesia)
- Abnormal vision, eye inflammation
- Tinnitus
- Heart failure
- Irregular heartbeat (arrhythmia), accelerated heartbeat
- Shortness of breath
- Respiratory infections
- Vomiting, excessive gas in the stomach and intestines, abdominal pain, constipation
- Increase in liver enzymes
- Itching
- Hair loss
- Muscle pain, joint pain
- Kidney failure
- Urinary tract infection
- Pain,
- Weakness
- Fainting
- Symptoms including shortness of breath, swelling in the legs and ankles, bluish discoloration of the skin and lips (pulmonary hypertension)

Rare:

- Chest pain (angina pectoris)
- Heart attack
- Low blood pressure
- Persistent abnormal heart rhythm (atrial fibrillation)
- Lung inflammation (pneumonia)
- Fluid accumulation in the pleura (pleural effusion)
- Asthma
- Gastritis (stomach inflammation)
- Loss of appetite
- Skin rash
- Frequent urination at night
- Flu symptoms (high fever, headache, cough, etc.)
- Malaise
- Tremor, general discomfort

[Page: 7]

Unknown:

- Torsade de pointes (a type of heart rhythm problem)
- Pulmonary fibrosis (a disease characterized by the scarring of the lungs)
- Tubulointerstitial nephritis (a disease characterized by rapid deterioration of kidney function within days and weeks)

The following side effects have been reported in the literature during treatment with THROMBOREDUCTIN.

- Decrease in red blood cell, white blood cell, and platelet counts below normal (pancytopenia)
- Fluid retention
- Weight loss
- Confusion
- Memory loss (amnesia)
- Drowsiness
- Loss of coordination
- Speech disorder (dysarthria)
- Double vision (diplopia)
- Heart enlargement
- Heart muscle disorder
- Pericardial effusion (abnormal fluid accumulation between the heart and the pericardium)
- Vasodilation
- Fluid accumulation in the pleura (pleural effusion)
- High blood pressure in the lungs (pulmonary hypertension)
- Liver infiltrate (pulmonary infiltrate)
- Allergic alveolitis (a type of lung disease)
- Eating disorder (anorexia)
- Pancreatitis (inflammation of the pancreas)
- Gastrointestinal bleeding (gastrointestinal hemorrhage)
- Gastrointestinal disorder
- Colitis (inflammation of the large intestine)
- Gum bleeding
- Dry skin
- Increase in serum creatinine indicating protein metabolism disorder
- Chest pain
- Fever
- Chronic fatigue (asthenia)
- Erection problems (impotence)

If you experience any side effects not mentioned in these instructions for use, inform your doctor or pharmacist.

Reporting of side effects

If you experience any side effects, whether or not listed in the Instructions for Use, talk to your doctor, pharmacist, or nurse. You can also report adverse effects to the Turkish Pharmacovigilance Centre (TÜFAM) by clicking on the "Drug Adverse Effect Notification" icon on www.titck.gov.tr or by calling the adverse effect notification line at 0 800 314 00 08.

[Page: 8]

By reporting side effects, you will contribute to obtaining more information on the safety of the medicine you are using.

5. How to store THROMBOREDUCTIN

Keep THROMBOREDUCTIN out of the sight and reach of children and in its packaging.

Store at room temperature below 30°C.

Use in accordance with the expiry date.

Do not use THROMBOREDUCTIN after the expiry date on the packaging.

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

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[Page: 9]