Patient Leaflet According to the Pharmacists' Regulations (Preparations) – 1986

This medicine is sold with a doctor's prescription only

Anagrid 0.5

Capsules

Active ingredient:
Each capsule of Anagrid 0.5 contains:
0.5 mg of Anagrelide (as HCl)

For the list of inactive ingredients, please see section 6. See also 'Important information about some of the medicine's ingredients' in section 2.
Read this entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. If you have any further questions, please refer to your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if you think their illness is similar to yours.

1. What is the medicine intended for?

The medicine is intended for treatment of patients with essential thrombocythemia in order to reduce the high blood platelet count and the risk of thrombosis, and to improve the associated symptoms.
Essential thrombocythemia is a condition which occurs when the bone marrow produces too many platelets (type of blood cells). A high level of platelets in the blood can cause clotting problems.

Therapeutic group:
Thrombolytic medicines

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients the medicine contains (for list of inactive ingredients, please see section 6).
- You are pregnant or breastfeeding.
- You suffer from moderate or severe liver problems.
- You suffer from moderate or severe kidney problems.

Special warnings regarding the use of this medicine:
When Anagrid is administered in combination with aspirin, there is an increased risk of major hemorrhages (bleeding). See next section.

Before treatment with Anagrid, tell your doctor if:

- You have or think you might have a heart problem.
- You suffer from a congenital disorder of prolonged QT interval (appears in ECG, which is a printout recording the heart's electrical activity) or if anyone in your family suffers from such a disorder.
- You are taking other medicines that might cause heart problems (that appear in the ECG). See next section.
- You suffer from low blood salt levels (e.g. potassium, magnesium or calcium).
- You suffer from liver or kidney problems.

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutrition supplements, please tell your doctor or pharmacist. Especially inform your doctor or pharmacist if you are taking the following medicines (it should be noted that the following list mentions the active ingredients in the medicines. If you are not sure whether you are using one of these medicines please check with your doctor or pharmacist):

- Medicines that affect the heart rate, such as: sotalol, amiodarone.

- Medicines that might affect elimination of Anagrid from the body, such as: fluvoxamine (for treatment of depression), certain antibiotics (such as enoxacin).
- Theophylline (used to treat asthma and breathing problems).
- Medicines used to treat heart disorders (for example, milrinone, enoximone, amrinone, olprinone and cilostazol).
- Aspirin (used to relieve pain or as a platelets aggregation inhibitor).
- Other medicines affecting the platelets in your blood.
- Oral contraceptives (pills to prevent pregnancy): if you experience severe diarrhea during use, you should use additional contraceptive means, such as a condom.

Use of this medicine and food:
The medicine can be taken regardless of mealtimes.

Pregnancy and breastfeeding:
- If you are planning to become pregnant, consult your doctor.
- This medicine should not be taken by pregnant women. Women who might become pregnant must use contraceptives (as recommended by the doctor) when using Anagrid.
- Tell your doctor if you are breastfeeding or if you are planning to breastfeed. Do not use this medicine if you are breastfeeding. You must stop breastfeeding if you are taking this medicine.

Driving and use of machines:
Use of this medicine may cause dizziness. Do not drive or operate machinery if you feel dizzy.

Use in children:
There is limited information on the use of Anagrid in children and adolescents and therefore it should be used with caution in this age group.

Important information about some of the medicine's ingredients:
The medicine contains lactose. If you are sensitive to lactose, inform your doctor before taking this medicine (see section 6).

3. How to use this medicine?
Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure.
The dosage and the manner of treatment will be determined by the doctor only.
The standard dosage is usually: The starting dosage is usually one capsule twice a day for at least a week. Afterwards, your doctor may increase or decrease the number of capsules that you take per day according to your condition.
Do not exceed the recommended dose.

Swallow the capsules whole with a glass of water. This medicine may be taken with food or on an empty stomach.
It is recommended to take the capsules at the same time every day.
Do not chew or crush and do not open the capsule and disperse its contents in liquid.

Tests and follow up: During the treatment, your doctor may ask you to perform blood and urine tests to check the effect of the medicine, the liver and kidney functions and the balance of salts in your body. You may also be sent for various heart tests before and during the treatment.

If you have accidentally taken a higher dosage: If you have taken an overdose or if a child or another person has accidentally swallowed the medicine, go immediately to a doctor or a hospital emergency room and bring the medicine package with you. Taking an overdose may cause a decrease in blood pressure, dizziness, vomiting and increased heart rate.

If you forgot to take the medicine at the required time take the forgotten dose as soon as you remember. Take the next dose at the usual time. Do not take two doses together.

Continue with the treatment as recommended by your doctor.
Even if your state of health improves, do not stop the treatment with this medicine without consulting your doctor or pharmacist. Stopping treatment with this medicine might cause the platelet count to rise to the level that it was before start of the treatment, within 14 days from the time of stopping the treatment.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

4. Side effects

Like any medicine, the use of Anagrid may cause side effects in some users. If these side effects persist or are bothersome or get worse, please consult your doctor. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

Contact your doctor immediately if the following serious side effects appear:
Uncommon side effects:

- Various heart problems, for instance: heart failure (symptoms can include shortness of breath, chest pain, leg swelling as a result of fluid build-up), severe problems with the rate or rhythm of the heart beat (e.g. tachycardia or atrial fibrillation).
- Inflammation of the pancreas, which may cause severe abdominal and back pain.
- Bloody vomit, bloody or black stool (bleeding from the digestive system).
- Severe decrease in blood cells, which may cause weakness, bruising, bleeding or infection (pancytopenia).

Rare side effects:

- Kidney failure - symptoms include passing little or no urine.
- Heart attack.

Additional side effects:

Very common side effects (appear in more than 1 user out of 10):
Headaches.

Common side effects (appear in 1-10 users out of 100):
Dizziness, tiredness, palpitations (strong, rapid or irregular heartbeats), nausea, diarrhea, stomachache, indigestion, flatulence, vomiting, anemia (decrease in the red blood cell count), fluid retention, rash, insomnia, high blood pressure, nosebleed.

Uncommon side effects (appear in 1-10 users out of 1,000):
Weakness, feeling unwell, irregular heartbeats, fainting, chills, or fever, decreased appetite, constipation, bruising, bleeding (including bleeding under the skin), edema (swelling), weight loss, muscle pains, joint pains, back pain, decrease in skin sensation and sensitivity, tingling or prickling sensation, depression, confusion, nervousness, dry mouth, memory loss, shortness of breath, breathing difficulties, pneumonia/lung inflammation (of different types, with symptoms including fever, cough, breathing difficulties, wheezing and scarring of the lungs), phlegm, hair loss, itching of skin or change of skin color, impotence, chest pain, decrease in blood platelets that increases the risk of bleeding or bruising (thrombocytopenia), accumulation of fluid around the lungs, increase in liver enzymes.

Rare side effects (appear in 1-10 users out of 10,000):
Bleeding gums, weight gain, severe chest pain (angina pectoris), heart muscle disease (which can manifest as tiredness, palpitations amongst other symptoms), enlarged heart, accumulation of fluid around the heart, loss of coordination, speaking difficulties, dry skin, migraine, vision disturbances

or double vision, ringing in the ears, dizziness when standing up, particularly when getting up from a sitting or lying down position, increased need to pass urine during the night, pain, flu-like symptoms, sleepiness, widening of the blood vessels , inflammation of the large bowel (symptoms can include diarrhea accompanied usually by blood and mucus, stomachache, fever), inflammation of the stomach (symptoms can include pain, nausea, vomiting), increased pressure in the lung arteries (symptoms can include: shortness of breath, and lips and skin turning blue), areas of abnormal density in the lung, high level of creatinine in blood test, which may be a sign of kidney problems.

Side effects of unknown frequency (effects whose frequency has not been determined yet):
Irregular heartbeats, which may be life-threatening (torsade de pointes); liver inflammation (hepatitis) whose symptoms include nausea, vomiting, itching, yellowing of the skin and eyes, change in color of stools and urine; inflammation of the kidneys.

In any case you experience side effects that are not mentioned in this leaflet or if there is a change in your general feeling, consult the doctor immediately!

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored in a safe place out of the reach of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 25°C.

6. Additional information

- **In addition to the active ingredient this medicine also contains the following inactive ingredients:**
  Lactose, microcrystalline cellulose, crosspovidone, povidone K25, magnesium stearate, water, titanium dioxide (E171), gelatin.
  Each capsule contains approximately 123 mg lactose.

- **What does the medicine look like and what does the package contain?**
  Off-white capsules in blister packs, 60 capsules per box.

Registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301.

Medicine registration number in the National Medicines Registry of the Ministry of Health:
1486433344

This leaflet was checked and approved by the Ministry of Health in June 2016.

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