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 the additional ingredients, 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 it seems to you that 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 where the bone marrow produces too many platelets (type of blood cells). A high level of platelets in the blood can cause serious problems in the blood circulation and clotting.

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 additional ingredients the medicine contains (for the list of the additional ingredients, see section 6). An allergic reaction is characterized amongst others by the appearance of a rash, itching, swelling of the face, lips or shortness of breath.
- You suffer from moderate or severe liver problems.
- You suffer from moderate or severe kidney problems (creatinine clearance below 50 ml/min).

Special warnings regarding the use of this medicine:
Before (and during) 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 (is seen on an ECG, which is a printout recording the heart's electrical activity) or if anyone in your family suffers from such a problem.
- You are taking other medicines that might cause heart problems (that are seen on an ECG). See in section 'Drug interactions'.
- You have low blood salt levels (e.g. potassium, magnesium or calcium).
- You suffer from liver or kidney problems.
- You have lung problems.

Additional warnings:

- When Anagrid is administered in combination with acetylsalicylic acid (aspirin), there is an increased risk of major hemorrhages (bleeding). See the section 'Drug interactions'.

- During the treatment period with Anagrid you should strictly follow the instructions for use and the dosage prescribed for you by your doctor. Do not stop taking the medicine without first consulting your doctor. Do not stop taking the medicine abruptly without consulting your doctor. Stopping to take the medicine abruptly could lead to an increased risk of stroke.

  Signs and symptoms of stroke may include the following symptoms that occur suddenly: numbness, tingling or weakness in the face, arm, or leg, especially on one side of the body; sudden confusion, trouble speaking or difficulty understanding speech; sudden trouble seeing in one eye or both eyes; sudden trouble walking, dizziness, problem with balance, loss of balance or lack of coordination; sudden severe headache with no known cause. In such cases seek immediate medical assistance.

Children and adolescents:

The information that exists on the use of Anagrid in children and adolescents is limited and therefore it should be used with caution in this age group.

Tests and follow-up:

During the treatment the doctor may send you to perform blood tests to check the effect of the medicine, tests for liver and kidney functions, and the balance of salts in the body. In addition, you may also be referred to various heart tests before and during the treatment.

Drug interactions:

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

- Medicines that affect the heart rhythm, such as: sotalol, amiodarone.
- Medicines that might affect the elimination of Anagrid from the body, such as: fluvoxamine (for treatment of depression), certain antibiotics (such as enoxacin).
- Theophylline (for the treatment of asthma and breathing problems).
- Medicines used to treat heart problems (for example, milrinone, enoximone, amrinone, olprinone and cilostazol).
- Acetylsalicylic acid (aspirin) used to relieve pain, reduce fever or as a blood clotting/platelets aggregation inhibitor). See 'Additional warnings'.
- Other medicines affecting the platelets in the blood, such as clopidogrel.
- Omeprazole (used to reduce the amount of acid produced in the stomach).
- Oral contraceptives (pills to prevent pregnancy): if severe diarrhea occurs during use, additional contraceptive means, such as a condom should be used.

Use of this medicine and food:

The medicine can be taken regardless of mealtimes.

Pregnancy and breastfeeding:

Consult your doctor if you are pregnant or are planning a pregnancy.

- This medicine should not be used by pregnant women. Women who might become pregnant need to use effective contraceptives (as recommended by the doctor) when using Anagrid.

- Tell your doctor if you are breastfeeding or are planning to breastfeed. Do not use this medicine if you are breastfeeding. You need to stop breastfeeding if you are taking this medicine.

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

Important information about some of the medicine's ingredients:
Each capsule contains approximately 123 mg lactose. If you have intolerance to certain sugars, consult the doctor before taking the medicine.

3. How to use this medicine?

Always use the medicine according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and manner of treatment with the medicine. The dosage and the manner of treatment will be determined by the doctor only.
The standard dosage is usually: The starting dose is usually one capsule twice a day for at least a week. After this time, the doctor may increase or decrease the number of capsules you take per day according to your condition.
Do not exceed the recommended dosage.
Do not take more or less capsules than the doctor instructed. Do not stop taking the medicine without first consulting your doctor. Do not stop taking the medicine on your own.
Swallow the capsules whole with a glass of water. The medicine may be taken with food, after 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.

If you have accidentally taken a higher dosage: If you took an overdose or if a child or another person has accidentally swallowed the medicine, proceed immediately to a doctor or 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 a double dose to compensate for the forgotten dose.

Adhere to the treatment as recommended by your doctor.
Even if your state of health improves, do not stop treatment with the medicine without consulting your doctor.

If you stop taking the medicine: Stopping to take the medicine might cause an increase in the platelet count within 4 days. Within 10-14 days the platelet level might reach the level that it was before starting the treatment (or even higher). The platelet count should be monitored frequently. See also 'Additional Warnings' in section 2.

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.
If you have further questions concerning the use of the medicine, consult a doctor or pharmacist.

4. Side effects

As with any medicine, the use of Anagrid may cause side effects in some users. 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, swelling of the legs as a result of fluid retention), serious heartbeat rate or rhythm problems (e.g., tachycardia or atrial fibrillation).
- Inflammation o the pancreas which may cause severe stomach and back pain.
- Bloody vomit, bloody or black stool (bleeding from the digestive system).
- Severe decrease in blood cells (pancytopenia), which may cause weakness, bruising (hematoma), bleeding or infection.
- Pulmonary hypertension (the symptoms include shortness of breath, swelling in legs/ankles, or lips and skin can turn bluish color).

Rare side effects:
- Kidney failure, symptoms include passing little or no urine.
- Heart attack.

Additional side effects:
Very frequent 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, rapid, irregular or strong heartbeats (palpitations), nausea, diarrhea, stomachache, flatulence, vomiting, anemia (decrease in the red blood cell count), fluid retention, rash.

Uncommon side effects (appear in 1-10 users out of 1,000):
Weakness, feeling unwell, high blood-pressure, irregular heartbeats, fainting, chills or fever, digestive difficulties/disorders, loss of appetite, constipation, bruising (hematoma), bleeding, edema (swelling), weight loss, muscle pains, joint pains, back pain, decrease, loss or change of sensation and sensitivity especially of the skin, feeling of tingling, prickling or itching, depression, confusion, insomnia, nervousness, dry mouth, memory loss, shortness of breath, nosebleed; serious lung infection with fever, shortness of breath, cough, phlegm; hair loss, itchiness or change in skin color, impotence, chest pain, decrease in blood platelets (thrombocytopenia) that increases the risk of bleeding or bruising, fluid retention around the lungs, increase in liver enzymes (can be seen in blood tests).

Rare side effects (appear in 1-10 users out of 10,000):
Bleeding gums, weight gain, severe chest pain (angina pectoris), heart muscle disease (symptoms include tiredness, chest pain, palpitations), enlarged heart, fluid retention around the heart, painful spasm of the blood vessels on the heart (while resting, usually at night or early in the morning - Prinzmetal angina), coordination disorders, speaking difficulties, dry skin, migraine, visual disturbances or double vision, ringing in the ears, dizziness when standing up, particularly when getting up from a sitting or lying position, increase in need to pass urine at night, pain, flu-like symptoms, drowsiness, widening of blood vessels, inflammation of the large bowel (symptoms include: diarrhea usually accompanied by blood and mucus, stomachache, fever), inflammation of the stomach (symptoms include pain, nausea, vomiting), areas of abnormal density in the lung, high level of creatinine in blood tests, which may be a sign of kidney problems.

Side effects of unknown frequency (effects whose frequency has not yet been determined):
Irregular heartbeats, which may be life-threatening (torsade de pointes); liver infection (hepatitis) with symptoms that include nausea, vomiting, itching, yellowing of the skin and eyes, change in color of stools and urine, lung inflammations of different types including allergy related (symptoms include fever, cough, breathing difficulties, wheezing, scarring of the lungs); kidney inflammation, stroke (see also 'Additional warnings" in section 2).
If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with your doctor.

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://sideeffects.health.gov.il/

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored in a closed place out of the reach and sight of children and/or babies, 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) that appears 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, the medicine also contains:**

Lactose, microcrystalline cellulose, crosspovidone, povidone K25, magnesium stearate, 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 of 60 capsules.

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

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

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