



PACKAGE LEAFLET

DAFANIB 20 mg Film Coated Tablets

Taken by mouth.

Cytotoxic

Active substance: Each film-coated tablet contains 20 mg dasatinib (anhydrous).

Excipients: *Tablet core:* Lactose monohydrate (from cow's milk), Microcrystalline cellulose PH 101, Croscarmellose sodium, Hydroxypropyl cellulose, Magnesium stearate. *Film coating:* Opadry® White 03H280006: HPMC 2910/Hypromellose, Titanium dioxide, Propylene glycol.

Read all of this LEAFLET carefully before you start using this medicine because it contains important information for you.

- *Keep this leaflet. You may need to read it again.*
- *If you have any further questions, please ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *When you visit a doctor or hospital while using this medicine, tell them that you are using this medicine.*
- *Please follow the instructions in this leaflet. Do not use any **higher or lower** doses than the recommended dose of this medicine.*

What is in this leaflet:

- 1. What DAFANIB is and what it is used for***
- 2. What you need to know before you use DAFANIB***
- 3. How to use DAFANIB***
- 4. Possible side effects***
- 5. How to store DAFANIB***

1. What DAFANIB is and what it is used for

DAFANIB is a medicine taken through mouth and contains dasatinib as active substance.

DAFANIB is a white to off-white, biconvex, round film-coated tablet. Each cardboard box contains 60 film-coated tablets.

This medicine is used to treat chronic myeloid leukemia (CML) in adults, adolescents and children at least 1 year of age. Leukemia is a cancer of white blood cells. These white cells usually help the body to fight infection. In people with CML, white cells called granulocytes start growing out of control. DAFANIB inhibits the growth of these leukemic cells.

DAFANIB is also used to treat Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL) in adults, adolescents and children at least 1 year of age, and lymphoid blast CML in adults who are not benefiting from prior therapies. In people with ALL, white cells called lymphocytes multiply too quickly and live too long. DAFANIB inhibits the growth of these leukemic cells.

If you have questions about how DAFANIB works or why this medicine has been prescribed for you, ask your doctor.



2. What you need to know before you use DAFANIB

DAFANIB must be given by a doctor experienced in the diagnosis and treatment of leukemia.

DO NOT use DAFANIB in the following conditions

If you are allergic to dasatinib or any of the ingredients of DAFANIB.

If there is a possibility that you may be allergic, consult your doctor.

Use DAFANIB with SPECIAL CARE in following conditions

Talk to your doctor or pharmacist before using DAFANIB.

- If you are taking medicines to thin the blood or prevent clots (see section ‘Using with other medicines’)
- If you have a liver or heart problem, or used to have one.
- If you start having difficulty breathing, chest pain, or a cough when taking DAFANIB: this may be a sign of fluid retention in the lungs or chest (which can be more common in patients aged 65 years and older), or due to changes in the blood vessels supplying the lungs.
- If you have ever had or might now have a hepatitis B infection. This is because DAFANIB could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.
- If you experience bruising, bleeding, fever, fatigue and confusion when taking DAFANIB, contact your doctor. This may be a sign of damage to blood vessels known as thrombotic microangiopathy (TMA).

If they apply to you, please tell your doctor. Your doctor will regularly monitor your condition to check whether DAFANIB is having the desired effect. You will also have blood tests regularly while you are taking DAFANIB.

If any of these warnings apply to you, even for a period in the past, please consult your doctor.

Children and adolescents

Do not give this medicine to children younger than 1 year of age. There is limited experience with the use of DAFANIB in this age group. Bone growth and development will be closely monitored in children taking DAFANIB.

The risk of swallowing difficulties in younger age groups should be taken into consideration when using film-coated tablets.

Using DAFANIB with food and drink

Do not take DAFANIB with grapefruit or grapefruit juice.

Pregnancy

Ask your doctor or pharmacist before you start to use this medicine.

DAFANIB is not to be used during pregnancy unless clearly necessary. Your doctor will discuss with you the potential risk of taking DAFANIB during pregnancy. Both men and women taking DAFANIB will be advised to use effective contraception during treatment.

Talk to your doctor immediately if you find out that you are pregnant during treatment.

Breastfeeding

Ask your doctor or pharmacist before you start to use this medicine.

If you are breastfeeding, tell your doctor. You should stop breastfeeding during DAFANIB use.



Driving and using machines

Take special care when driving or using machines in case you experience side effects such as dizziness and blurred vision.

Important information about some of the excipients of DAFANIB

If you have been told by the doctor that you cannot tolerate some forms of sugar, talk to your doctor before taking DAFANIB because of its lactose ingredient.

Using with other medicines

Tell your doctor if you are taking, have recently taken or might take any other medicines.

DAFANIB is mainly processed by the liver. Certain medicines may interfere with the effect of DAFANIB when taken together.

These medicines are not to be used with DAFANIB:

- Ketoconazole, itraconazole (antifungal medicines)
- Erythromycin, clarithromycin, telithromycin (antibiotics)
- Ritonavir (an antiviral medicine)
- Phenytoin, carbamazepine, phenobarbital (medicines for treatment of epilepsy)
- Rifampicin (an antibiotic used for the treatment of tuberculosis)
- Famotidine, omeprazole (medicines that block stomach acids)
- Astemizole, terfenadine (medicines used for allergic conditions)
- Cisapride (a medicine used for stomach disorders)
- Pimozide (a medicine used to treat psychotic mental disorders)
- Quinidine (a medicine used for heart rhythm disorders)
- Bepridil (a medicine used in cardiovascular diseases)
- Ergot alkaloids such as ergotamine, dihydroergotamine (medicines used to treat a type of headache)
- St. John's wort – an herbal preparation obtained without a prescription, used to treat depression and other conditions (also known as *Hypericum perforatum*)

Do not take medicines that neutralize stomach acids (antacids such as aluminum hydroxide or magnesium hydroxide) in the **2 hours before or 2 hours after taking DAFANIB**.

Tell your doctor if you are taking medicines to **thin the blood** or prevent clots.

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

3. How to use DAFANIB

Instructions for appropriate use and dose/frequency of administration

DAFANIB will only be prescribed to you by a doctor with experience in treating leukemia. Always take DAFANIB exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. DAFANIB is given for adults and children at least 1 year of age.

The recommended starting dose for adults with chronic phase CML is 100 mg daily.



The starting dose recommended for adult patients with accelerated or blast crisis CML or Ph+ ALL is 140 mg once a day.

Dosing for children with chronic phase CML or Ph+ ALL is on the basis of body weight. DAFANIB is administered orally once daily in the form of DAFANIB tablet. DAFANIB tablets are not recommended for patients weighing less than 10 kg.

Your doctor will adjust dosage based on your weight, any side effects and response to treatment.

Depending on how you respond to the treatment, your doctor may suggest a higher or lower dose, or stopping treatment. For higher or lower doses, you may need to take combinations of the different tablet strengths. Take your tablets at the same time every day.

Take DAFANIB daily until your doctor tells you to stop.

Route and method of administration

To maintain dose consistency and minimize the risk of exposure to skin, do not crush, cut, or chew the film-coated tablets; swallow the tablets whole. Film-coated tablets should not be dispersed as the exposure in patients receiving a dispersed tablet is lower than in those swallowing a whole tablet. It can be taken with or without a meal.

Special handling instructions

It is unlikely that the DAFANIB tablets will get broken. But if they do, persons other than the patient should use gloves when handling DAFANIB.

Special age groups

Use in children

The starting dose of DAFANIB for children is calculated by body weight as shown below:

Body weight (kg)^a	Daily dose (mg)
10 to less than 20 kg	40 mg
20 to less than 30 kg	60 mg
30 to less than 45 kg	70 mg
at least 45 kg	100 mg

^a The tablet is not recommended for patients weighing less than 10 kg.

There is no dose recommendation for DAFANIB with children under 1 year of age.

Use in the elderly

No specific dose recommendation is necessary in elderly.

Special conditions for use

Kidney/Liver failure

In patients with moderate to severe liver failure, DAFANIB should be used with caution. No clinical studies have been conducted with DAFANIB in patients with reduced kidney function.

If you think that the effect of DAFANIB is too strong or too weak, see your doctor or pharmacist.



If you use more DAFANIB than you should

If you have accidentally taken too many tablets, you may require medical attention.

Talk to a doctor or pharmacist if you have used more DAFANIB than you should.

If you forget to use DAFANIB

Take the next scheduled dose at the regular time.

Do not use a double dose to make up for a forgotten dose.

Possible effects if you stop using DAFANIB

The effects that may occur when treatment is stopped are unknown. Use until your doctor stops your treatment.

4. Possible side effects

Like all other medicines, DAFANIB may cause side effects in people with hypersensitivity to its ingredients.

Stop taking DAFANIB and IMMEDIATELY tell your doctor or refer to your nearest hospital emergency department if one of the following occurs:

- If you have chest pain, difficulty breathing, cough and fainting
- If you experience unexpected bleeding or bruising without having an injury
- If you find blood in your vomit, stools or urine, or have black stools
- If you get signs of infections such as fever, severe chills
- If you get fever, sore mouth or throat, blistering or peeling of your skin and/or mucous membranes

These are all very serious side effects. If you have one of them, you are severely allergic to DAFANIB. Urgent medical care or hospitalization may be needed. These very serious side effects occur quite rarely.

Side effects are listed as shown in the categories below:

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

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

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

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

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

Not known : Cannot be estimated from the available data.

Very common

- Infections (including bacterial, viral and fungal)
- Shortness of breath
- Diarrhea, feeling or being sick (nausea, vomiting)
- Skin rash, fever, swelling around the face, hands and feet, headache, feeling tired or weak, bleeding
- Pain in the muscles (during or after discontinuing treatment), tummy (abdominal) pain
- Low blood platelet (thrombocyte) count (thrombocytopenia), low white blood cells count (neutropenia), anemia, fluid around the lungs



Common

- Inflammation of the lungs (pneumonia), herpes virus infection (including cytomegalovirus), upper respiratory tract infection, serious infection of the blood or tissues (including fatal outcomes and uncommon cases).
- Palpitations, irregular heartbeat, congestive heart failure (an illness marked by respiratory failure, edema, enlargement of the liver due to heart failure), weak heart muscle, high blood pressure, increased blood pressure in the vessels of the lungs, cough
- Appetite disturbances, taste disturbance, bloated or distended tummy (abdomen), inflammation of the colon, constipation, heartburn, sores in the mouth, weight increase, weight decrease, gastritis (inflammation of the stomach mucosa)
- Skin tingling, itching, dry skin, acne, inflammation of the skin, persistent noise in ears, hair loss, excessive sweating, visual disorder (including blurred vision and disturbed vision), dry eyes, bruises, depression, insomnia, flushing, dizziness, contusion (bruising), loss of appetite, somnolence, generalized edema
- Joint pain, muscle weakness, chest pain, pain in hands and feet, chills, stiffness in muscles and joints, muscle spasm
- Fluid around the membranes of the heart, fluid around the membranes of the lungs, arrhythmia, a condition that develops due to the decrease in the number of defense cells in the body (febrile neutropenia), gastrointestinal bleeding, high uric acid levels in the blood.

Uncommon

- Heart attack (including fatal outcome), inflammation of the lining (fibrous sack) surrounding the heart, irregular heartbeat, chest pain due to lack of blood supply to the heart (angina), low blood pressure, narrowing of the airways that may cause breathing difficulties, asthma, increased blood pressure in blood vessels of the lungs
- Inflammation of the pancreas, peptic ulcer, inflammation of the food pipe, swollen tummy (abdomen), tear in the skin of the anal canal, difficulty in swallowing, inflammation of the gallbladder, blockage of bile ducts, gastro-esophageal reflux (a condition where acid and other stomach contents come back up into the throat)
- Allergic reaction including tender, red lumps on the skin (erythema nodosum), anxiety, confusion, mood swings, lower sexual drive, fainting, tremor, eye inflammation which causes redness or pain, a skin disease characterized by tender, red, well-defined blotches with the sudden onset of fever and raised white blood cell count (neutrophilic dermatosis), loss of hearing, sensitivity to light, visual impairment, increased eye tearing, skin color disturbance, inflammation of fatty tissue under the skin, skin ulcer, blistering of the skin, nail disorder, hair disorder, hand-foot disorder, renal failure, urinary frequency, breast enlargement in men, menstrual disorder, general weakness and discomfort, low thyroid function, losing balance while walking, osteonecrosis (a disease of reduced blood flow to the bones, which can cause bone loss and bone death), arthritis, skin swelling anywhere in the body
- Vein inflammation that can cause redness, tenderness and swelling, tendon inflammation
- Memory loss
- Abnormal blood test results and possibly impaired kidney function caused by the waste products of the dying tumor (tumor lysis syndrome), low levels of albumin in the blood, low levels of lymphocytes (a type of white blood cell) in the blood, high level of cholesterol in the blood, swollen lymph nodes, bleeding in the brain, irregularity of the electrical activity of the heart, enlarged heart, inflammation of the liver, protein in the urine, raised creatine phosphokinase (an enzyme mainly found in the heart, brain and skeletal muscles), raised



troponin (an enzyme mainly found in the heart and skeletal muscles), raised gamma-glutamyltransferase (an enzyme mainly found in the liver), milky-appearing fluid around the lungs (chylothorax)

Rare

- Enlargement of the right ventricle in the heart, heart muscle inflammation, collection of conditions resulting from blockage of blood supply to the heart muscle (acute coronary syndrome), cardiac arrest (stopping of blood flow from the heart), coronary (heart) artery disease, inflammation of the tissue covering the heart and lungs, blood clots, blood clots in the lungs
- Loss of vital nutrients such as protein from your digestive tract, bowel obstruction, anal fistula (an abnormal opening from the anus to the skin around the anus), impairment of kidney function, diabetes
- Convulsion, inflammation of the optic nerve that may cause a complete or partial loss of vision, blue-purple mottling of the skin, abnormally high thyroid function, inflammation of the thyroid gland, ataxia (a condition associated with lack of muscular coordination), difficulty walking, miscarriage, inflammation of the skin blood vessels, skin fibrosis
- Stroke, temporary episode of neurologic dysfunction caused by loss of blood flow, facial nerve paralysis, dementia
- Severe allergic reaction
- Delayed fusion of the rounded ends that form joints (epiphyses); slower or delayed growth

Unknown

- Inflammation of the lungs
- Bleeding in the stomach or bowels that can cause death
- A reaction with fever, blisters on the skin, and ulceration of the mucous membranes
- Recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past (a liver infection)
- Disease of the kidneys with symptoms including edema and abnormal laboratory test results such as protein in the urine and low protein level in the blood
- Damage to blood vessels known as thrombotic microangiopathy (TMA), including decreased red blood cell count, decreased platelets, and formation of blood clots

Your doctor will check for some of these effects during your treatment.

If you notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get any side effects including any possible side effects not listed in this leaflet, talk to your doctor, pharmacist or nurse. You can also report side effects directly via the national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store DAFANIB

Keep DAFANIB out of the reach and sight of children and in its original package.

Store at room temperature under 30°C.

In case of tablet breakage, the patient and others are advised to wear gloves when handling DAFANIB.



Use it in accordance with the expiry date.

Do not use DAFANIB after the expiry date stated on the label or package.

The expiry date refers to the last day of the specified month.

Do not use DAFANIB in cases of any defects in the product and/or the package.

Waste materials/equipment of the inner packaging of cytotoxic and cytostatic medicinal products for human use are considered as **HAZARDOUS WASTE MATERIALS** and the management of these waste materials is carried out in accordance with local regulations and guidelines.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Marketing authorization holder:

DEVA Holding A.Ş.

Küçükçekmece – İSTANBUL / TÜRKİYE

Manufacturing site:

DEVA Holding A.Ş.

Kapaklı – TEKİRDAĞ / TÜRKİYE

This package leaflet was approved on 21/12/2023.