**TASIGNA®**

**Important note:** Before prescribing, consult full prescribing information.

**Presentation:** Hard capsules containing 200 mg of nilotinib.

Indications: Treatment of adult patients with newly diagnosed philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP). Patients who have been treated with TASIGNA for at least 3 years and have achieved a sustained deep molecular response may be eligible for treatment discontinuation; treatment of adult patients with chronic or accelerated phase (AP) Ph+ CML resistant to or intolerant of at least one prior therapy including imatinib. Ph+ CML patients in chronic phase, who have been previously treated with imatinib and whose treatment has been switched to TASIGNA for at least 3 years and have achieved a sustained deep molecular response may be eligible for treatment discontinuation.

**Dosage:** ♦Patients with newly diagnosed Ph+ CML-CP: 300 mg twice daily; patients with CP and AP Ph+ CML resistant to or intolerant to at least one prior therapy including imatinib: 400 mg twice daily. ♦Discontinuation of treatment may be considered in eligible Ph+ CML-CP patients who have been treated with TASIGNA for a minimum of 3 years if a deep molecular response is sustained for a minimum of one year immediately prior to discontinuation of therapy. Discontinuation of TASIGNA treatment should be initiated by a physician experienced in the treatment of patients with CML. ♦Increases in blood glucose and serum cholesterol levels have been reported with TASIGNA therapy. Blood glucose levels and lipid profiles should be assessed prior to initiating TASIGNA therapy and monitored during treatment. ♦TASIGNA capsules should be taken twice daily, at approximately 12 hours intervals and must not be taken with food. ♦No food should be consumed for 2 hours before the dose and for at least one hour after the dose. ♦For patients who are unable to swallow capsules, the content of each capsule may be dispersed in one teaspoon of applesauce (pureed apple) and should be taken immediately. Not more than one teaspoon of applesauce and no food other than applesauce must be used.

**Contraindications:** ♦Hypersensitivity to nilotinib or to any of the excipients.

**Warnings and precautions:** ♦Treatment with TASIGNA associated with thrombocytopenia, neutropenia and anemia, generally reversible and usually managed by withholding TASIGNA temporarily or dose reduction. Complete blood counts to be performed every two weeks for the first 2 months and then monthly thereafter or as clinically indicated. ♦Caution in patients who have or may develop prolongation of QTc (e.g., patients with hypokalemia, hypomagnesemia, congenital long QT syndrome; with uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina or clinically significant bradycardia; patients taking anti-arrhythmic medicines or other drugs that may lead to QT prolongation). ♦A baseline ECG is recommended prior to initiating therapy with TASIGNA and should be repeated as clinically indicated. ♦Hypokalemia or hypomagnesemia must be corrected prior to TASIGNA administration. ♦Uncommon cases (0.1 to 1%) of sudden death have been reported in clinical trials in patients with significant cardiac risk factors (including ventricular repolarization abnormalities) or with comorbidities/concomitant medications (not in the newly diagnosed Ph+ CML-CP study). The estimated reporting rate for spontaneous reports of sudden death is 0.02% per patient-year. ♦Cardiovascular events (peripheral arterial occlusive disease, ischemic heart disease and ischemic cerebrovascular events) were reported in newly diagnosed Ph+ CML study and observed in the post-marketing reports. If acute signs or symptoms of cardiovascular events occur, advise patients to seek immediate medical attention. The cardiovascular status of patients should be evaluated and cardiovascular risk factors should be monitored and actively managed during TASIGNA therapy according to standard guidelines. ♦Unexpected, rapid weight gain should be carefully investigated. If signs of severe fluid retention appear during treatment with nilotinib, the etiology should be evaluated and patients treated accordingly. ♦It is recommended that the lipid profiles be determined before initiating treatment with TASIGNA, assessed at month 3 and 6 after initiating therapy, and at least yearly during chronic therapy. If a HMG-CoA reductase inhibitor (a lipid lowering agent) is needed, refer to section 8 Interactions, before starting treatment since certain HMG-CoA reductase inhibitors are metabolized by the CYP3A4 pathway. ♦Blood glucose levels should be assessed before initiating treatment with TASIGNA and monitored during treatment. If test results warrant therapy, physicians should follow their local standards of practice and treatment guidelines. ♦Test for hepatitis B infection before initiating treatment with TASIGNA. In patients with positive hepatitis B serology (including those with active disease) and for patients who test positive for hepatitis B infection during treatment, consult experts before initiating treatment. Closely monitor for signs and symptoms of active hepatitis B infection in carriers of hepatitis B virus throughout therapy and for several months following termination of therapy. ♦Must not be taken with food. ♦Eligible patients who are confirmed to express the typical BCR-ABL transcripts, can be considered for treatment discontinuation. Monitoring of BCR-ABL transcript levels in patients eligible for treatment discontinuation must be performed with a quantitative diagnostic test validated to measure molecular response levels with a sensitivity of at least MR4.5. BCR-ABL transcript levels must be assessed prior to and during treatment discontinuation. Frequent monitoring of BCR-ABL transcript levels and complete blood count with differential is required to detect possible loss of remission. ♦Avoid grapefruit juice and other foods that are known to inhibit CYP3A4. ♦Caution in patients with hepatic impairment. ♦Caution in patients with previous history of pancreatitis. Interrupt treatment in case of lipase elevations accompanied by abdominal symptoms. ♦The bioavailability of nilotinib might be reduced in patients with total gastrectomy. ♦Due to possible occurrence of tumor lysis syndrome, correction of clinically significant dehydration and treatment of high uric acid levels are recommended prior TASIGNA administration.♦Not recommended in patients with rare hereditary problems of galactose intolerance, of severe lactase deficiency or of glucose-galactose malabsorption.

**Pregnancy:** ♦Women of child-bearing potential must use highly effective method of contraception while receiving TASIGNA and for up to 2 weeks after ending treatment. ♦Should not be used during pregnancy unless clearly necessary.

**Breast-feeding:** ♦Breast-feeding is not recommended.

**Interactions:** ♦Avoid in patients treated with medicines known to prolong the QT interval (e.g., chloroquine, methadone, halofantrine, clarithromycin, haloperidol, moxifloxacin, bepridil, pimozide). ♦Avoid in patients treated with anti-arrhythmic medicines (e.g. amiodarone, disopyramide, procainamide, quinidine, sotalol). ♦Avoid administration of strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, itraconazole, voriconazole, telithromycin). ♦Caution with CYP3A4 inducers (e.g., phenytoin, rifampicin, carbamazepine, phenobarbital, or St. John's Wort). ♦TASIGNA may be used concurrently with esomeprazole or other proton pump inhibitors. ♦TASIGNA can be used concurrently with warfarin. ♦Caution with medicines that affect P-glycoprotein. ♦Nilotinib is a moderate CYP3A4 inhibitor. The systemic exposure of other drugs primarily metabolized by CYP3A4 (e.g. certain HMG-CoA reductase inhibitors) may be increased when co-administered with nilotinib. Appropriate monitoring and dose adjustment may be necessary for drugs that are CYP3A4 substrates and have a narrow therapeutic index (including but not limited to alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, sirolimus and tacrolimus) when co-administered with nilotinib. ♦Avoid grapefruit juice and other foods that are known to inhibit CYP3A4. ♦In concurrent use: the H2 blocker (e.g. famotidine) may be administered approximately 10 hours before and approximately 2 hours after TASIGNA dose; antacids (e.g., aluminum hydroxide, magnesium hydroxide, simethicone) may be administered approximately 2 hours before or approximately 2 hours after TASIGNA dose.

Adverse drug reactions:

**Very common**: headache, nausea, constipation, vomiting, abdominal pain upper, rash, pruritus, alopecia, myalgia, arthralgia, fatigue, myelosuppression (thrombocytopenia, neutropenia, anaemia), hypophosphataemia (including blood phosphorus decreased), hyperbilirubinaemia (including blood bilirubin increased), alanine aminotransferase increased, aspartate aminotransferase increased, lipase increased, lipoprotein cholesterol (including low density and high density) increased, total cholesterol increased, blood triglycerides increased, musculoskeletal pain, myalgia, pain in extremity, arthralgia, bone pain and spinal pain upon discontinuing treatment with TASIGNA.

**Common**: folliculitis, upper respiratory tract infection (including pharyngitis, nasopharyngitis, rhinitis), skin papilloma, leukopenia, eosinophilia, febrile neutropenia, pancytopenia, lymphopenia, anorexia, electrolyte imbalance (including hypomagnesaemia, hyper/hypokalaemia, hyponatraemia, hyper/hypocalcaemia, hyperphosphataemia), diabetes mellitus, hyperglycaemia, hypercholesterolaemia, hyperlipidaemia, hypertriglyceridaemia, decreased appetite, depression, insomnia, anxiety, dizziness, peripheral neuropathy, hypoaesthesia, paraesthesia, eye haemorrhage, periorbital oedema, eye pruritus, conjunctivitis, dry eye (including xerophthalmia), vertigo, angina pectoris, arrhythmia (including atrioventricular block, cardiac flutter, extrasystoles, atrial fibrillation, tachycardia, bradycardia), palpitations, electrocardiogram QT prolonged, hypertension, flushing, dyspnoea, dyspnoea exertional, epistaxis, cough, dysphonia, abdominal pain, diarrhoea, pancreatitis, abdominal discomfort/distension, dyspepsia, dysgeusia, flatulence, hepatic function abnormal, night sweats, eczema, urticaria, hyperhidrosis, contusion, acne, dermatitis (including allergic exfoliative and acneiform), muscle spasms, bone pain, pain in extremity, musculoskeletal chest pain, musculoskeletal pain, back pain, neck pain, flank pain, muscular weakness, pollakiuria, asthenia, oedema peripheral, pyrexia, chest pain (including non-cardiac chest pain), pain, chest discomfort, malaise, haemoglobin decreased, blood amylase increased, gamma-glutamyltransferase increased, blood creatine phosphokinase increased, blood alkaline phosphatase increased, blood insulin increased, weight decreased, weight increased, globulins decreased.

**Uncommon:** pneumonia, urinary tract infections, gastroenteritis, bronchitis, herpes virus infection, candidiasis including oral candidiasis, hyperthyroidism, hypothyroidism, gout, dehydration, increased appetite, dyslipidaemia, intracranial haemorrhage, ischaemic stroke, transient ischaemic attack, cerebral infarction, migraine, loss of consciousness (including syncope), tremor, disturbance of attention, hyperaesthesia, vision impairment, vision blurred, visual acuity reduced, eyelid oedema, photopsia, hyperaemia (scleral, conjunctival, ocular), eye irritation, conjunctival haemorrhage, cardiac failure, myocardial infarction, coronary artery disease, cardiac murmur, pleural and pericardial effusions, cyanosis, hypertensive crisis, peripheral arterial occlusive disease, intermittent claudication, arterial stenosis limb, haematoma, arteriosclerosis, pulmonary oedema, interstial lung disease, pleuric pain, pleurisy, pharyngolaryngeal pain, throat irriation, gastrointestinal haemorrhage, melena, mouth ulceration, gastroesophageal reflux, stomatitis, oesophageal pain, dry mouth, gastritis, sensitivity of teeth, hepatotoxicity, toxic hepatitis, jaundice, exfoliative rash, drug eruption, pain of skin, ecchymosis, swelling face, musculoskeletal stiffness, joint swelling, dysuria, micturation urgency, nocturia, breast pain, gynaecomastia, erectile dysfunction, face oedema (including swelling face), gravitational oedema, influenza-like illness, chills, feeling body temperature change (including feeling hot, feeling cold), blood lactate dehydrogenase increased, blood urea increased.

**Frequency not known**: sepsis, subcutaneous abscess, anal abscess, furuncle, tinea pedis, oral papilloma, paraproteinaemia, thrombocythaemia, leukocytosis, hypersensitivity, hyperparathyroidism secondary, thyroiditis, hyperuricaemia, hypoglycaemia, disorientation, confusional state, amnesia, dysphoria, cerebrovascular accident, basilar artery stenosis, brain oedema, optic neuritis, lethargy, dysaesthesia, restless legs syndrome, papilloedema, diplopia, photophobia, eye swelling, blepharitis, eye pain, chorioretinopathy, conjunctivitis allergic, ocular surface disease, hearing impaired, ear pain, tinnitus, ventricular dysfunction, pericarditis, ejection fraction decreased, shock haemorrhagic, hypotension, thrombosis, peripheral artery stenosis, pulmonary hypertension, wheezing, oropharyngeal pain, gastrointestinal ulcer perforation, retroperitoneal haemorrhage, haematemesis, gastric ulcer, oesophagitis ulcerative, subileus, enterocolitis, haemorrhoids, hiatus hernia, rectal haemorrhage, gingivitis, cholestasis, hepatomegaly, psoriasis, erythema multiforme, erythema nodosum, skin ulcer, palmar-plantar erythrodysaesthesia syndrome, petechiae, photosensitivity, blister, dermal cyst, sebaceous hyperplasia, skin atrophy, skin discolouration, skin exfoliation, skin hyperpigmentation, skin hypertrophy, hyperkeratosis, arthritis, renal failure, haematuria, urinary incontinence, chromaturia, breast induration, menorrhagia, nipple swelling, localized oedema, troponin increased, blood bilirubin unconjugated increased, blood insulin decreased, insulin C-peptide decreased, blood parathyroid hormone increased, tumour lysis syndrome, and hepatitis B reactivation.

**you can report any undesirable effects through:**
- **Toll free phone: 8002490000**
- **Fax: +966-11-205-7662**
- **E-mail: npc.drug@sfda.gov.sa**
- **Or by online: https://ade.sfda.gov.sa/**

**Or Novartis drug safety:**
**Phone: +99611 265 8100**
**Fax: +966 11 265 8107**
**Email: adverse.events@novartis.com**

NOVARTIS





# Tasigna® (nilotinib)

# Important Information About How to Take Your Medication

NOVARTIS

## What is Tasigna® (nilotinib) used for?

Tasigna is a prescription medicine used to treat a type of leukemia called Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in adult patients who either:

- Are newly diagnosed
- Are no longer benefiting from previous other treatments, including Glivec® (imatinib)
- Have taken other treatments, including imatinib, and cannot tolerate them

## The Do's and Don'ts of taking Tasigna

### What to do

- **Take 2 capsules twice every day,** around the same time each day, as prescribed by your doctor. This is different from Glivec®, which is taken once daily by most patients. Please keep this in mind.
- **Swallow the capsules whole, followed by a full glass of water.** Do not chew the capsules
- **Take each dose about 12 hours apart.** For example, if you take the first dose at 10 am, wait until 10 pm before you take the second dose.
- **Take Tasigna when it is first prescribed.** Whatever is left of your previous medication should be discarded. If a dose is missed, patients should not make up the dose, but take the next dose as scheduled.
- Under the supervision of a doctor, in case you have achieved a long-lasting deep molecular response (e.g. at least MR4.5), you may perhaps be eligible to discontinue Tasigna. If you do discontinue Tasigna, you will need to have frequent blood and molecular testing to monitor your CML disease status, and see if you need to restart Tasigna treatment.



### What NOT to do

- **Do NOT take Tasigna with food.** Taking food with Tasigna will increase the amount of Tasigna circulating in your blood, and can cause severe side effects such as QT prolongation.
- No food should be eaten for 2 hours before and at least 1 hour after taking a dose.
- **Do NOT consume grapefruit or grapefruit juice at any time during treatment with Tasigna.**
- Grapefruit interacts with an enzyme in the body that may increase the amount of Tasigna circulating in your blood, possibly to a harmful level.
- Please ask your doctor about any other foods that should be avoided with Tasigna.
- **Do NOT take any other medicines without talking to your doctor or pharmacist.** This includes over-the-counter and herbal remedies (e.g. St. John's wort). The doctor will decide if any changes need to be made to the medicines that you are taking.
- Do not stop taking Tasigna unless your doctor tells you to do so.

### What should I do if I take more Tasigna than I should?

- If you have taken more Tasigna than prescribed, or if someone else accidentally takes your medication, contact a doctor or the hospital for advice right away. Show them the pack of capsules. Medical treatment may be necessary.

### What to do if you feel sick

- If you are sick and experience vomiting after taking Tasigna, you should NOT take another dose. Speak to your doctor immediately.



### Tell your doctor if:

- You have QT prolongation or a family history of it.
- You experience fainting or have an irregular heartbeat while taking Tasigna® (nilotinib). — These can be signs of QT prolongation.
- You know that you suffer from low blood levels of electrolytes, such as potassium or magnesium.
- You develop swelling of feet or hands, generalized swelling or rapid weight gain, as these may be signs of severe fluid retention. Uncommon cases of severe fluid retention have been reported.
- You have a heart disorder, liver disorder, high cholesterol, or diabetes or are taking medicines for these conditions.
- You are pregnant, breast-feeding or lactose intolerant.
- You have any side effects during treatment with Tasigna.
- You develop chest pain or discomfort, numbness or weakness, problems with walking or with your speech, pain, discoloration or a cool feeling in a limb, **tell your doctor immediately,** as these may be signs of a cardiovascular event. Serious cardiovascular events, including problems with the blood flow to the leg (peripheral arterial occlusive disease), ischemic heart disease, and problems with blood supply to the brain (ischemic cerebrovascular disease) have been reported. Your doctor should assess the level of fats (lipids) and sugar in your blood before initiating treatment and during Tasigna treatment.
- If you get pain in muscles, joints, limbs or your back after Tasigna has been discontinued.