NOVARTIS

TASIGNA®

(nilotinib)

50mg, 150 mg and 200 mg Hard Capsules

Basic Succinct Statement

CODE: BSS RD 25 MAR 2019; APPR 14 JAN 2020

This material is only meant for Healthcare Professionals

TASIGNA®

Important note: Before prescribing, consult full prescribing information.

Presentation: Hard capsules containing 50mg, 150 mg or 200 mg of nilotinib.

Indications: Treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP); treatment of pediatric patients 2 years of age and older with newly diagnosed Ph+ CML-CP; treatment of chronic phase (CP) and accelerated phase (AP) Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML) in adult patients resistant to or intolerant of at least one prior therapy including imatinib; treatment of pediatric patients 2 years of age and older with Ph+ CML-CP with resistance or intolerance to prior therapy including imatinib.

Dosage: ♦Treatment should be continued as long as clinical benefit is observed or until unacceptable toxicity occurs. ♦ 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.

Adults: ♦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.

Children and adolescents: ♦Dosing in pediatric patients is individualized and is based on body surface area (mg/m2). ♦Pediatric patients with newly diagnosed Ph+ CML-CP, or with Ph+ CML-CP with resistance or intolerance to prior therapy including imatinib: 230 mg/m2 twice daily, rounded to the nearest 50 mg dose (to a maximum single dose of 400 mg). There is no experience in pediatric patients below 2 years of age or in pediatric patients with Ph+ CML-AP or blast crisis (BC).

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). ♦ 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 “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. ♦In pediatric patients the long-term effects of prolonged treatment with TASIGNA is unknown. Close monitoring of growth in pediatric patients under TASIGNA treatment is recommended. ♦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.

Adverse drug reactions: ♦**Very common**: headache, nausea, abdominal pain upper, rash, pruritus, alopecia, myalgia, 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: constipation, vomiting, folliculitis, upper respiratory tract infection (including pharyngitis, nasopharyngitis, rhinitis), skin papilloma, leukopenia, eosinophilia, febrile neutropenia, pancytopenia, lymphopenia, electrolyte imbalance (including hypomagnaesemia, hyper/hypokalaemia, hyponatraemia, hyper/hypocalcaemia, hyperphosphataemia), diabetes mellitus, hyperglycaemia, hypercholesterolaemia, hyperlipidaemia, hypertriglyceridaemia, decreased appetite, anorexia, 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, peripheral artery stenosis, dyspnoea, dyspnoea exertional, epistaxis, cough, dysphonia, abdominal pain diarrhoea, pancreatitis, abdominal discomfort/distension, dyspepsia, dysgeusia, flatulence, hepatic function abnormal, erythema, night sweats, eczema, urticaria, hyperhidrosis, contusion, acne, dermatitis (including allergic exfoliative and acneiform), dry skin, arthralgia, muscle spasms, bone pain, pain in extremity, musculoskeletal chest pain, musculoskeletal pain, back pain, neck pain, flank pain, muscular weakness, growth retardation, 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, thrombocythaemia, leukocytosis, 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, pleural effusion, 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,blood glucose decreased.

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, hepatitis B reactivation.