NOVARTIS

GLIVEC® (imatinib mesilate)
100 mg and 400 mg Film-coated Tablets

Basic Succinct Statement (BSS)

Version 2.3

CODE: BSS RD 03 JUN 2019; APPR 18 MAY 2020

This material is only meant for Healthcare Professionals

GLIVEC®

Important note: Before prescribing, consult full prescribing information.

Presentation: Imatinib mesilate. ♦Film-coated tablets containing 100 mg or 400 mg of imatinib (as mesilate beta crystals).

Indications:

Glivec is indicated for the treatment of :

- adult and pediatric patients with newly diagnosed chronic myeloid leukaemia (CML) as well as for the treatment of adult and pediatric patients with CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.
- adult patients with unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST).
- adjuvant treatment of adult patients following resection of GIST. Patients who have a low or very low risk of recurrence should not receive adjuvant treatment.
- adult and paediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy.
- adult patients with relapsed or refractory Ph+ ALL as monotherapy.
- adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements.
- adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukaemia (CEL) with F1P1L1-PDGFRα rearrangement.
- adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP).
- adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown.

The effectiveness of Glivec is based on overall haematological and cytogenetic response rates and progression-free survival in CML, on haematological and cytogenetic response rates in Ph+ ALL, MDS/MPD, on haematological response rates in HES/CEL and ASM and on objective response rates in GIST and DFSP, and on recurrence-free survival in adjuvant GIST (see section PHARMACODYNAMICS). The experience with Glivec in patients with MDS/MPD associated with PDGFR gene re-arrangements is very limited. Except in newly diagnosed chronic phase CML, there are no controlled trials demonstrating a clinical benefit or increased survival in diseases.

Dosage: Adults: Adults: ♦For CML: 400 mg a day for patients in chronic phase CML administered orally once daily; 600 mg a day for patients in accelerated phase or blast crisis, administered orally once daily. ♦**For Ph+ALL**: 600 mg a day. ♦**For ASM**: 400 mg a day; for SM associated with eosinophilia, 100 mg a day to be increased to 400 mg a day if well tolerated and insufficient response to therapy. ♦**For HES/CEL**: 400 mg a day; for HES/CEL with demonstrated FIP1L1-PDGFR-alpha fusion kinase, 100 mg a day to be increased to 400 mg a day if well tolerated and insufficient response to therapy. Treatment should be continued as long as the patient continues to benefit. ♦**For GIST, GIST adjuvant treatment, MDS/MPD**: 400 mg a day. ♦**For DFSP:** 800 mg a day (400 mg twice daily). ♦For CML and GIST, under certain circumstances, a dose of 800 mg could be considered and should be administered as 400 mg

twice daily. ♦Patients with hepatic or renal impairment should be given 400 mg daily as a starting dose. ♦Dose adjustment may be required due to side-effects or insufficient response to therapy.

Children: ♦For CML and Ph+ALL: 340 mg/m^2 daily (not to exceed the total dose of 600 mg a day). No experience in children for CML below 2 years of age and for Ph+ALL below 1 year of age.

Contraindications: Hypersensitivity to imatinib or to any of the excipients.

Warnings and precautions: ♦Caution should be used when taking other medicines (see section Interactions). ♦Should be taken with food and a large glass of water to minimize the risk of gastrointestinal disturbances. ♦Beware of severe fluid retention. It is recommended that patients be weighed regularly. ♦Regular monitoring of complete blood counts and liver function tests. Monitoring of hepatic function is recommended when used concomitantly with hepatotoxic chemotherapy regimens in Ph+ ALL patients. ♦Monitoring renal function prior to the start of therapy and during therapy. ♦Test for hepatitis B infection before initiating treatment with Glivec. 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.♦ Caution in patients with history of cardiac disease or history of renal failure. Careful monitoring of patients with cardiac disease, risk factors for cardiac failure or history of renal failure. Cardiac screening should be considered in patients with HES/CEL, and patients with MDS/MPD or ASM with high level of eosinophils (echocardiogram, serum troponin level); if either is abnormal, prophylactic use of systemic steroids to be considered for 1 to 2 weeks concomitantly with imatinib at the initiation of therapy. ♦Monitoring of TSH levels in thyroidectomy patients undergoing levothyroxine replacement. ♦Reports of gastrointestinal hemorrhage and hemorrhages at the site of tumor deposits in GIST patients. Reports of gastric antral vascular ectasia (GAVE) in patients with CML, ALL and other diseases. Monitoring for gastrointestinal symptoms at the start of and during treatment. Glivec discontinuation may be considered. ♦Reports of tumor lysis syndrome (TLS). Correction of clinically significant dehydration and treatment of high uric acid levels prior to initiation of Glivec®. ♦Should not be used during pregnancy unless clearly necessary. Reports of spontaneous abortions/infant congenital anomalies in women who have taken Glivec. Women of child-bearing potential must be advised to use highly effective contraception. Women of child-bearing potential who open capsules should handle contents with caution and avoid skin-eye contact or inhalation. Hands to be washed immediately after handling open capsules. Women taking Glivec should not breast-feed. ♦Children/adolescents: close monitoring of growth due to growth retardation reports. ♦Caution recommended when driving a car or operating machinery.

Adverse drug reactions: ♦***Very common (>10%)****:* neutropenia, thrombocytopenia, anaemia, headache, nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, periorbital oedema, dermatitis, eczema, rash, muscle spasm or cramps, musculoskeletal pain including myalgia, arthralgia, bone pain, fluid retention and edema, fatigue, weight increased,

musculoskeletal pain upon treatment discontinuation (including myalgia, pain in extremity, arthralgia, bone pain, spinal pain). ♦***Common(1 to 10%)***: pancytopenia, febrile neutropenia, anorexia, insomnia, dizziness, paraesthesia, taste disturbance, hypoaesthesia, eyelid oedema, lacrimation increased, conjunctival haemorrhage, conjunctivitis, dry eye, blurred vision, flushing, haemorrhage, dyspnoea, epistaxis, cough, flatulence, abdominal distension, gastro-esophageal reflux, constipation, dry mouth, gastritis, increased hepatic enzymes, pruritus, face oedema, dry skin, erythema, alopecia, night sweats, photosensitivity reaction, joint swelling, weakness, pyrexia, anasarca, chills, rigors, weight decreased. ♦***Uncommon(01 to 1%)***: herpes zoster, herpes simplex, nasopharyngitis, pneumonia, sinusitis, cellulitis, upper respiratory tract infection, influenza, urinary tract infection, gastroenteritis, sepsis, thrombocythaemia, lymphopenia, bone marrow depression, eosinophilia, lymphadenopathy, hypokalaemia, increased appetite, hypophosphataemia, decreased appetite, dehydration, gout, hyperuricaemia, hypercalaemia, hyperglycaemia, hyponatraemia, depression, libido decreased, anxiety, migraine, somnolence, syncope, peripheral neuropathy, memory impairment, sciatica, restless leg syndrome, tremor, cerebral haemorrhage, eye irritation, orbital oedema, scleral oedema, retinal haemorrhage, blepharitis, macular oedema, vertigo, tinnitus, hearing loss, palpitations, tachycardia, cardiac failure congestive, pulmonary oedema, hypertension, haematoma, subdural haematoma, peripheral coldness, hypotension, Raynaud's phenomenon, pleural effusion, pharyngolaryngeal pain, pharyngitis, stomatitis, mouth ulceration, gastrointestinal haemorrhage, eructation, melena, oesophagitis, ascites, gastric ulcer, haematemesis, cheilitis, dysphagia, pancreatitis, hyperbilirubinaemia, hepatitis, jaundice, rash pustular, contusion, sweating increased, urticaria, ecchymosis, increased tendency to bruise, hypotrichosis, skin hypopigmentation, exfoliative dermatitis, onychoclasis, folliculitis, petechiae, psoriasis, purpura, skin hyperpigmentation, bullous eruptions, joint and muscle stiffness, renal pain, haematuria, acute renal failure, urinary frequency increased, gynaecomastia, erectile dysfunction, menorrhagia, menstruation irregular, sexual dysfunction, nipple pain, breast enlargement, scrotal oedema, chest pain, malaise, blood creatinine increased, blood creatine phosphokinase increased, blood lactate dehydrogenase increased, blood alkaline phosphatase increased, cerebral oedema, thrombosis/embolism, acute respiratory failure, interstitial lung disease, ileus/intestinal obstruction, tumour haemorrhage/necrosis, gastrointestinal perforation, palmar-plantar erythrodysaesthesia syndrome. ♦***Rare*****:** Fungal infection, haemolytic anaemia, hyperkalaemia, hypomagnesaemia, confusional state, increased intracranial pressure, convulsions, optic neuritis, cataract, glaucoma, papilloedema, arrhythmia, atrial fibrillation, cardiac arrest, myocardial infarction, angina pectoris, pericardial effusion, pleuritic pain, pulmonary fibrosis/hypertension/haemorrhage, colitis, ileus, inflammatory bowel disease, hepatic failure/necrosis, acute febrile neutrophilic dermatosis (Sweet's syndrome), nail discolouration, angioneurotic oedema, rash vesicular, erythema multiforme, leucocytoclastic vasculitis, Stevens-Johnson syndrome, acute generalized exanthematous pustulosis (AGEP), muscular weakness, arthritis, blood amylase increased, vitreous haemorrhage, pericarditis, cardiac tamponade, diverticulitis, gastric antral vascular ectasia (GAVE), lichenoid keratosis, lichen planus, avascular necrosis/ hip osteonecrosis, rhabdomyolysis/myopathy, tumour lysis syndrome. ♦***Very rare*****:** anaphylactic shock, toxic epidermal necrolysis, and haemorrhagic corpus luteum/haemorrhagic ovarian cyst. ♦***Not known:*** growth retardation in children/adolescents, drug rash with eosinophilia and systemic symptoms (DRESS), pseudoporphyria and hepatitis B reactivation.