United Kingdom Prescribing Information (CML and GIST)

GLIVEC® (imatinib) 100mg and 400mg Tablets

Important note: Before prescribing, consult Summary of Product Characteristics (SmPC).

Presentation: Imatinib (as mesilate) 100 mg and 400 mg film-coated tablets
Indication(s): Chronic myeloid leukaemia (CML) Treatment of adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+)CML for whom bone marrow transplantation is not considered as the first line oftreatment. Treatment of adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy or in accelerated phase or blast crisis. Gastrointestinal stromal tumours (GIST) Treatment of adult patients with Kit (CD117) positive unresectable and/or metastatic malignant GIST. Adjuvant treatmentof adult patients who are at significant risk of relapse following resection of Kit(CD117)-positive GIST. Patients who have a low or very low risk of recurrence should not receive adjuvant treatment.
Dosage and administration: Oral with a meal and a large glass of water. CML *Adults:* 400mg/day for patients in chronic phase CML and 600mg/day for patients in accelerated phase or blast crisis. Increases to 600mg or 800mg (given as 400mg twice daily) may be considered. Patients should be monitored closely following dose escalation, given the potential for an increased incidence of adverse reactions at higher dosages. Dosing for children should be on the basis of body surface area (mg/m^2). *Children:* 340mg/m^2 daily. Increases to 570mg/m^2 daily (not to exceed the total dose of 800mg) may be considered. There is no experience with the treatment of children below 2 years of age.
GIST: The recommended dosage is 400mg/day.
Refer to the SmPC for dose adjustments due to adverse reactions. Patients with liver dysfunction or renal insufficiency should be given the minimum recommended dose of 400mg daily.
Contraindications: Hypersensitivity to the active substance or to any of the excipients Cellulose microcrystalline, Crospovidone, Hypromellose, Magnesium stearate, Silica, colloidal anhydrous, Iron oxide red (E172), Iron oxide yellow (E172), Macrogol, Talc.
Warnings/Precautions: *Paediatric population:* There have been case reports of growth retardation occurring in children and pre-adolescents receiving imatinib, Close monitoring of growth in children under imatinib treatment is recommended. *Hypothyroidism:* Use with caution in patients receiving levothyroxine, closely monitor TSH levels. *Hepatotoxicity:* Cases of liver injury, including hepatic failure and hepatic necrosis, have been observed with imatinib. Peripheral blood counts and liver enzymes should be carefully monitored in patients with hepatic dysfunction. Hepatic function should be carefully monitored in circumstances where imatinib is combined with chemotherapy regimens also known to be associated with hepatic dysfunction. *Fluid retention:* Occurrences of severe fluid retention have been reported. Weigh patients regularly. An unexpected rapid weight gain should be carefully investigated.
Cardiac disease: Patients with cardiac disease or risk factors for cardiac failure or history of renal failure should be monitored carefully and any patient with signs or symptoms consistent with cardiac or renal failure should be evaluated and treated.
Gastrointestinal haemorrhage: Gastrointestinal and intra-tumoural haemorrhages have been reported in patients with GIST. Gastric antral vascular ectasia (GAVE) has been reported in patients with CML, ALL and other diseases. When needed, discontinuation of imatinib treatment may be considered. *Tumour lysis syndrome (TLS):* Correct dehydration and treat high uric acid levels prior to treatment. *Hepatitis B (HBV) reactivation:* Reactivation of HBV has been reported and some cases resulted in acute hepatic failure, liver transplantation or a fatal outcome. Test for HBV before treatment initiation. Carriers of HBV should be closely monitored for HBV infection during therapy and after therapy for several months. *Phototoxicity:* Avoid or minimise exposure to direct sunlight. *Thrombotic Microangiopathy:* BCR-ABL tyrosine kinase inhibitors (TKIs) have been associated with thrombotic microangiopathy (TMA), including individual case reports for Glivec. If laboratory or clinical findings associated with TMA occur in apatient receiving Glivec, treatment should be discontinued and thorough evaluation for TMA, including ADAMTS13 activity and anti-ADAMTS13-antibody determination, should be completed. If anti-ADAMTS13-antibody is elevated in conjunction with low ADAMTS13 activity, treatment with Glivec should not be resumed. *Laboratory tests:* Complete blood counts must be performed regularly during treatment. Treatment of CML patients with Glivec has been associated with neutropenia or thrombocytopenia. Liver and renal function should be monitored regularly. Renal function should be evaluated prior to the start of imatinib therapy and closely monitored during therapy. Patients with severe renal impairment should be treated with caution. Long-term treatment with imatinib maybe associated with a clinically significant decline in renal function. Patients with renal impairment should be given the minimum starting dose.
Interactions: Use caution administering imatinib with CYP3A4 inhibitors (e.g. protease inhibitors, azole antifungals, and certain macrolides). Concomitant use of imatinib and CYP3A4 inducers (e.g. dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital, fosphenytoin, primidone or St. John's Wort) may significantly reduce exposure to imatinib, potentially increasing the risk of therapeutic failure. Therefore, concomitant use of strong CYP3A4 inducers and imatinib should be avoided. Patients who require anticoagulation should receive low-molecular-weight or standard heparin, instead of coumarin derivatives such as warfarin. Caution is advised when administering Glivec with CYP3A4 and CYP2D6 substrates with a narrow therapeutic window. Exercise caution when using high doses of Glivec and paracetamol concomitantly. Glivec may increase plasma concentration of other CYP3A4 metabolised drugs.
Fertility, pregnancy and lactation: Use effective contraception during treatment and for at least 15 days after stopping treatment with Glivec. Do not use during pregnancy unless clearly necessary. If it is used during pregnancy, the patient must be informed of the potential risk to the foetus. Women should not breast-feed during treatment and for at least 15 days after stopping treatment with Glivec. Patients concerned about their fertility on Glivec treatment should consult with their physician.
Effects on ability to drive and use machines: Caution should be recommended when driving a car or operating machinery.
Undesirable effects: *Very common (≥1/10)*: neutropenia, thrombocytopenia, anaemia, headache, nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, periorbital oedema, dermatitis/eczema/rash, muscle spasm and cramps, musculoskeletal pain including myalgia, arthralgia, bone pain, fluid retention and oedema, fatigue, weight increased. *Common (≥1/100 to <1/10)*: 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-oesophageal 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 (≥1/1,000 to <1/100): 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, hypercalcaemia, hyperglycaemia, hyponatraemia, depression, libido decreased, anxiety, migraine, somnolence, syncope, peripheral neuropathy, memory impairment, sciatica, restless leg syndrome, tremor, cerebral haemorrhage, eye irritation, eye pain, orbital oedema, scleral haemorrhage, 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, melaena, 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, dermatitis exfoliative, onychoclasis, folliculitis, petechiae, psoriasis, purpura, skin hyperpigmentation, bullous eruptions, panniculitis (including erythema nodosum), joint and muscle stiffness, osteonecrosis, renal pain, haematuria, renal failure acute, 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. *Rare (≥1/10,000 to <1/1,000)*: fungal infection, tumour lysis syndrome, haemolytic anaemia, thrombotic microangiopathy, 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, pulmonary hypertension, pulmonary haemorrhage, colitis, ileus, inflammatory bowel disease, hepatic failure, hepatic necrosis, acute febrile neutrophilic dermatosis (Sweet's syndrome), nail discolouration, angioneurotic oedema, rash vesicular, erythema multiforme, leucocytoclastic vasculitis, Stevens- Johnson syndrome, acute generalised exanthematous pustulosis, pemphigus, muscular weakness, arthritis, rhabdomyolysis/myopathy, haemorrhagic corpus luteum/haemorrhagic ovarian cyst, blood amylase increased. *Not known*: HBV reactivation, tumour haemorrhage/tumour necrosis, anaphylactic shock, cerebral oedema, vitreous haemorrhage, pericarditis, cardiac tamponade, thrombosis/embolism, acute respiratory failure, interstitial lung disease, ileus/intestinal obstruction, gastrointestinal perforation, diverticulitis, GAVE, palmoplantar erythrodysesthesia syndrome, lichenoid keratosis, lichen planus, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms, pseudoporphyria, growth retardation in children, renal failure chronic.
Other Adverse Effects: Please consult the Summary of Product Characteristics fora detailed listing of all adverse events before prescribing.
Legal classification: POM.
Marketing Authorisation number, quantities and NHS price:
PLGB 00101/1080– 100mg x 60 tablets, £973.32
PLGB 00101/1081– 400mg x 30 tablets, £1,946.67

Date of last revision of prescribing information: January 2025
Full Prescribing Information available from: Novartis Pharmaceuticals UK Ltd,2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ, UK. Tel: 01276 692255.

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report or alternatively email medinfo.uk@novartis.com or call 01276 698370

UK | FA-11338206 | January 2025