

Important Safety Information¹

GLIVEC® (imatinib) is indicated for the treatment of adult patients with KIT (CD 117)-positive unresectable and/or metastatic, malignant gastrointestinal stromal tumours (GIST).

- **Contraindications:** Hypersensitivity to imatinib or to any of the excipients
- **Precautions/Warnings:** Should be taken with food and a large glass of water to minimise 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. Caution in patients with history of cardiac disease. Careful monitoring of patients with cardiac disease or risk factors for cardiac failure. Monitoring of TSH levels in thyroidectomy patients undergoing levothyroxine replacement. Should not be used during pregnancy unless clearly necessary. Should not be used by breast-feeding mothers
- **Interactions:** Caution with CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin). Caution with CYP3A4 inducers (e.g. dexamethasone, rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort). Caution with substrates of CYP3A4 (e.g. triazolo-benzodiazepines, dihydropyridine calcium channel blockers, simvastatin, cyclosporin, pimozone), CYP2C9 (e.g. warfarin) or CYP2D6 (e.g. metoprolol). Caution with concomitant use of paracetamol/acetaminophen

Adverse reactions:

- **Very common:** headache, nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, myalgia, arthralgia, muscle spasm or cramps, bone pain, dermatitis, eczema, rash, fatigue, weight increase
- **Common:** anorexia, insomnia, dizziness, paraesthesia, taste disturbance, hypoaesthesia, flushing, photosensitivity reaction, weakness, pyrexia, chills, weight decreased, lacrimation increased, conjunctivitis, dry eye, blurred vision, dyspnoea, epistaxis, cough, flatulence, abdominal distension, gastro-oesophageal reflux, constipation, dry mouth, gastritis, increased hepatic enzymes, pruritus, dry skin, erythema, alopecia, night sweats, joint swelling



Novartis Pharma AG
CH-4002 Basel, Switzerland

© 2007 Novartis

3/07

G-GLI-10089

HELP YOUR PATIENTS WITH KIT+ GIST ACHIEVE OPTIMAL RESPONSES TO GLIVEC®



Manage mild-to-moderate side effects with supportive care to maximise therapeutic results with GLIVEC¹

- Most side effects are mild to moderate in severity, and some can be managed without compromising the GLIVEC dose^{1,2}
- Continue daily dosing whenever possible to help maintain ongoing suppression of the tyrosine kinase receptor KIT^{2,3}
 - Some side effects may require dose reduction, treatment interruption, and in rare cases, permanent discontinuation of GLIVEC¹
 - Treatment with GLIVEC is associated with anemia, neutropenia, and thrombocytopenia¹
 - Dose reduction or treatment interruptions for severe neutropenia and thrombocytopenia are recommended¹
 - In severe nonhaematologic adverse reactions, GLIVEC should be withheld until the event has resolved, then resumed thereafter, as appropriate, depending on the initial severity of the event¹
 - Discontinuation rates due to adverse events are generally low, at 4%¹

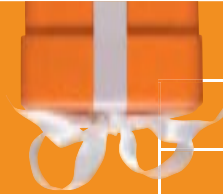
PLEASE SEE IMPORTANT SAFETY INFORMATION AND ENCLOSED SUMMARY OF PRODUCT CHARACTERISTICS.



Manage mild-to-moderate side effects with supportive care to provide the full potential benefit of GLIVEC^{1,2}

FOR PATIENTS WITH KIT+ GIST

Event	Examples of Supportive Care
Oedema	Diuretic; topical and anti-inflammatory agent (for periorbital oedema)
Diarrhoea	Antidiarrhoeal
Nausea	Take GLIVEC with a meal and a large glass of water
Muscle cramps	Calcium and magnesium supplements, quinine
Rash	Antihistamine; topical or systemic steroids
Musculoskeletal pain	Nonsteroidal anti-inflammatory agent



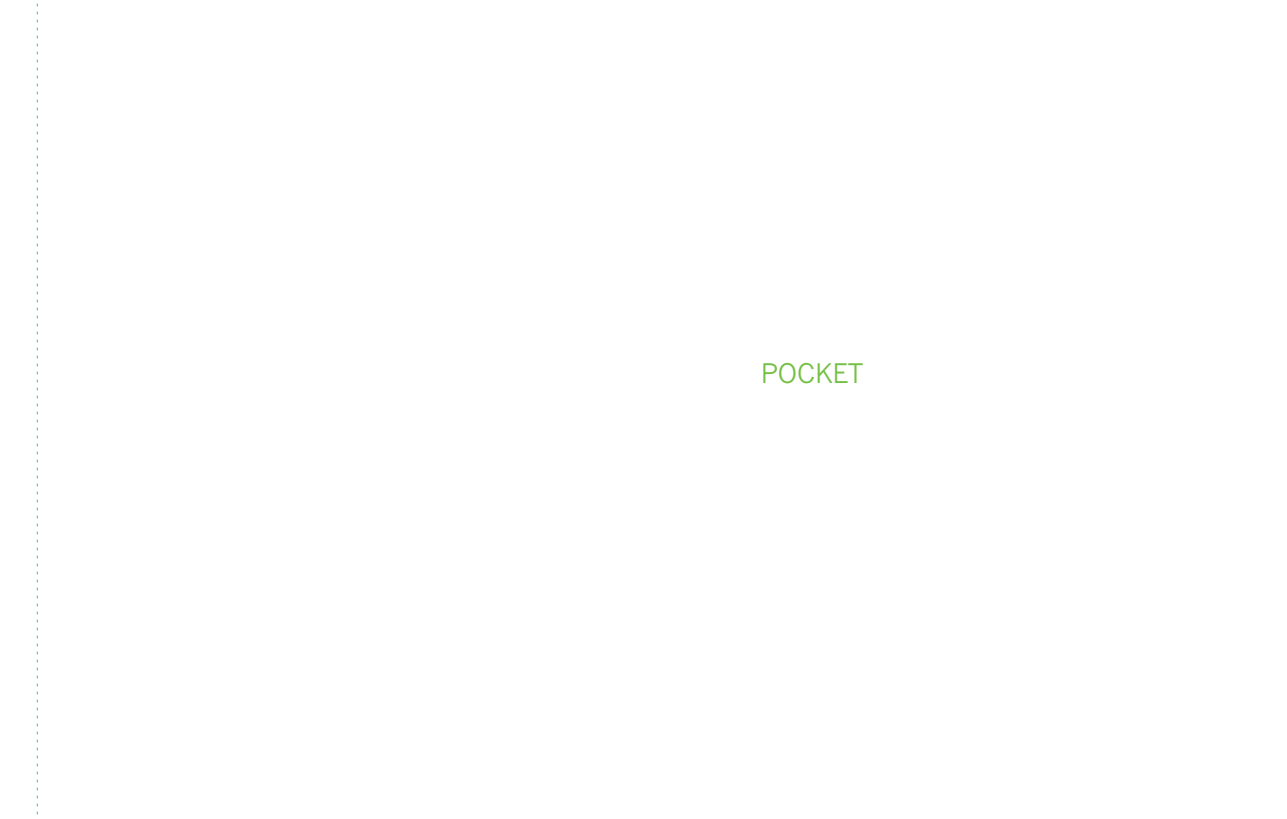
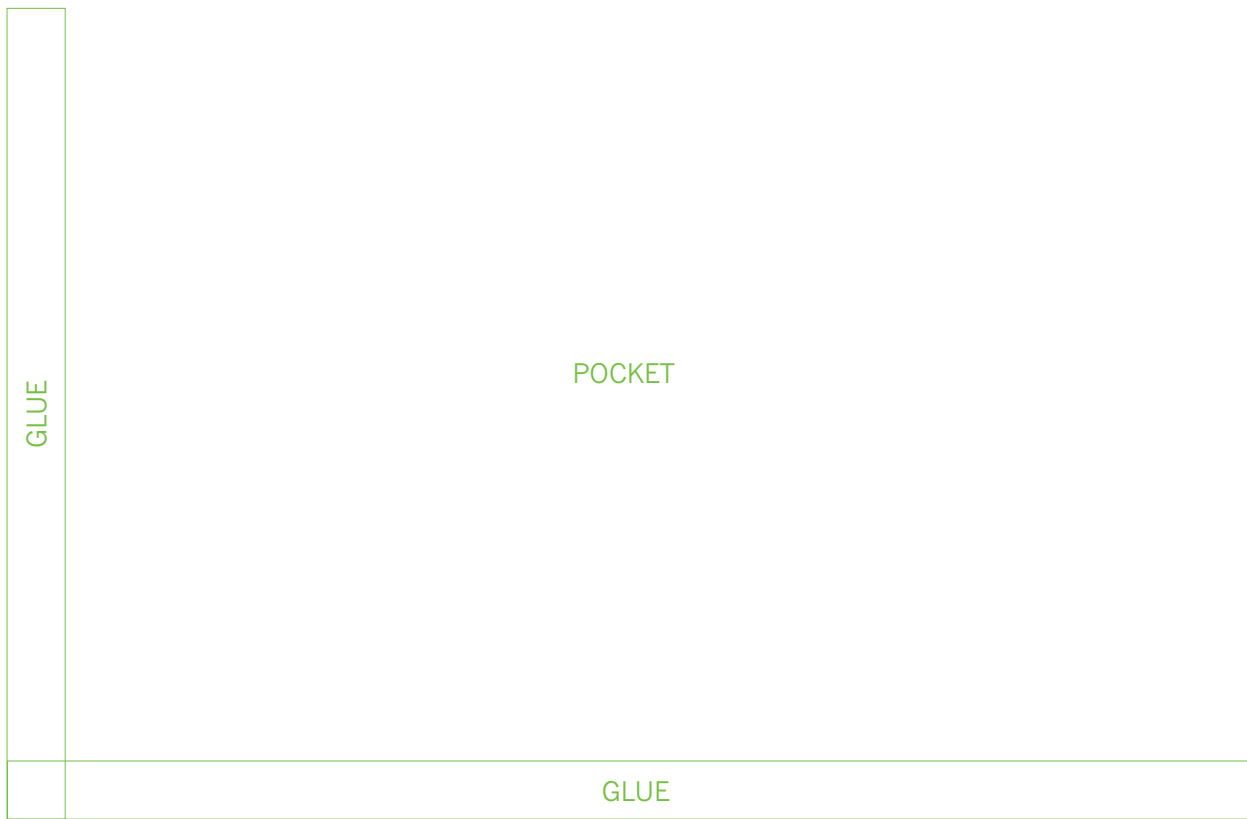
HELP PATIENTS ACHIEVE THE FULL POTENTIAL BENEFIT OF GLIVEC®

Most mild-to-moderate side effects may be managed with supportive care to maintain dose and to help achieve the best possible response¹

- GLIVEC has a mostly mild-to-moderate side-effect profile and 5 years of post-approval data^{1,4}
- Some side effects may resolve with supportive care, while others may require dose interruption or adjustment¹
- Managing side effects may help patients achieve optimal responses to GLIVEC
- GLIVEC is generally well tolerated when it is taken as instructed
 - Dose GLIVEC daily to provide continuous KIT suppression^{2,3}

GLIVEC® (imatinib) is indicated for the treatment of adult patients with KIT (CD 117)-positive unresectable and/or metastatic, malignant gastrointestinal stromal tumours (GIST).

PLEASE SEE IMPORTANT SAFETY INFORMATION AND ENCLOSED SUMMARY OF PRODUCT CHARACTERISTICS.



- **Potentially serious:** fluid retention, anasarca, oedema (including brain, eye, pericard, abdomen and lung), neutropenia, thrombocytopenia or anaemia, pancytopenia, haemolytic anaemia, sepsis, cellulitis, fungal infection, upper respiratory tract infection, interstitial lung disease, pneumonia, pericardial/pleural effusion, pleuritic pain, pulmonary hypertension/haemorrhage/fibrosis, cardiac failure congestive, arrhythmia, atrial fibrillation, cardiac arrest, myocardial infarction, angina pectoris, pericarditis, cardiac tamponade, thrombosis/embolism, ileus/intestinal obstruction, pancreatitis, hepatic failure/necrosis, hepatitis, exfoliative dermatitis, angioneurotic oedema, Stevens-Johnson syndrome, erythema multiforme, leucocytoclastic vasculitis, Sweet's syndrome, anaphylactic shock, syncope, hypotension, acute respiratory failure, interstitial lung disease, acute renal failure, haemorrhage (including brain, eye, kidney and gastrointestinal tract), melaena, haematemesis, diverticulitis, colitis, inflammatory bowel disease, gastrointestinal perforation, ascites, tumour haemorrhage/necrosis, hip osteonecrosis/avascular necrosis, sciatica, optic neuritis, cataract, glaucoma, hearing loss, Raynaud's phenomenon, increased intracranial pressure, peripheral neuropathy, paresthesia, depression, convulsions

Note: Before prescribing, please read full Summary of Product Characteristics.

References: **1.** GLIVEC® (imatinib mesilate) Summary of Product Characteristics. Basel, Switzerland: Novartis Pharma AG; 2006. **2.** Harrison ML, Goldstein D. Management of metastatic gastrointestinal stromal tumour in the Glivec era: a practical case-based approach. *Intern Med J.* 2006;36:367-377. **3.** Demetri GD, von Mehren M, Blanke CD, et al. Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med.* 2002;347:472-480. **4.** Data on file. Novartis Pharma AG, Basel, Switzerland.