Imatinib Therapy - GIST

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved Reimbursement Status*
Treatment of adult patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST).	C16	00335a	N/A
Adjuvant treatment of adult patients who are at significant risk of relapse following resection of Kit (CD117)-positive GIST.	C16	00335b	N/A

* This applies to post 2012 indications

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Unresectable/Metastatic GIST:
Imatinib 400mg is taken orally, once daily until disease progression or unacceptable toxicity develops. The dose may be increased to 800mg daily in progressing disease.

Adjuvant:
Imatinib 400mg is taken orally, once daily continuously for up to 3 years after resection unless the patient experiences disease progression or unacceptable toxicity.

Drug	Dose	Route	Cycle
Imatinib	400mg once daily*	PO with food	Continuous
*For daily doses of 800mg, the dose should be administered as 400mg twice a day, in the morning and in the evening			
Imatinib is commonly available as 100mg and 400mg/tablets			

ELIGIBILITY:

- Indications as above
- ECOG status 0-3
- Adequate bone marrow, renal and liver function

EXCLUSIONS:

- Hypersensitivity to imatinib or any of the excipients
- Patients who have a low risk of recurrence are not eligible for adjuvant treatment
- Pregnancy
- Breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- ECG
- Virology screen -Hepatitis B (HBsAg, HBcoreAb)*

*(Regimen Specific Complications for information on Hepatitis B reactivation)

Regular tests:

- Renal and liver profile monthly
- FBC every 2 weeks for first 12 weeks and then monthly or as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Haematological:

Table 1: Dose modification of imatinib in haematological toxicity

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
1.5-1.99	or	<LLN* to 75	400mg daily
1-1.49	or	50-74	400mg daily
0.5-0.99	or	10-49	Hold until toxicity ≤ Grade 1, then resume at 300mg daily. For second occurrence, hold until toxicity ≤ Grade 1, then resume at 200mg daily.
<0.5	or	<10	
No dose reductions for Grade 3 or 4 anaemia. Patients can be transfused or treated with erythropoietin			
*LLN=Lower Limit Normal			

Renal and Hepatic Impairment:

Table 2: Dose modification of imatinib in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No dose adjustment is needed Haemodialysis: no dose adjustment is needed	No dose adjustment is needed *In patients with hepatic dysfunction (mild, moderate or severe), peripheral blood counts and liver enzymes should be carefully monitored. It should be noted that GIST patients may have hepatic metastases which could lead to hepatic impairment.
Renal and hepatic recommendations aligned to Giraud et al 2023 *As per SPC	

Management of adverse events:

Table 3: Hepatotoxic Adverse Events

Bilirubin		Liver Transaminases	Dose
> 3 x ULN	or	> 5 x ULN	Hold until bilirubin < 1.5 x ULN and transaminase levels < 2.5 x ULN, then resume at 300 mg daily.

Table 4: Dose Modification for Non-Haematological Adverse Reactions

Toxicity	Occurrence	Recommended dose modification and measures
Grade 2	1st occurrence	Hold until toxicity ≤ Grade 1, then resume at the same daily dose.
	2nd occurrence	Hold until toxicity ≤ Grade 1, then resume at 300mg daily
	3rd occurrence	Hold until toxicity ≤ Grade 1, then resume at 200mg daily
Grade 3 or 4	1st occurrence	Hold until toxicity ≤ Grade 1, then resume at 300mg daily
	2nd occurrence	Hold until toxicity ≤ Grade 1, then resume at 200mg daily

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting Available on the NCCP website

Imatinib doses ≤400mg/day: Minimal to low (**Refer to local policy)**
Imatinib doses >400mg/day: Moderate to high (**Refer to local policy)**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS

- **Hypothyroidism**: Hypothyroidism has been reported in thyroidectomy patients undergoing thyroxine replacement during treatment with imatinib.
- **Fluid retention:** Monitor regularly for signs and symptoms of fluid retention caused by imatinib. Probability increases with higher doses, age greater than 65 years and patients with a prior history of cardiac disease. If severe fluid retention occurs treatment should be withheld until resolved.
- **Cardiac Disease:** Patients with cardiac disease, 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:** In the study in patients with unresectable and/or metastatic GIST, both gastrointestinal and intra-tumoural haemorrhages were reported. Based on the available data, no predisposing factors (e.g. tumour size, tumour location, coagulation disorders) have been identified that place patients with GIST at a higher risk of either type of haemorrhage. Since increased vascularity and propensity for bleeding is a part of the nature and clinical course of GIST, standard practices and procedures for the monitoring and management of haemorrhage in all patients should be applied.
- **Reactivation of Hepatitis B Virus (HBV):** Cases of reactivation of HBV have occurred in patients who are chronic carriers of HBV after they received BCR-ABL tyrosine kinase inhibitors (TKIs). Some cases of HBV reactivation resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or a fatal outcome.
    - Patients should be tested for HBV infection before initiating treatment with BCR-ABL TKIs
    - Experts in liver disease and the treatment of HBV should be consulted before treatment in patients with positive HBV serology (including those with active disease) is initiated and for patients who test positive for HBV infection during treatment.
    - Patients who are carriers of HBV requiring treatment with BCR-ABL TKIs should be closely monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

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2. Gastrointestinal Stromal Tumor Meta-Analysis, Group. Comparison of two doses of imatinib for the treatment of unresectable or metastatic gastrointestinal stromal tumors: a meta-analysis of 1,640 patients. J Clin Oncol 2010;28(7):1247-1253.
3. Verweij J, Paolo G Casali PG et al. Progression-free survival in gastrointestinal stromal tumours with high-dose imatinib: randomised trial. Lancet 2004; 364:1127-1134.
4. Dematteo, RP, Ballman KV, Antonescu CR, et al. Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebo-controlled trial. Lancet 2009;373(9669):1097-1104.
5. Joensuu H, Eriksson M, Sundby Hall K, et al. One vs three years of adjuvant imatinib for operable gastrointestinal stromal tumor: a randomized trial. JAMA 2012;307(12):1265-1272
6. BC Cancer Protocol Summary for Adjuvant Treatment of C-Kit Positive High Risk Gastrointestinal Stromal Cell Tumours Using iMAtinib SAAJGI Revised May 2018
7. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
8. Glivec® Summary of Product Characteristics Last updated 04/08/2025. Accessed September 2025 Available at https://www.ema.europa.eu/en/documents/product-information/glivec-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	20/06/2016		Prof Maccon Keane
2	20/06/2018	Updated with new NCCP template	Prof Maccon Keane
3	15/07/2020	Updated treatment table Updated emetogenic potential Updated adverse events Updated references	Prof Maccon Keane
4	18/10/2025	Regimen reviewed. Updated exclusion criteria Update renal and hepatic impairment to align with Giraud et al 2023 Updated regimen specific complications Updated regimen in line with NCCP standardisation.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.