# SORAFENIB

1. For unresectable hepatocellular carcinoma, only for patients with Child-Pugh score A (see separate guide in Hepato-biliary section for calculating a Child-Pugh score)

2. For papillary or follicular thyroid cancer

*Blueteq registration is required before treatment may start*

Drug/Dosage: **Sorafenib** initiate at 400mg po bd continuous therapy

(but see Hepatic and Renal Impairment sections)

Administration: Sorafenib is available as 200mg tablets, which may be taken at least one hour before, or 2 hours after, a meal. Alternatively, they may be taken with a low or moderate fat meal (but not a high fat meal). Swallow with a glass of water.
Grapefruit and grapefruit juice should be avoided while on sorafenib.

Frequency: continue for as long as there is clinical benefit, or unacceptable toxicity.

Main Toxicities: hand-foot syndrome; diarrhoea; hypertension; rash; alopecia; fatigue; hypophosphataemia

Anti- emetics: mildly emetogenic – anti-emetics not routinely needed

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| Regular: | FBC | every 4 weeks |
| Investigations: | LFTs | every 4 weeks |
| | U&Es (including phosphate) | every 4 weeks |
| | $Ca^{2+}$ | as indicated; monitor closely in thyroid cancer patients |
| | Blood pressure | weekly for 1st cycle (ideally via GP, with patient making a record of the readings for the next oncology appointment), then every 4 weeks |

Comments: Patients should be advised to apply moisturiser to their hands and feet regularly throughout treatment, and to minimise activities that put pressure on feet or hands if they start to develop sore hands or feet. Recommended moisturisers are Udderly Smooth or urea-containing moisturisers eg Eucerin.

Elimination of sorafenib is mainly through hepatic metabolism. Concomitant use of enzyme inducers (e.g. rifampicin, phenytoin, carbamazepine, St Johns wort) with sorafenib should be avoided, as this may increase the risk of therapeutic failure.

Interactions of sorafenib with CYP3A4 enzyme inhibitors are unlikely.

If the patient is taking warfarin, monitor the INR closely when initiating sorafenib.

Sorafenib has been shown to prolong the QT interval, so use with caution in patients taking other medicines that lead to QT prolongation (e.g. amiodarone, quinidine, sotalol, chloroquine, clarithromycin), and those with electrolyte disturbances such as hypokalaemia, hypocalcaemia, or hypomagnesaemia. When using sorafenib in these patients, periodic ECG, plus monitoring of magnesium and calcium should be considered.

**Dose Modifications** Management of suspected adverse drug reactions may require temporary interruption or dose reduction of therapy.
HCC: reduce to 400mg once daily, when dose reduction is necessary.
Thyroid cancer: SPC advice is to reduce to 600mg daily (400mg om and 200mg on) initially. If a further dose reduction is required, then reduce to 400mg daily.

a) Patients tolerating re-introduction of sorafenib at a reduced dose may be considered for a dose escalation back to 400mg twice daily.

b) If there is further toxicity at a dose of 400mg once daily, treatment should be interrupted until resolution of the toxicity to ≤ Grade 1.
Then reduce further to 200mg once daily.

Haematological Toxicity: An increased risk of bleeding may occur while on sorafenib. Discontinue sorafenib if any bleeding event requires medical intervention.

Hypertension: If hypertension develops, it should be treated (usually by GP) and monitored closely until stabilised. It is not a reason to stop sorafenib, unless patient develops severe hypertension.

Skin Toxicity: Grade 2 + hand-foot syndrome or rash may require a 1-2 week break in treatment until resolved to Grade ≤ 1. The patient should be advised to moisturise their hands and feet regularly, and to keep them cool.
Once symptoms have resolved to ≤ Grade 1, sorafenib may be re-introduced at a reduced dose, with a step-wise reduction as above.

Hepatic Impairment: Sorafenib is mainly eliminated via the hepatic route. The SPC states that no dose adjustment required in patients with Child Pugh A or B hepatic impairment. However the table below, *adapted* from a pharmacokinetic study by Miller[1], is a useful guide for choosing a start dose in patients with hepatic impairment.

| Hepatic function | Starting sorafenib dose |
|---|---|
| Bilirubin > ULN but ≤ 1.5 x ULN and/or AST > ULN | 400mg twice daily |
| Bilirubin 1.5 – 3 x ULN and any AST | 400mg once daily |
| Bilirubin 3 – 10 x ULN and any AST | Not even 200mg every 3rd day was tolerable |
| Albumin < 25 g/l, any bilirubin and any AST | 200mg once daily |

If sorafenib is well tolerated at the starting dose, then a dose increase should be considered. If in doubt, discuss with Consultant.

Renal Impairment: The SPC states that no dose adjustment is required in mild, moderate or severe renal impairment. However the table below, *adapted* from the pharmacokinetic study by Miller[1], is a useful guide for choosing a start dose in patients with renal impairment.

| Renal function (CrCl ml/min) | Starting sorafenib dose |
|---|---|
| 40 – 59 | 400mg twice daily |
| 20 – 39 | 400mg once daily |
| < 20 | Insufficient data |
| Patient on haemodialysis | 200mg once daily |

If sorafenib is well tolerated at the starting dose, then a dose increase should be considered. If in doubt, discuss with consultant.

References:
Llovet, JM et al; NEJM 2008; 359 (4): 378 – 390 (HCC)
[1]Miller, A et al; JCO 2009; 27 (11): 1800 - 1805

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| Reason for Update: access for Child-Pugh B7 removed; dose reductions reviewed | Approved by Consultant: Dr T Dhillon |
| Version: 4 | Approved by Lead Chemotherapy Nurse: S Wills-Percy |
| Supersedes: Version 3 | Date: 20.12.17 |
| Prepared by: S Taylor | Checked by: C Tucker |