SORAFENIB (Nexavar®)
FOR 1ST LINE HCC

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Cycle length	Drug	Daily Dose	Route	Schedule
Days 1 to 28	4 weeks	**SORAFENIB**	**400 mg**	Oral	TWICE DAILY

Presented as 200mg film-coated tablet. Sorafenib should be taken without food or with a low or moderate fat meal.

NUMBER OF DAYS PER CYCLE
Sorafenib is administered orally at a standard dosage is 400mg twice daily (a total daily dose of 800mg continuously). One cycle equals 4 weeks of treatment.

APPROVED INDICATIONS
Sorafenib is recommended as an option for treating advanced hepatocellular carcinoma only for people with Child-Pugh grade A liver impairment. (**NICE TA474**)

ELIGIABILITY CRITERIA
- ECOG PS 0 or 1.
- Radiologically or clinically evaluable disease
- Able to take oral medication

EXCLUSION CRITERIA
Hypersensitivity to the active substance or to any of the excipients.

PREMEDICATION
None

RECOMMENDED TAKE HOME MEDICATION
Metoclopramide 10 mg three times daily as required
Loperamide 2mg prn (max 16mg in 24 hours) for diarrhoea as required
Emollients (for skin rash) as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED
Baseline assessment of cardiac function and ECG during therapy for patients with cardiac risk factors. BP, FBC, U&Es (including phosphate & calcium), LFTs & tumour markers as appropriate prior to each cycle
Thyroid function test if patients develop symptoms suggestive of hypothyroidism or hyperthyroidism. Blood pressure should be monitored weekly during the first 6 weeks of treatment, and periodically thereafter

ASSESSMENT OF RESPONSE
Radiological and clinical assessment will be performed at baseline and then at appropriate intervals during therapy.

REVIEW BY CLINICIAN
Day 28 of each cycle

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NURSE / PHARMACIST LED REVIEW
Each cycle as applicable according to local protocols

ADMINISTRATION NOTES
- An increased incidence of arterial hypertension was observed in Sorafenib treated patients. Hypertension was usually mild to moderate, occurred early in the course of treatment, and was amenable to management with standard antihypertensive therapy. Blood pressure should be monitored regularly and treated, if required, in accordance with standard medical practice.
- Drugs that are CYP3A4 inducers such as rifampicin and to a lesser extent dexamethasone, phenytoin, carbamazepine, phenobarbital or *Hypericum perforatum* (St John's wort) may increase metabolism and decrease sorafenib plasma concentrations. Current data suggest that clinical pharmacokinetic interactions of sorafenib with CYP3A4 inhibitors is unlikely.
- Co-administration of neomycin or other antibiotics that cause major ecological disturbances of the gastrointestinal microflora may lead to a decrease in sorafenib bioavailability.
- Sorafenib inhibits CYP2B6, CYP2C8 and CYP2C9, however in most cases the effect is not likely to be clinically significant. Patients taking narrow therapeutic-index CYP2C9 substrates such as warfarin or other vitamin K antagonists should be monitored regularly for changes in prothrombin time, International Normalised Ratio (INR) or clinical bleeding episodes as an effect on INR has been found in trials.

TOXICITIES
- Fatigue
- Diarrhoea
- Nausea
- Vomiting
- Hand-foot syndrome (palmar plantar erythrodysaesthesia)
- Alopecia
- Rash
- Pruritus
- Erythema
- Dry skin
- Laboratory test abnormalities (Increased lipase and amylase)
- Hypophosphatemia, hypocalcaemia
- Hypertension, headache
- Rarely, arrhythmias, cardiac ischemia/infarction/failure

DOSE MODIFICATION
Haematological toxicity
Dose delay: If ANC < 1.0 or Platelets < 60 until counts recovered.

Non-Haematological Toxicity, e.g. Diarrhoea, Skin Rash

CTC grade 0 - 1	No change.
CTC grade 2	Therapy withheld until toxicity resolves to grade 1. No change in subsequent dose.
CTC grade 3 - 4	Therapy withheld until toxicity resolves to grade 1. Decrease subsequent dose to 400mg once daily. Dose reduction maintained for ongoing cycle and remainder of therapy.

Renal impairment
No dose adjustment is required in patients with mild, moderate or severe renal impairment. Monitoring of fluid balance and electrolytes in patients at risk of renal dysfunction is advised.

Hepatic impairment
No dose adjustment is required in patients with Child Pugh A and B (mild to moderate) hepatic impairment. No data available in severe hepatic impairment (refer to consultant if bilirubin > 2.5 x ULN or ALT > 3 x ULN).

TREATMENT LOCATION Cancer Centre and Cancer Units

REFERENCES:

1. Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. NEJM 2008: 359; 378-90.
2. Llovet J, Ricci S, Mazzaferro V, Hilgard P, Raoul J, Zeuzem S, et al. Sorafenib improves survival in advanced hepatocellular carcinoma (HCC): results of a phase III randomized placebo-controlled trial (SHARP trial) [abstract]. J Clin Oncol. 2007;25(18 Suppl):LBA1.
3. Summary of Product Characteristics: Nexavar® 200mg film-coated tablets. Last updated 13 Oct 2017, https://www.medicines.org.uk/emc/product/226
4. NICE TA474, Sorafenib for treating advanced hepatocellular carcinoma (https://www.nice.org.uk/guidance/ta474). Published date: 06 September 2017.

Document Control

Document Title:	SORAFENIB (Nexavar®) FOR 1ST LINE HCC		
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Reviewer:	Chris Beck – Chemo Pharmacist NCA	**Date Approved:**	13.03.2018
Approved by:	Steve Williamson Consultant Pharmacist Northern Cancer Alliance	**Due for Review:**	13.03.2021
Due for Review:			
Summary of Changes	1.1	Protocol reviewed and reissued, Antiemetic advice updated	
	1.2	Updated against Chemocare parameters, updated approved indications.	