SORAfenib Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of hepatocellular carcinoma (HCC).	C22	00294a	CDS
Treatment of patients with advanced renal cell carcinoma (RCC) who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.	C64	00294b	CDS
Treatment of patients with progressive, locally advanced or metastatic differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine	C73	00294c	Reimbursement not approved[i]

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.

SORAfenib is taken twice daily continuously until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Cycle
SORAfenib	400mg Twice Daily	PO	Continuous therapy
It is recommended that SORAfenib should be administered without food or with a low or moderate fat meal. If the patient intends to have a high-fat meal, SORAfenib tablets should be taken at least 1 hour before or 2 hours after the meal. The tablets should be swallowed with a glass of water.			

ELIGIBILTY:

- Indications as above
- ECOG status 0-2
- Adequate haematological, renal and liver status
  - Applicable to HCC only; Child Pugh Class A

EXCLUSIONS:

- Hypersensitivity to SORAfenib or any of the excipients
- Uncontrolled hypertension

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Blood pressure
- Baseline thyroid function tests
- Assessment of cardiac function

Regular tests:

- Consider FBC**,** renal and liver profile at 14 days for first cycle.
- FBC, renal and liver profile, TSH and thyroid function every 28 days
- Blood pressure weekly for first month and then every 28 days
- INR tests if patient is on warfarin 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.
- Management of suspected adverse drug reactions may require temporary interruption or dose reduction of SORAfenib therapy.
- **Hepatocellular carcinoma (HCC) and Advanced Renal Cell Carcinoma (RCC):**
  - When dose reduction is necessary the dose of SORAfenib should be reduced to two tablets of 200 mg SORAfenib once daily (400mg OD).
- **Differentiated thyroid carcinoma (DTC)**:
  - When dose reduction is necessary during the treatment of the dose of SORAfenib should be reduced to 600 mg SORAfenib daily in divided doses (two tablets of 200 mg and one tablet of 200 mg twelve hours apart or 400mg AM, 200mg PM).
  - If additional dose reduction is necessary, SORAfenib may be reduced to 400 mg SORAfenib daily in divided doses (two tablets of 200 mg twelve hours apart, 200mg AM, 200mg PM), and if necessary further reduced to one tablet of 200 mg once daily.
  - After improvement of non-haematological adverse reactions, the dose of SORAfenib may be increased.

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

Renal Impairment		**Hepatic Impairment**	
CrCl (ml/min)	**Dose**	**Class**	**Dose**
>40	No adjustment	Child-Pugh A	No dose adjustment
20-39	200mg Twice Daily, dose escalate based on tolerability	Child-Pugh B	
<20 or haemodialysis	200mg once daily, dose escalate based on tolerability.	Child-Pugh C	200mg once daily, dose escalate based on tolerability.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal to low (**Refer to local policy).**

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

Medication may be required for the management of diarrhoea **(Refer to local policy).**
See local skin care policy for treatment and prevention of PPE.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Dermatologic reactions:** Hand foot skin reaction (palmar-plantar erythrodysaesthesia (PPE)) and rash represent the most common adverse drug reactions with SORAfenib. Rash and hand foot skin reaction are usually CTC (Common Toxicity Criteria) Grade 1 and 2 and generally appear during the first six weeks of treatment with SORAfenib. Management of dermatological toxicities may include topical therapies for symptomatic relief, temporary treatment interruption and/or dose modification of SORAfenib, or in severe or persistent cases, permanent discontinuation of SORAfenib.
- **Hypertension**: 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. In cases of severe or persistent hypertension, or hypertensive crisis despite institution of antihypertensive therapy, permanent discontinuation of SORAfenib should be considered.
- **Haemorrhage:** An increased risk of bleeding may occur following SORAfenib administration. If any bleeding event necessitates medical intervention it is recommended that permanent discontinuation of SORAfenib should be considered.
- **Cardiac Toxicity**: Temporary or permanent discontinuation of SORAfenib should be considered in patients who develop cardiac ischaemia and/or infarction
- **QT Interval Prolongation:** SORAfenib has been shown to prolong the QT/QTc interval which may lead to an increased risk for ventricular arrhythmias. Use SORAfenib with caution in patients who have, or may develop prolongation of QTc, such as patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking certain anti-arrhythmic medicines or other medicinal products that lead to QT prolongation, and those with electrolyte disturbances such as hypokalaemia, hypocalcaemia, or hypomagnesaemia. When using SORAfenib in these patients, periodic monitoring with on-treatment electrocardiograms and electrolytes (magnesium, potassium, calcium) should be considered.
- **Wound healing complications:** Temporary interruption of SORAfenib therapy is recommended for precautionary reasons in patients undergoing major surgical procedures. The decision to resume SORAfenib therapy following a major surgical intervention should be based on clinical judgement of adequate wound healing.
- **Hypoglycemia:** Decreases in blood glucose, in some cases clinically symptomatic and requiring hospitalization due to loss of consciousness, have been reported during sorafenib treatment. In case of symptomatic hypoglycaemia, sorafenib should be temporarily interrupted. Blood glucose levels in diabetic patients should be checked regularly in order to assess if anti-diabetic medicinal product's dosage needs to be adjusted.
- **Aneurysms and artery dissections:** The use of VEGF pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating SORAfenib, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm.

- **Disease specific warnings**
  - Haemorrhage in DTC : Due to the potential risk of bleeding, treatment of tracheal, bronchial and oesophageal infiltration with localized therapy should be considered prior to administering SORAfenib in patients with DTC.
  - Hypocalcaemia in DTC: When using SORAfenib in patients with DTC, close monitoring of blood calcium level is recommended. Severe hypocalcaemia should be corrected to prevent complications such as QT-prolongation or torsade de pointes.
  - TSH suppression in DTC: Increases in TSH levels above 0.5mU/L were observed in SORAfenib treated patients during a phase III trial. When using SORAfenib in DTC patients, close monitoring of TSH level is recommended.
  - Acute diarrhea may occur within 24 hours of first dose. If Grade1 or less, can be managed conservatively and may settle without dose reduction requirement.

DRUG INTERACTIONS:

- Caution is recommended when administering SORAfenib with compounds that are metabolised/eliminated predominantly by the UGT1A1 (e.g. irinotecan) or UGT1A9 pathways.
- Co-administration of neomycin or other antibiotics that cause major ecological disturbances of the gastrointestinal microflora may lead to a decrease in SORAfenib bioavailability. The risk of reduced plasma concentrations of SORAfenib should be considered before starting a treatment course with antibiotics.
- Patients taking concomitant warfarin or phenprocoumon should be monitored regularly for changes in prothrombin time, International Normalised Ratio (INR) or clinical bleeding episodes.
- CYP3A4 inducers may increase metabolism of SORAfenib and thus decrease SORAfenib concentrations.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

SORAfenib - L01XE05

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Version	Date	Amendment	Approved By
1	3/5/2016	Applied new NCCP regimen template	Prof Maccon Keane
2	30/06/2018	Updated with new NCCP regimen template	Prof Maccon Keane
3	27/05/2020	Reviewed. Update of dose modifications for renal and hepatic impairment, emetogenic potential and adverse events.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] Post 2012 indication. Not reimbursed through the ODMS or Community Drug Schemes (including the High Tech arrangements of the PCRS community drug schemes). Please check https://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/new.html for the most up to date reimbursement approvals.

ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes