SORAfenib Therapy

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of hepatocellular carcinoma (HCC).</td>
<td>C22</td>
<td>00294a</td>
<td>CDS</td>
</tr>
<tr>
<td>Treatment of patients with advanced renal cell carcinoma (RCC) who have</td>
<td>C64</td>
<td>00294b</td>
<td>CDS</td>
</tr>
<tr>
<td>failed prior interferon-alpha or interleukin-2 based therapy or are</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>considered unsuitable for such therapy.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Treatment of patients with progressive, locally advanced or metastatic</td>
<td>C73</td>
<td>00294c</td>
<td></td>
</tr>
<tr>
<td>differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>refractory to radioactive iodine</td>
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</tbody>
</table>

*If the reimbursement status is not defined*, the indication has yet to be assessed through the formal HSE reimbursement process.

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 patient's individual clinical circumstances.

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>SORAfenib</td>
<td>400mg BD</td>
<td>PO</td>
<td>Continuous therapy</td>
</tr>
</tbody>
</table>

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.

ELIGIBILITY:
- 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

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician, and is subject to HSE’s terms of use available at [http://www.hse.ie/eng/Disclaimer](http://www.hse.ie/eng/Disclaimer). This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens).
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

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dose modification required.</td>
<td>Child Pugh A</td>
</tr>
<tr>
<td>No data is available in patients requiring dialysis. Monitoring of fluid balance and electrolytes in patients at risk of renal dysfunction is advised.</td>
<td>No dose modification required</td>
</tr>
<tr>
<td></td>
<td>Child Pugh B</td>
</tr>
<tr>
<td></td>
<td>No data available</td>
</tr>
<tr>
<td></td>
<td>Child Pugh C</td>
</tr>
<tr>
<td></td>
<td>No data available</td>
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</tbody>
</table>

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal (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.

- **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

REFERENCES:
6. Brose MS, Nutting CM et al. Sorafenib in radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer: a randomized, double-blind, phase 3 trial. Lancet 2014;384(9940):319-328

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
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<tr>
<td>1</td>
<td>3/5/2016</td>
<td>Applied new NCCP regimen template</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>30/06/2018</td>
<td>Updated with new NCCP regimen template</td>
<td>Prof Maccon Keane</td>
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</table>
NCCP Chemotherapy Regimen

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at; http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/

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