Chemotherapy Protocol

RENAL CELL

AXITINIB

This regimen may require funding

Regimen

- Renal Cell - Axitinib

Indication

- Second line treatment of advanced or metastatic renal cell carcinoma after failure or intolerance to a first line therapy such as sunitinib
- WHO Performance status 0, 1
- Palliative intent

Toxicity

Drug	Adverse Effect
Axitinib	Cardiac failure, hypertension, hypothyroidism, fatigue, skin/hair colour changes, palmar-plantar erythrodysaesthesia, diarrhoea, taste disturbances, oedema, epistaxis, mucositis

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

Monitoring

Drugs

- FBCs, LFTs and U&Es prior to each cycle for the first three cycles, this may reduce to every other cycle if stable
- Blood pressure weekly for the first 4 weeks then every 6 - 12 weeks
- Thyroid function tests at baseline then every 3 months.
- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems or in the elderly. Repeat every three to six months as clinically indicated.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

For axitinib dose modifications should occur in incremental steps and are applied based on individual safety and tolerability. For example 5mg twice a day to 3mg twice a day to 2mg twice a day.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to cycle 1 the following criteria should be met;

Criteria	Eligible Level
Neutrophil	≥1x10^9/L
Platelets	≥75x10^9/L

Thereafter;

Neutrophils (x10^9/L)	Dose Modifications
1 or greater	100%
less than 1	Delay until recovery to 1x10^9/L or greater. If recovery occurs within 7 days then continue with the last dose dose. If the recovery takes longer than 7 days then reduce the dose as described above.
Platelets (x10^9/L)	**Dose Modifications**
75 or greater	100%
Less than 75	Delay until recovery to 75x10^9/L or greater. If the recovery occurs within 7 days then continue with full dose. If recovery takes longer than 7 days then reduce the dose as described above.

Hepatic Impairment

Drug	Child Pugh Class	Starting Dose
Axitinib	A	5mg twice a day
	B	2mg twice a day
	C	No information

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Axitinib	15 or less	No information

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Cardiovascular

Hypertension should be treated initially as per the NICE guidelines[(1)]. For persistently high blood pressure of more than 140/90mmHg despite standard hypertensive therapy, reduce the axitinib dose and continue to monitor. If hypertension persists discontinue the axitinib.

Gastro-intestinal

Diarrhoea is a known complication of axitinib therapy. Patients should be advised to limit consumption of high fibre or spicy foods, caffeine, alcohol and dairy products. Laxatives should be avoided. For a NCI-CTC grade 1 or 2 diarrhoea continue treatment at the same dose and attempt dietary and dehydration management. Anti-diarrhoeal medicines, such as loperamide, may be necessary. For a NCI-CTC grade 3 adverse reaction reduce the dose by one dose level. For a NCI-CTC grade 4 adverse reaction stop the axitinib until it resolves to at least NCI-CTC grade 2. Treatment may be re-started with a dose reduction of one dose level in the first instance.

Endocrine

Hypothyroidism can occur and should be managed according to standard medical practice. There is no need to discontinue or dose reduce the axitinib.

Skin

Palmar-plantar erythrodysaesthesia can occur. 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. Refer to a chiropodist if appropriate.

A NCI-CTC grade 1 reaction should be treated symptomatically. There is no need to interrupt therapy with axitinib or reduce the dose. For a NCI-CTC grade 2 effect delay treatment with axitinib until it resolves to at least NCI-CTC grade 1. The axitinib may be re-started with a dose reduction. The development of palmar-plantar erythrodysaesthesia at NCI-CTC grade 3 should result in treatment being delayed until it resolves to NCI-CTC grade 1. The axitinib can be re-started with a reduced dose.

Regimen

28 day cycle until disease progression or unacceptable toxicity occurs (10 cycles will be set in ARIA)

Patients who tolerate the starting dose of 5mg twice a day with no adverse effects greater than NCI-CTC grade 2 in severity for two consecutive weeks may have the dose increased to 7mg twice a day unless the patient has;

1. a blood pressure greater than 150/90 mmHg
2. receiving antihypertensive medication

Patients who tolerate the dose of 7mg twice a day may have their dose increased to a maximum of 10mg twice a day following the same criteria.

Cycle 1

Drug	Dose	Days	Administration
Axitinib	5mg twice a day	1-14 incl.	Oral
	7mg twice a day	15-28 incl.	Oral

Cycle 2 Onwards

Drug	Dose	Days	Administration
Axitinib	10mg twice a day	1-28 incl.	Oral

Dose Information

- Axitinib is available as 1mg, 3mg, 5mg and 7mg tablets

Administration Information

- Swallow this medicine whole. Do not chew or crush

Additional Therapy

- Mouthwashes according to local or national policy on the treatment of mucositis.
- Loperamide 4mg oral after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to axitinib.
- It must be made clear to all staff, including those in the community, that axitinib should only be prescribed under the supervision of an oncologist.

Coding (OPCS)

- Procurement – X71.5
- Delivery – X73.1

References
1. Rini BL, Escudier B, Tomczak P et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial. Lancet 2011; 378 (9807): 1931-1939.

REGIMEN SUMMARY

Axitinib

Cycle One – Day 1

Take Home Medicines

1. Axitinib 5mg twice a day for 14 days (days 1-14 inclusive) oral

Cycle One – Day 15

Take Home Medicines

2. Warning – Dose escalation
   Administration instructions
   Please note this dose has been automatically escalated by ARIA; please check the dose is appropriate for the patient.

3. Axitinib 7mg twice a day for 14 days (days 15-28 inclusive) oral

Cycle Two – Day 1

Take Home Medicines

4. Warning – Dose escalation
   Administration instructions
   Please note this dose has been automatically escalated by ARIA; please check the dose is appropriate for the patient.

5. Axitinib 10mg twice a day for 28 days oral

Cycle Three Onwards – Day 1

Take Home Medicines

6. Axitinib 10mg twice a day for 28 days oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	April 2016	Header changed Tablet strengths updated Hepatic impairment guidelines updated “dose” changed to “starting dose” Mucositis recommendation changed Administration information added No days treatment at 7mg bd corrected in regimen summary OPCS codes updated Warnings added at each dose escalation Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	April 2013	Correction made to the name at the top of the summary sheet. Changed from sunitinib to axitinib.	Dr Deborah Wright Pharmacist	Donna Kimber System Manager
1	March 2013	None	Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheater Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.