Chemotherapy Protocol

RENAL CELL

EVEROLIMUS

This protocol may require funding

Regimen

- Renal Cell - Everolimus

Indication

- Advanced renal cell carcinoma that has progressed on or after treatment with VEGF-targeted therapy
- Performance status 0, 1
- Palliative intent

Toxicity

Drug	Adverse Effect
Everolimus	Diarrhoea, rash, dry skin, fatigue, non-infectious pneumonitis, increased risk of infection, hyperglycaemia, hypertriglyceridaemia

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

Monitoring

- FBC, U&Es and LFTs every 4 weeks
- Blood glucose levels at baseline and after 4 weeks of treatment. Thereafter every 4-8 weeks
- Triglycerides at baseline then every 8 weeks

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.

Haematological

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

Neutrophils ($x10^9$/L)	**Dose Modifications**
1 or greater	Full dose
0.5 - 1	1st Occurrence Interrupt treatment until recovery to $1x10^9$/L or greater then restart at the full dose 2nd Occurrence Interrupt treatment until recovery to $1x10^9$/L or greater then restart at 5mg once a day
less than 0.5 or NCI-CTC grade 3 febrile neutropenia	1st Occurrence Interrupt treatment until the fever has resolved and the neutrophils are $1x10^9$/L or greater then restart at 5mg once a day 2nd Occurrence Discontinue treatment permanently
NCI-CTC grade 4 febrile neutropenia	Discontinue treatment permanently
Platelets ($x10^9$/L)	**Dose Modifications**
75 or greater	Full dose
50-75	1st Occurrence Interrupt treatment until recovery to $75x10^9$/L or greater then restart at the full dose 2nd Occurrence Interrupt treatment until recovery to $75x10^9$/L or greater then restart at 5mg once a day
less than 50	1st Occurrence Interrupt treatment until recovery to $75x10^9$/L or greater then restart at 5mg once a day 2nd Occurrence Discontinue treatment permanently

Hepatic Impairment

Drug	**Child Pugh Class**	**Dose**
Everolimus	A	7.5mg once a day
	B	5mg once a day
	C	Not recommended

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Everolimus	N/A	No dose modification required

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.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 5mg once a day or discontinued as appropriate.

Mucositis

NCI-CTC Grade	Action
2	Continue the everolimus without dose adjustments if the patient can tolerate it. Alternatively interrupt until symptoms have resolved to NCI-CTC grade 1 or below and then re-challenge at the same dose
3 or recurrence of grade 2 mucositis	Interrupt treatment until symptoms have resolved to NCI-CTC grade 1 or below then restart the everolimus at 5mg once a day
4 or recurrence of grade 3 mucositis	Discontinue everolimus

Non-infectious Pneumonitis

NCI-CTC Grade	Action
1	Continue everolimus without dose adjustments
2	Interrupt therapy. Consider short term use of corticosteroids e.g. prednisolone 20mg once a day for 10-14 days. Restart everolimus at 5mg once a day when symptoms have resolved to NCI-CTC grade 1 or below.
3	Interrupt therapy. Prescribe corticosteroids e.g. prednisolone 40mg as indicated. Restart everolimus at 5mg daily once symptoms have resolved to NCI-CTC grade 1 or below or discontinue as appropriate.
4	Discontinue the everolimus. Treat appropriately.

Regimen

28 day cycle continued as long as clinical benefit is observed or until unacceptable toxicity occurs (6 cycles will be set in Aria)

Drug	Dose	Days	Administration
Everolimus	10mg once a day	1-28 incl.	Oral

Dose Information

- Everolimus is available as 2.5mg, 5mg and 10mg tablets.

Administration Information

- Take at the same time of day each day consistently with or without food. Tablets should be swallowed whole.

Additional Therapy

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to everolimus.
- It must be made clear to all staff, including those in the community, that everolimus should only be prescribed under the supervision of an oncologist.
- Everolimus interacts with many other agents. Always check for drug interactions.

Coding (OPCS)

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

References
1. R Motzer, B Escudier, S Oudard et al. Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial. Lancet 2008; 372 (9637): 449 – 556

REGIMEN SUMMARY

Everolimus

Day 1

1. Everolimus 10mg once a day oral
   Administration Instructions
   Please supply an original pack per 28 day cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2016	Header changed Haematological and hepatic toxicity guidance updated Administration information updated Available tablet strengths updated Mucositis recommendation changed Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Jan 2013	None	Rebecca Wills Pharmacist 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.