Chemotherapy Protocol

PANCREATIC NEUROENDOCRINE CARCINOMA

EVEROLIMUS

This protocol may require funding

Regimen

- PNET - Everolimus

Indication

- The first or second line treatment of moderately differentiated PNET carcinomas
- Performance status 0, 1

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 or the prescription of an erythropoietin produce according to NICE TA 323 if the patient is 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
25-50	1st Occurrence Interrupt treatment until recovery to 75x10^9/L or greater then restart at 5mg once a day 2nd Occurrence Discontinue treatment permanently
less than 25	Discontinue treatment permanently

Hepatic Impairment

Drug	Child Pugh Class	Dose
Everolimus	A	10mg 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

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.
3	Interrupt therapy. Prescribe corticosteroids e.g. prednisolone 40mg as indicated. Restart everolimus at 5mg daily once symptoms have resolved 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 every day with or without food, but not after a high fat meal.
- If a dose is missed do not take an additional but rather take the next scheduled dose

Additional Therapy

- Mouthcare for the prophylaxis or treatment of mucositis in accordance with CSCCN guidelines. Avoid mouthwashes containing alcohols.
- 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

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

References

1. Yao JC, Shah MH, Ito T et al. Everolimus for advanced pancreatic neuroendocrine tumours. N Engl J Med 2011; 364 (6): 514-23.

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	May 2015	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Judith Cave 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 NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Trust

All actions have been taken to ensure these protocols are correct. However, it remains the responsibility of the prescriber to ensure the correct drugs and doses are prescribed for patients.