

Chemotherapy Protocol

CNS CANCER

BEVACIZUMAB

This protocol may require funding. This is an unlicensed indication for bevacizumab.

Regimen

- CNS-Bevacizumab

Indication

- Recurrent GBM
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Bevacizumab	Haemorrhage, hypertension, proteinuria, impaired wound healing, gastrointestinal perforations, fistulae, arterial thrombosis

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- Blood pressure and dipstick urinalysis for proteinuria prior to treatment with bevacizumab

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

There is little need to adjust the dose of bevacizumab for haematological toxicity.

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT units	Dose
Bevacizumab	n/a		n/a	No information available

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Bevacizumab	n/a	No information available

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.

Bevacizumab

Bevacizumab doses should be omitted and not reduced for adverse reactions. If more than two doses are missed due to adverse events treatment should be stopped. It should be noted that the half life of bevacizumab is approximately twenty days. Discontinuation of treatment in response to adverse effects is not expected to influence the short term clinical evolution of the event, symptomatic treatment is often necessary.

Bevacizumab should be stopped if the individual develops;

- Gastrointestinal perforation
- Arterial thromboembolic events
- NCI-CTC grade 3 and above haemorrhagic events (requiring a blood transfusion or a major non-elective intervention)
- NCI-CTC grade 3 and above congestive heart failure or left ventricular function
- NCI-CTC grade 4 fistula

If a NCI-CTC symptomatic grade 4 venous thromboembolic event occurs bevacizumab should be stopped. However, if this is a pulmonary embolism bevacizumab may be re-

started once a full recovery has been made and the individual is anti-coagulated with a subcutaneous low molecular weight heparin. An oral anticoagulant must not be used. Hypertension is a common consequence of bevacizumab therapy. For a NCI-CTC grade 1 hypertension no treatment is necessary. NCI-CTC grade 2 hypertension, consider anti-hypertensive therapy. For a NCI-CTC grade 3 and above hypertension that is persistent consider stopping treatment.

Bevacizumab may be continued for a NCI-CTC grade 1 proteinuria or the first occurrence of a grade 2 proteinuria. For the second occurrence of a NCI-CTC grade 2 proteinuria or any NCI-CTC grade 3 proteinuria give the bevacizumab as scheduled. A 24 hour urine collection or UPCR should be conducted at most three days before the next dose. If there is less than 2g protein per 24 hours or a UPCR 0-1 administer the bevacizumab and return to dipstick monitoring. If there is more than 2g protein per 24 hours omit the bevacizumab. Repeat the 24 hour urine collection prior to the next scheduled dose. If this is less than 2g per 24 hours administer the bevacizumab and continue 24 hour urine collection until the protein is 1g per 24 hours or less.

[Regimen](#)

21 day cycle until unacceptable toxicity or disease progression occurs (six cycles will be set in Aria)

Drug	Dose	Days	Administration
Bevacizumab	10mg/kg	1	Intravenous infusion in 100ml sodium chloride 0.9% over 90 minutes (see administration information)

[Dose Information](#)

- Bevacizumab will be dose banded according to the CSCCN agreed bands

[Administration Information](#)

Extravasation

- Bevacizumab – neutral

Other

- The first infusion of bevacizumab will be over 90 minutes. If this is well tolerated the second infusion may be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

[Additional Therapy](#)

- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding

- Procurement – X71.5
- Delivery – X72.3

References

1. Friedman HS, Prados MD, Wen PY et al. Bevacizumab alone or in combination with irinotecan in recurrent glioblastoma. J Clin Oncol 2009; 27 (28): 4733-4738.

REGIMEN SUMMARY

Bevacizumab

Days 1

1. Bevacizumab 10mg/kg intravenous infusion in 100ml sodium chloride 0.9% over 90 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Oct 2015	None	Dr Deborah Wright Pharmacist	Dr O Al-Salihi Consultant Clinical 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 Hospital 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.