

# Bevacizumab (in combination with chemotherapy)

## Indication

In combination with platinum and paclitaxel for the 1st line treatment of metastatic cervical cancer

In combination with carboplatin and paclitaxel for the 1st line treatment of ovarian cancer

## Regimen details

### Cervical Cancer:

Bevacizumab 15mg/kg IV in 100ml 0.9% sodium chloride

### Ovarian Cancer (HRD positive with maintenance olaparib & bevacizumab planned post chemotherapy):

Bevacizumab 15mg/kg IV in 100ml 0.9% sodium chloride

### Ovarian Cancer (HRD negative or unknown):

Bevacizumab 7.5mg/kg IV in 100ml 0.9% sodium chloride

## Cycle frequency

Every 3 weeks

Therapy should be withheld for elective surgery

## Number of cycles

### Cervical cancer:

Only give with chemotherapy, stop when chemotherapy completed

### Ovarian Cancer (HRD positive with maintenance olaparib & bevacizumab planned post chemotherapy):

Give with chemotherapy then switch to olaparib and bevacizumab regimen post chemotherapy (see separate protocol)

### Ovarian cancer (HRD negative or unknown):

Give with chemotherapy and continue following completion of chemotherapy to a total of 18 doses

## Administration

Give first dose over 90 minutes, second dose over 60 minutes and subsequent doses over 30 minutes if tolerated

Check blood pressure before infusion. Be aware of 'white coat syndrome' which can elevate BP.

## Pre-medication

None

## Emetogenicity

Minimal

## Additional supportive medication

None

## Extravasation

Neutral

### Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Blood pressure	14 days
Urine dipstick for proteinuria	14 days

Pre-existing blood pressure must be controlled before starting treatment

Prior radiotherapy is a risk factor for the development of fistulae

The use of VEGF pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating bevacizumab, this risk should be carefully considered in patients with risk factors such as hypertension, history of aneurysm, or dissection.

### Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), blood pressure, urine dipstick for proteinuria

### Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Note investigations refer to bevacizumab only. If given with chemotherapy, please refer to the relevant chemotherapy protocol

Investigation	Limit
Neutrophil count	$\geq 1.5 \times 10^9/L$
Platelet count	$\geq 100 \times 10^9/L$
Bilirubin	$\leq 1.5 \times \text{ULN}$
Hb	$\geq 95 \text{ g/L}$
Blood pressure	<140/90 mmHg

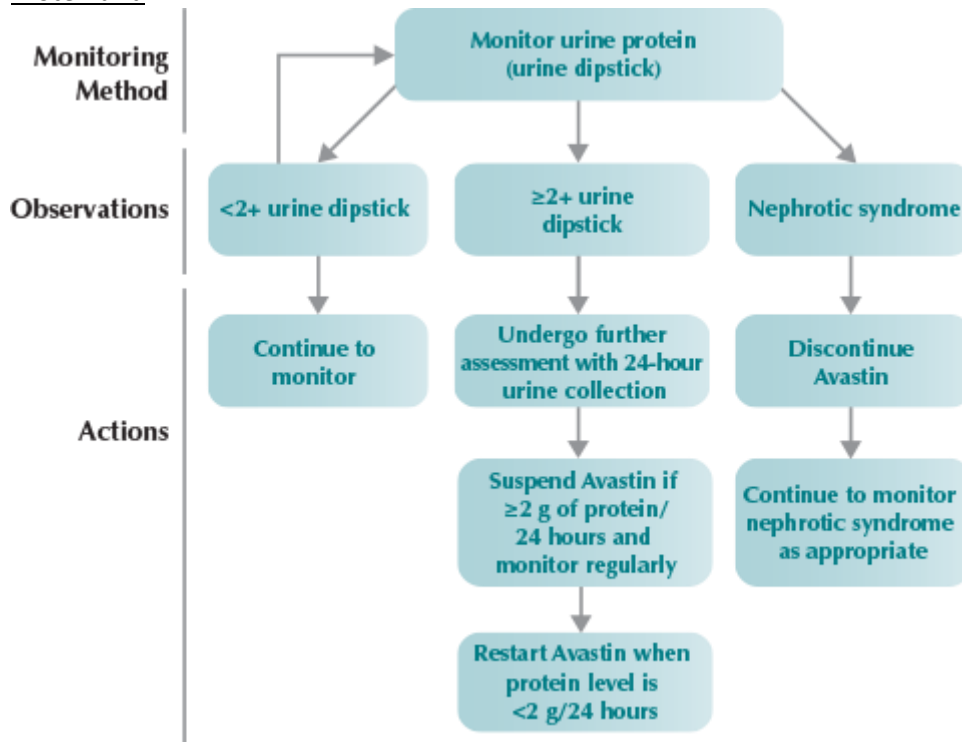
If only Hb is low (below 95g/dl) please contact doctor to arrange for blood transfusion but continue with chemotherapy

## Dose modifications

Do not reduce the dose of bevacizumab. Dosing should be interrupted or discontinued as described below

Toxicity	Grade	Dose adjustment
Infusion related reactions	Grade ≤2	90 minute infusion: continue with dose as normal, but give premedication (paracetamol and chlorphenamine) with the next dose and give over 90 minutes. If well tolerated subsequent infusions can be reduced by 30 minutes as long as use premedication.
		60 minute infusion: all subsequent doses should be given over 90 minutes (with pre-medication)
	30 minute infusion: all subsequent doses should be given over 60 minutes (with pre-medication)	
	Grade ≥2	Discontinue permanently
Proteinuria (on dipstick)	<2	Continue with bevacizumab as normal
	≥2+	See algorithm below
	Nephrotic syndrome	Permanently discontinue
Gastro-intestinal perforation or dehiscence		Discontinue permanently
Wound healing complications		Bevacizumab should not be initiated for at least 28 days following surgery or until wound is fully healed Bevacizumab should be withheld for 42 days (6 weeks) prior to elective surgery If wound healing complications occur during treatment it should be withheld until the wound is fully healed.
Fistula or intra-abdominal abscess		Discontinue permanently
Venous thromboembolic event	Grade 3 Deep DVT or cardiac thrombosis needing anticoagulation or incidental first PE	Hold bevacizumab for 2 weeks May be resumed after initiation of therapeutic dose anticoagulant
	Grade 4 Embolic event including PE with life-threatening thrombus	Discontinue permanently
Arterial thrombotic event	ANY grade	Permanently discontinue
Haemorrhage	Grade 1 or 2	No modification but institute appropriate treatment
	Grade 3 or 4	Discontinue and institute appropriate treatment

## Proteinuria



## Hypertension

	Definition	Action
Grade 1	Asymptomatic transient (<24 hours) increase by >20 mmHg (diastolic) or to >140/90 mmHg if previously normal.	Recheck BP 1 hour later If BP <140/90 mmHg: administer as normal If BP 140/90-150/100 mmHg administer but recheck BP 48 hours later If >150/100 mmHg omit bevacizumab and recheck BP 48 hours later  If BP after 48 hours still >140/90 mmHg commence antihypertensive therapy
Grade 2	Recurrent or persistent (>24 hour) increase by 20 mmHg (diastolic) or to >140/90 mmHg if previously normal	Anti-hypertensive therapy should be commenced. Once controlled to <140/90 mmHg bevacizumab can be continued
Grade 3	Requiring more than one antihypertensive or more intensive therapy than previously	Withhold bevacizumab for persistent hypertension >140/90 mmHg If hypertension cannot be controlled, discontinue permanently
Grade 4	Life threatening (hypertensive crisis)	Medical emergency Permanently discontinue

## Adverse effects –

for full details consult product literature/ reference texts

Fistulae and perforations  
Wound healing complications  
Hypertension  
Posterior Reversible Encephalopathy Syndrome (PRES)  
Proteinuria  
Arterial thromboembolism  
Venous thromboembolism  
Haemorrhage  
Aneurysms and artery dissections  
Congestive heart failure (CHF)  
Neutropenia and infections  
Hypersensitivity and infusion reactions

## References

Avastin SPC - <https://www.medicines.org.uk/emc/product/3885>

---

**THIS PROTOCOL HAS BEEN DIRECTED BY DR YIANNAKIS, DESIGNATED LEAD CLINICIAN FOR GYNAECOLOGICAL CANCER**

**RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE**

Date: April 2021

Review: April 2023

VERSION: 2

---