BEVACIZUMAB (AVASTIN) for use in gynaecological cancers

1. The front-line treatment of advanced (FIGO stages IIIB, IIIC and IV) epithelial ovarian, fallopian tube or primary peritoneal cancer, in combination with paclitaxel and carboplatin
2. For first-line palliative treatment of recurrent or metastatic cervical cancer, in combination with paclitaxel and carboplatin (or cisplatin)

Individual funding must be agreed before treatment with bevacizumab may start

Drug/Dosage/ Administration:

Indication	Bevacizumab Dose & Administration	Bevacizumab Frequency and Duration
Ovarian: front-line use with paclitaxel and carboplatin	**7.5** mg/kg in 100ml sodium chloride 0.9% over 15 minutes[2]	every 3 weeks for a total of 18 doses
Cervical cancer: with paclitaxel and platinum	**15**mg/kg in 100ml sodium chloride 0.9% over **30** minutes[2]	every 3 weeks only while on chemotherapy (no funding for maintenance bevacizumab)

Bevacizumab may be administered in combination with chemotherapy, and may be administered before or after chemotherapy
(but avoid bevacizumab within at least 4 weeks of surgery – see Comments).

If a patient experiences a mild infusion-related reaction, give the next infusion over 60 - 90 minutes +/- chlorphenamine cover. If this is tolerated, reduce the infusion time for the next doses in a step-wise fashion to a minimum of 30 minutes, and maintain that infusion time for all remaining doses.

Main Toxicities: hypertension; proteinuria; arterial thromboembolism; haemorrhage; gastrointestinal perforations and fistulae (serious but rare)

Anti-emetics: none needed

Regular Investigations:

Blood pressure	before each dose
Urinalysis for proteinuria	before each dose
FBC	} as chemotherapy protocol (then, for ovarian patients on
U&Es and LFTs	} maintenance bevacizumab, every 3 months, once
CA 125	} chemotherapy completed)

Comments: Bevacizumab may adversely affect the wound healing process.
Therapy should not be initiated for at least 28 days following major surgery or until the surgical wound is fully healed. Therapy should also be withheld for at least 28 – 60 days before elective surgery.[1]
For minor surgery, including port placement, it is recommended that bevacizumab is withheld for 7 days after surgery.

Reason for Update: removal of 2nd line ovary indication	Approved by Consultant: Dr S Essapen
Version: 5	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 4	Date: 2.6.15
Prepared by: S Taylor	Checked by: C Tucker

Pre-existing hypertension should be adequately controlled (usually by GP) before starting bevacizumab treatment.

Dose Modifications Dose reduction is not recommended. If indicated, therapy should either be permanently discontinued or temporarily suspended.

When receiving in combination with chemotherapy, if a cycle of chemotherapy is delayed for any reason, the bevacizumab dose should also be delayed until the patient is fit enough for the chemotherapy.

Hypertension: Baseline blood pressure should be < 150/100mmHg.
A suggested assessment of blood pressure results is:
If diastolic increase > 20mmHg above baseline or blood pressure rises to > 150/100mmHg, antihypertensive therapy may be required. Treatment, and initial monitoring until stabilised, is usually best managed via the patient's GP.
If blood pressure > 180/110mmHg, it is advised that bevacizumab therapy is withheld until blood pressure controlled.

Proteinuria: A suggested assessment of urine dipstick results is:
1+ or 2+ on dipstick (0.3 – 2.9g/L): continue with bevacizumab. (No additional evaluation required)
3+ on dipstick (3 - 19g/L): May have dose of bevacizumab as scheduled, but will need 24-hour urine to measure 24 hour protein to be done a few days before next cycle due.
If 24 hr protein result < 2g, continue with bevacizumab, with continued proteinuria monitoring via 24 hour urine before each dose. If the 24 hour protein level falls to < 1g/24hr, return to dipstick analysis.
If ≥ 2g, withhold bevacizumab until repeat 24 hour urine collection shows < 2g protein. Then re-introduce bevacizumab, with continued proteinuria monitoring via 24 hour urine.
4+ on dipstick (≥ 20g/L): withhold bevacizumab. 24-hour urine required. Follow 24 hour urine monitoring and guidance as for 3+ on dipstick.

Renal Impairment: There are no data for bevacizumab in patients with impaired renal function. However, dose adjustments would not be expected to be required.

Hepatic Impairment: There are no data for bevacizumab in patients with impaired liver function. However, dose adjustments would not be expected to be required.

References:
Perren, TJ et al; NEJM 2011; 365: 2484 - 2496 (ICON 7)
Tewari, K et al; NEJM 2014; 370: 734 – 743 (cervical use)
[1]Letter on file from Roche, December 2010
[2] Reidy, DL et al; JCO 2007; 25 (19): 2691 – 2695
Miles, D et al; Using Bevacizumab to treat metastatic cancer: UK consensus guidelines; Br J Hosp Med 2010; 71: 12