AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression

September 2020

ONE WALES INTERIM COMMISSIONING DECISION

Bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression

Date of original advice: July 2019
Date of review: September 2020

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria, bevacizumab (Avastin®) 7.5 mg/kg dose in combination with carboplatin and paclitaxel can continue to be made available within NHS Wales for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression. High risk is defined as: International Federation of Gynaecology and Obstetrics [FIGO] stage III debulked but residual disease more than 1.0 cm or stage IV disease, or stage III disease at presentation and requiring neoadjuvant chemotherapy due to low likelihood of optimal primary surgical cytoreduction.

Bevacizumab (Avastin®) 7.5 mg/kg is not licensed to treat this indication and is therefore off-label. Each provider organisation must ensure all internal governance arrangements are completed before this medicine is prescribed.

The risks and benefits of the off-label use of bevacizumab (Avastin®) for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Interim Commissioning decision.

Health board and trust responsibility
Health boards and trusts will take responsibility for implementing One Wales Interim Commissioning decisions at the lowest acquisition cost and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

Starting and stopping criteria for bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression

These criteria are adapted from the NHS England National Cancer Drugs Fund List[1].

Starting and stopping criteria:

Starting criteria:
Patients with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer with sufficient performance status to undergo treatment with carboplatin, paclitaxel and bevacizumab in one of the following groups:

- patients with FIGO stage III debulked but residual disease more than 1 cm
- patients with stage IV disease
- patients with stage III disease at presentation and requiring neoadjuvant chemotherapy due to low likelihood of optimal primary surgical cytoreduction.

These criteria also apply to patients entered into the ICON 8b trial. Clinicians should be aware that for patients randomised to the non-bevacizumab arm of the ICON 8b, the use of bevacizumab in subsequent lines of treatment is not approved under One Wales Interim Pathways Commissioning.

Patients who satisfy the eligibility criteria will be prescribed bevacizumab following consultation with the patient and/or carer taking into account potential adverse effects, cautions and contraindications. This consultation should be recorded in the patient's notes.

Bevacizumab is prescribed at a dose of 7.5 mg/kg every three weeks up to a maximum of 18 cycles. Bevacizumab should be given with the:

- first or second cycle of chemotherapy following primary debulking surgery or for those patients with stage IV disease or inoperable disease
- first or second cycle of chemotherapy following interval debulking surgery performed after three to four cycles of neoadjuvant chemotherapy
- first cycle of neoadjuvant chemotherapy.

Stopping criteria:

- radiological or clinical evidence of disease progression
- toxicity
- patient request
- after 18 cycles of bevacizumab.

Reference

1. NHS England. National Cancer Drugs Fund version 1.141. July 2019. Available at: https://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/. Accessed July 2019.

This is a summary of new evidence available and patient outcome data collected, to inform the review.

Background
Ovarian cancer is the leading cause of death from gynaecological cancer in the UK[1]. The outcome for women with ovarian cancer is generally poor, with an overall five-year survival rate of 42.6%[2]. Women with advanced ovarian cancer (FIGO stage III or IV) have a five-year survival rate of 26.9% and 13.4%, respectively[3]. Bevacizumab 7.5 mg/kg is on the Cancer Drugs Fund in England for patients with FIGO stage III debulked but residual disease more than 1.0 cm or stage IV disease, or stage III disease at presentation and requiring neoadjuvant chemotherapy due to low likelihood of optimal primary surgical cytoreduction[4]. A cohort of patients was identified in Wales based on data from individual patient funding request panels. Clinicians in Wales considered there to be an unmet need and based on these two factors this medicine was deemed suitable for a One Wales Interim Commissioning decision.

Current One Wales Interim Commissioning Decision
Bevacizumab (Avastin®) 7.5 mg/kg dose in combination with carboplatin and paclitaxel can be made available within NHS Wales for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression. High risk is defined as: International Federation of Gynaecology and Obstetrics [FIGO] stage III debulked but residual disease more than 1.0 cm or stage IV disease, or stage III disease at presentation and requiring neoadjuvant chemotherapy due to low likelihood of optimal primary surgical cytoreduction. July 2019.

Licence status
Bevacizumab (Avastin®) 7.5 mg/kg dose in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression is off label.

Guidelines
There have been no new relevant guidelines or updates to existing guidelines identified.

Licensed alternative medicines/Health Technology Appraisal advice for alternative medicines
Cancer Drugs Fund
Bevacizumab is the only drug available on the Cancer Drugs Fund for first line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression[4].

The poly(adenosine diphosphate-ribose) polymerase (PARP) inhibitor, olaparib, is available on the Cancer Drugs Fund (NICE TA598, August 2019) as maintenance treatment for patients whose disease has a deleterious or suspected deleterious germline and/or somatic breast cancer gene (BRCA) mutation and has responded to first line platinum chemotherapy[4]. Other PARP inhibitors are included on the Cancer Drugs Fund but are utilised in later line therapy and so are not detailed here.

In progress
NICE ID1652: Olaparib with bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer. Expected publication date November 2020[5].

Efficacy/Effectiveness
No new clinical trials were identified in the repeat literature search. The results of the OSCAR study have now been published[6]. The results are as previously reported.

Safety
No relevant safety analyses were identified in the repeat literature search.

Cost effectiveness
No relevant cost-effectiveness analyses were identified in the repeat literature search.

Budget impact
The European patent for bevacizumab (Avastin®) expires in June 2020, subsequent availability of biosimilars may affect the future price of bevacizumab.

Based on the patient numbers reported below, it is likely that the budget impact for the last 12 months is slightly lower than estimated in the original evidence status report. However, a number of eligible patients have been unable to start bevacizumab treatment due to the COVID-19 pandemic and therefore the original estimates are likely to be a good prediction of true patient numbers.

Impact on health and social care services
The impact on the service remains minimal.

Patient outcome data
Across Wales, 25 patients have received bevacizumab for advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression. [Confidential information removed]. Of the 25 patients who started treatment, 11 have stopped treatment. [Confidential information removed]. A total of 13 patients are still receiving treatment (median of 5 cycles; range: 5-17 cycles). [Confidential information removed]. It is difficult to draw meaningful comparisons between these data and outcomes reported in published clinical evidence. The median follow up for 23/25 patients is currently 5 months. The data suggest that discontinuation rates are lower than those published in the real life study by Bertelli et al[7] but the median follow up in that study was longer at 8 months (12 cycles). Additionally, some patients have had their treatment plan altered due to the presence of BRCA mutations making them eligible for olaparib or due to the COVID-19 pandemic. We welcome these data provided by clinicians and expect to be in a better position to compare the real-world outcomes for patients in Wales with those previously reported at the next 12 month review in 2021.

References

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3. Cancer Research UK. Ovarian cancer survival statistics. Ovarian cancer survival by stage at diagnosis. 2014. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/ovarian-cancer/survival. Accessed Jun 2020.
4. NHS England. National Cancer Drugs Fund. May 2020. Available at: https://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/. Accessed Jun 2020.
5. National Institute for Health and Care Excellence. Technology Appraisal in development GID-TA10526. Olaparib with bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer. Expected publication date: Nov 2020. Available at: https://www.nice.org.uk/guidance/indevelopment/gid-ta10526. Accessed Jun 2020.
6. Hall M, Bertelli G, Li L, et al. Role of front-line bevacizumab in advanced ovarian cancer: the OSCAR study. *International Journal of Gynecologic Cancer.* 2020;30:213-220.
7. Bertelli G, Drews F & Lutchman-Singh K. Bevacizumab for Ovarian Cancer at High Risk of Progression: Reproducibility of Trial Results in 'Real-world' Patients. *Anticancer Research.* 2016;36(9):4947-4950.