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

Bevacizumab 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 (OW01)

December 2022

ONE WALES INTERIM DECISION

Bevacizumab 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

Date of original advice: Monday 24 June 2019
Date of review: December 2022

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria, bevacizumab 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 7.5mg/kg dose is not licensed to treat this indication and is therefore ‘off-label’. Each provider organisation must ensure all internal governance arrangements are completed before these medicines are prescribed in combination.

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

Providers should consult the relevant 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 Medicines Assessment Group decision.

Health board responsibility

Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

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

One Wales advice assists consistency of access across NHS Wales.

Starting and stopping criteria for bevacizumab 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

Prescribers should note that front-line treatment with bevacizumab is available for patients with stage III and IV homologous recombination deficiency (HRD)-positive disease who are eligible to receive olaparib plus bevacizumab maintenance therapy in line with the National Institute for Health and Care Excellence (NICE) guidance TA693 and should refer to this for full eligibility criteria[1].

These criteria are adapted from the NHS England National Cancer Drugs Fund List[2].

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

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
- first or second cycle of chemotherapy for those patients with inoperable stage IV disease or inoperable stage III disease or who are unable to undergo surgery due to increased risk during COVID19
- first or second cycle of chemotherapy following interval debulking surgery performed after three to four cycles of non-bevacizumab-containing neoadjuvant chemotherapy
- first or second cycle of neoadjuvant chemotherapy.

Stopping criteria:

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

References:

1. National Institute for Health and Care Excellence. Technology Appraisal TA693. April 2021. Available at: https://www.nice.org.uk/guidance/ta693. Accessed October 2022.
2. NHS England. National Cancer Drugs Fund. October 2022. Available at: https://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/. Accessed October 2022.

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

Bevacizumab 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 of progression.

This report was prepared by the All Wales Therapeutics and Toxicology Centre in September 2022. It summarises any new evidence available and patient outcome data collected since the last review in September 2021.

Background: Ovarian cancer is the leading cause of death from gynaecological cancer in the UK. Cancer survival statistics for Wales show that outcome for women with ovarian cancer is generally poor with an overall five-year survival rate for women diagnosed between 2014-2018 of 46.2%; women with advanced ovarian cancer (FIGO stage III or IV) have a five-year survival rate of 28.1% and 10.8%, respectively. Bevacizumab 7.5 mg/kg dose 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. 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 considered suitable for assessment via the One Wales Medicines process.

Current One Wales decision: Supported

Licence status: Off-label use for this licensed medicine

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

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines: Bevacizumab, both at its licensed dose of 15 mg/kg and the off-label 7.5 mg/kg dose, continues to be made available through NHS England clinical policy and listed on the Cancer Drugs Fund for use in combination with platinum-based chemotherapy as induction therapy for up to six cycles. Eligible patients may then go on to receive olaparib plus bevacizumab (15 mg/kg) as maintenance treatment in accordance with NICE recommendation TA693: Olaparib plus bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer. Patients who have not received bevacizumab as induction therapy but have stage III-IV disease associated with homologous recombination deficiency positive status are also eligible to receive olaparib plus bevacizumab maintenance therapy. For those patients not eligible to receive olaparib, the option for patients who have received bevacizumab 7.5 mg/kg as induction therapy to continue to receive bevacizumab 7.5 mg/kg monotherapy for up to 18 cycles in total is retained. A review of TA693 is currently underway with an expected publication date of 16 August 2023.

Effectiveness: No new relevant clinical effectiveness evidence was identified in the repeat literature search.

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

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

Budget impact: Since the last review, 41 patients across Wales have received bevacizumab (7.5 mg/kg) for advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression. This is higher than the estimated number of 30 patients in the original evidence status report from 2019. However, as this includes patients going on to receive olaparib and bevacizumab maintenance who achieved complete or partial response in line with NICE TA693, which would be funded under the new treatment fund, this figure is similar to the original estimate. The budget impact analysis assumed that all patients would receive the maximum of 18 cycles of low dose bevacizumab whereas the outcome data reported below shows that around a half of patients ceased treatment before completion. Four biosimilar bevacizumab preparations are now available in the UK. The list price for these biosimilars is 2–15% lower than the cost of the reference medicine, Avastin® although this doesn't take in to account any current or future contract prices which may be significantly different to the published list prices. Considering both these factors, it would seem reasonable to assume that the budget impact for the last 12 months is unlikely to exceed that predicted in 2019.

Impact on health and social care services: Minimal.

Patient outcome data: Of the 41 patients who started treatment, [confidential text removed] patients have completed 18 cycles and 14 patients are still receiving treatment. Eleven patients have stopped treatment due to disease progression, [confidential text removed], [confidential text removed] and [confidential text removed]. Seven patients who achieved complete or partial response have converted to olaparib plus bevacizumab (15 mg/kg) maintenance treatment.

The median and range of the number of bevacizumab treatment cycles received by 34 patients (of the 41 patients) is also available. A median of nine cycles (range 2-18 cycles) were received; of these 34 patients, six had carboplatin alone plus bevacizumab due to concerns on the risk of toxicity during the COVID-19 pandemic. Fifteen patients have either completed or are still receiving treatment. [confidential text removed] and 12 continue on treatment and have received 2-17 (median 13) cycles. Of the remaining 19 patients, 10 have stopped treatment due to disease progression after 4-13 (median 7) cycles, five have converted to olaprib plus bevacizumab (15 mg/kg) in accordance with NICE TA693 after 2-8 (median 2) cycles, [confidential text removed].

It is difficult to draw meaningful comparisons between these data and outcomes reported in published clinical evidence due to differences in follow up periods.

Evaluation of evidence

No significant new evidence has been published which challenges the current One Wales advice. AWTTC recommends continuing access in Wales to low dose bevacizumab for the treatment of advanced ovarian cancer.

Next review date: 12 months

References: A full reference list is available on request
This document includes evidence published since the last review or full assessment of this medicine for the indication under consideration. It does not replace the original full

evidence status report. Any previous reviews and the original full evidence status report are available on request by email to AWTTC@wales.nhs.uk.

Care has been taken to ensure the information is accurate and complete at the time of publication. However, the All Wales Therapeutics and Toxicology Centre (AWTTC) do not make any guarantees to that effect. The information in this document is subject to review and may be updated or withdrawn at any time. AWTTC accept no liability in association with the use of its content. An Equality and Health Impact Assessment (EHIA) has been completed in relation to the One Wales policy and this found there to be a positive impact. Key actions have been identified and these can be found in the One Wales Policy EHIA document.

Information presented in this document can be reproduced using the following citation: One Wales Interim Decision. low dose bevacizumab for the treatment of advanced ovarian cancer. (OW01). December 2022.