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

December 2017

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 advice: December 2017

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

It is the view of the Interim Pathways Commissioning Group (IPCG) that bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel should not be supported 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.

Individual Patient Funding Request (IPFR) consideration remains appropriate for those patients who are likely to obtain significantly more clinical benefit from the intervention than would normally be expected at a reasonable value for money.

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

One Wales advice promotes consistency of access across NHS Wales.

KEY FINDINGS: This is an abbreviated summary of the evidence provided to IPCG

Report background

Bevacizumab at a dose of 15 mg/kg, in combination with paclitaxel and carboplatin, has marketing authorisation for the front-line treatment of adults with advanced (International Federation of Gynaecology and Obstetrics [FIGO] stages IIIB, IIIC and IV) epithelial ovarian, fallopian tube or primary peritoneal cancer[1,2]. In 2013, the National Institute for Health and Care Excellence (NICE) assessed bevacizumab in combination with paclitaxel and carboplatin for the first-line treatment of advanced ovarian cancer at the licensed dose (15 mg/kg) and did not recommend its use based on grounds of cost effectiveness[3].

Bevacizumab at a dose of 7.5 mg/kg is not a licensed dose for the first-line treatment of advanced ovarian cancer and so its use is off-label. Commissioning representatives and patient experts have confirmed that bevacizumab at the unlicensed dose of 7.5 mg/kg is the dose most commonly used in NHS England for the treatment of advanced ovarian cancer. 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 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.

In August 2016, a One Wales decision was endorsed not to support the use of bevacizumab 7.5 mg/kg dose in combination with carboplatin and paclitaxel within NHS Wales for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer. In August 2017, the Interim Pathways Commissioning Group reviewed the evidence published subsequent to the original One Wales decision and deemed that the new evidence was sufficient to warrant a full review.

Clinicians in Wales consider that the group of patients who are most likely to benefit from treatment are those defined as high-risk based on the criteria applied by the Cancer Drugs Fund (see above). This evidence status report therefore focuses on this high-risk population.

Efficacy/Clinical Effectiveness

- In the high-risk subgroup of patients in the International Collaboration on Ovarian Neoplasms 7 (ICON7) trial, the addition of bevacizumab 7.5 mg/kg to standard chemotherapy increased progression-free survival by 4.1 months compared with standard chemotherapy alone, based on the restricted mean data in the final analysis[5].
- The addition of bevacizumab 7.5 mg/kg to standard chemotherapy also improved overall survival in the high-risk for progression subgroup, increasing overall survival by 4.8 months (from 34.5 to 39.3 months) based on the restricted mean data in the final analysis[5].

Safety

Adding bevacizumab to standard chemotherapy was associated with more adverse events[6]. In the ICON7 trial, adverse events of grade 3 or higher were reported in 56% of the women in the standard chemotherapy group and in 66% of women in the bevacizumab plus standard chemotherapy group. Treatment with bevacizumab plus standard chemotherapy appeared to be associated with: an increase in bleeding, particularly grade 1 or 2 mucocutaneous bleeding (7% versus 36%); hypertension ≥ grade 2 (2% versus 18%); thromboembolic events of ≥ grade 3 (3% versus 7%); and ≥ grade 3 GI perforations (< 1% versus 1%)[6].

Patient factors

Adding bevacizumab to standard chemotherapy was not associated with a decrease in quality of life for high-risk patients[7].

Cost effectiveness

According to one published model-based cost-utility analysis using the mature results of the high-risk subgroup of ICON7, the addition of 7.5 mg/kg bevacizumab to carboplatin plus paclitaxel chemotherapy produced 0.381 more quality-adjusted life-years (QALY) per patient at an additional cost of £18,684. This resulted in a base case incremental cost effectiveness ratio of £48,975 per QALY gained with ranges from £32,898 to £65,519 in scenario analyses[8].

Budget impact
The addition of bevacizumab 7.5 mg/kg to standard chemotherapy is estimated to increase the spend associated with this patient group in Wales by £689,857 in year one and £730,436 in year two, if all estimated eligible patients (30 per year) receive the recommended dose of 18 cycles[4].

Welsh commercial access agreement
This medicine is currently not licensed for the indication under consideration (i.e. off-label) and therefore as the Pharmaceutical Industry's code of practice prevents a company from promoting an off-label use of a medicine, a commercial agreement cannot be offered by the company.

Impact on health and social care services
Although there will be an increased use of existing services to administer bevacizumab and monitor for toxicity, the impact is expected to be minimal.

Innovation and/or advantages
Bevacizumab in combination with paclitaxel and carboplatin offers an additional treatment option.

References

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