### Avastin® (bevacizumab) and PARP inhibitor approvals in ovarian cancer as of June 2018

The following graphic illustrates where Avastin and PARP inhibitors are currently approved in ovarian cancer.1-4

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<th>1L</th>
<th>2L PLATINUM-SENSITIVE</th>
<th>2L PLATINUM-RESISTANT</th>
<th>3L PLATINUM-SENSITIVE</th>
<th>3L PLATINUM-RESISTANT</th>
<th>4L+</th>
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<tbody>
<tr>
<td>Induction</td>
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<tr>
<td>Avastin® (bevacizumab) plus chemotherapy</td>
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<td>Zejula® (niraparib)</td>
<td>Lynparza® (olaparib)</td>
<td>Rubraca® (rucaparib)</td>
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<td>Chemotherapy</td>
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### Indications

- Avastin, in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.
- Avastin, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens.
- Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

### Boxed WARNINGS

- **Surgery and wound healing complications**
  - The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in Avastin-treated patients.
  - Withhold Avastin for at least 28 days prior to elective surgery. Do not administer Avastin for at least 28 days after surgery and until the wound is fully healed.
  - Discontinue in patients with wound healing complications requiring medical intervention.

- **Hemorrhage**
  - Severe or fatal hemorrhage, including hemoptysis, GI bleeding, hematemesis, central nervous system hemorrhage, epistaxis, and vaginal bleeding, occurred up to 5-fold more frequently in patients receiving Avastin. In clinical studies, the incidence of grade ≥3 hemorrhagic events among patients receiving Avastin ranged from 0.4% to 7%.
  - Do not administer Avastin to patients with serious hemorrhage or a recent history of hemoptysis (≥1/2 tsp of red blood).
  - Discontinue Avastin in patients who develop grade 3-4 hemorrhage.

*Please see reverse for Zejula®, Lynparza®, and Rubraca® indication statements.*

Please see accompanying full Prescribing Information, including Boxed WARNINGS, and reverse for additional important safety information.
Important safety information (continued)

Additional serious adverse events

- Additional serious and sometimes fatal adverse events with increased incidence in the Avastin-treated arm vs chemotherapy arm included:
  - Non-GI fistulae (<1% to 1.8%, highest in patients with cervical cancer)
  - Arterial thromboembolic events (grade ≥3, 5%, highest in patients with GBM)
  - Renal injury and proteinuria
    - Grade 3–4 proteinuria ranged from 0.7% to 7% in clinical studies
    - Nephrotic syndrome (<1%)
- Additional serious adverse events with increased incidence in the Avastin-treated arm vs chemotherapy arm included:
  - Venous thromboembolism (grade ≥3, 11% seen in GOG-0240)
  - Hypertension (grade 3–4, 5%–18%)
  - Posterior reversible encephalopathy syndrome (PRES) (<0.5%)
  - Congestive heart failure (CHF) (1%)
- Infusion reactions with the first dose of Avastin occurred in <3% of patients, and severe reactions occurred in 0.2% of patients
- Avoid use in patients with ovarian cancer who have evidence of recto-sigmoid involvement by pelvic examination or bowel involvement on CT scan or clinical symptoms of bowel obstruction
- Inform females of reproductive potential of the risk of ovarian failure prior to initiating treatment with Avastin

Pregnancy warning

- Based on the mechanism of action and animal studies, Avastin may cause fetal harm
- Advise female patients that Avastin may cause fetal harm, and to inform their healthcare provider of a known or suspected pregnancy
- Advise females of reproductive potential to use effective contraception during treatment with Avastin and for 6 months after the last dose of Avastin
- Advise nursing women that breastfeeding is not recommended during treatment with Avastin and for 6 months following their last dose of treatment
- Avastin may impair fertility

Most common adverse events

- Across studies, the most common adverse reactions observed in Avastin patients at a rate >10% were:
  - Epistaxis
  - Proteinuria
  - Lacrimation disorder
  - Headache
  - Taste alteration
  - Back pain
  - Hypertension
  - Dry skin
  - Exfoliative dermatitis
  - Rhinitis
  - Rectal hemorrhage
  - Across all studies, Avastin was discontinued in 8% to 22% of patients because of adverse reactions

Other Indications

ZEJULA® (niraparib) is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Lynparza® (olaparib) is indicated

- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy
- for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with 3 or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza®

Rubraca® (rucaparib) is indicated

- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy
- for the treatment of adult patients with deleterious BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 2 or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca®

Please see accompanying full Prescribing Information, including Boxed WARNINGS, and reverse for additional important safety information.


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