CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17 July - August

BRAND NAME
Zejula™

GENERIC NAME
Niraparib

MANUFACTURER
Tesaro Inc

DATE OF APPROVAL
March 27, 2017

PRODUCT LAUNCH DATE
April 2017

REVIEW TYPE

☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Reviews for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
Zejula 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.

OFF-LABEL USES
Not applicable

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CLINICAL EFFICACY

The safety and efficacy of niraparib were investigated in a randomized, double-blind, placebo-controlled phase 3 trial. A total of 553 patients were enrolled into two cohorts, 203 in the gBRCA cohort (presence of germline BRCA mutation) and 350 in the non-gBRCA cohort (absence of a germline BRCA mutation). All patients had shown sensitivity to platinum-based treatment and received at least two such regimens. Patients were randomly assigned in a 2:1 ratio to receive niraparib 300 mg once daily or placebo once daily.

The primary endpoint was progression-free survival (PFS).

- gBRCA cohort: 21 months (95% CI 12.9, Not Reached) for niraparib vs. 5.5 months (95% CI 3.8, 7.2) for placebo. The hazard ratio was 0.26 (95% CI 0.17, 0.41).
- non-gBRCA cohort: 9.3 months (95% CI 7.2, 11.2) for niraprib vs. 3.9 months (95% CI 3.7, 5.5) for placebo. The hazard ratio was 0.45 (95% CI 0.34, 0.61).
- Homologous recombination deficiency (HRD)-positive subgroup of non-gBRCA cohort: 12.9 months vs. 3.8 months for placebo. The hazard ratio was 0.38 (95% CI 0.24, 0.59).

All outcomes were statistically significant ($p<0.001$).

CONTRAINDICATIONS

Not applicable

BLACK BOX WARNINGS

Not applicable

DRUG INTERACTIONS

Not applicable

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥10%) are thrombocytopenia, anemia, neutropenia, leukopenia, palpitations, nausea, constipation, vomiting, abdominal pain/distention, mucositis/stomatitis, diarrhea, dyspepsia, dry mouth, fatigue/asthenia, decreased appetite, urinary tract infection, AST/ALT elevation, myalgia, back pain, arthralgia, headache, dizziness, dysgeusia, insomnia, anxiety, nasopharyngitis, dyspnea, cough, rash, and hypertension.

DOSAGE AND ADMINISTRATION

The recommended dose is 300 mg orally once daily.

PRODUCT AVAILABILITY

Capsules: 100 mg

CENTENE PHARMACY AND THERAPEUTICS
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THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Rubraca (rucaprib)	600 mg orally twice daily	Approved only in those with deleterious BRCA mutation (germline and/or somatic) after two or more chemotherapies
Lynparza (olaprib)	400 mg orally twice daily	Approved only in those with deleterious or suspected deleterious germline BRCA mutation after 3 or more chemotherapies
carboplatin (Paraplatin)	Varies	
cisplatin (Platinol-AQ)	Varies	
carboplatin/docetaxel	Varies	
carboplatin/gemcitabine	Varies	
carboplatin/gemcitabine/ bevacizumb	Varies	
carboplatin/liposomal doxorubicin	Varies	
carboplatin/paclitaxel	Varies	
cisplatin/gemcitabine	Varies	

Boldface indicates generic availability

Utilization Management Recommendation

- There is significant potential for inappropriate use and utilization management should be considered for the following reason(s):

  i) To prevent inappropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcomes.
  ii) Zejula is being evaluated in clinical trials for lung, breast and prostate cancer.
  iii) Zejula has only been evaluated in patients that received and experienced a complete or partial response to prior platinum-containing chemotherapy regimens.

  iv) Recommended utilization management tool(s): (check all that apply)
  (1) ☒ Prior authorization
  (2) ☐ Quantity limits
  (3) ☐ Provider newsletter
  (4) ☐ Hard block (plan exclusion)
  (5) ☐ Messaging
  (6) ☐ Electronic step therapy

CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
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(7) ☐ Clinical Program
Product Comparison
• CPAC score: 68 vs. Rubraca - Modest benefits over current therapies • For BRCA negative, it would not be clinically appropriate to require a trial of Rubraca prior to Zejula. • For BRCA positive, it would be clinically appropriate to provide equal access to Rubraca and Zejula, or require a trial of one before the other.

REFERENCES:

1. Zejula Prescribing Information. Waltham, MA: Tesaro, Inc., March 2017. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208447lbl.pdf. Accessed March 30, 2017.
2. Mirza MR, Monk BJ, Herrstedt J et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1;375(22):2154-2164. Epub 2016 Oct 7.
3. National Comprehensive Cancer Network. Ovarian Cancer Version 1.2016. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed March 29, 2017.