Zejula™ (niraparib) – New orphan drug approval

- On March 27, 2017, the FDA announced the approval of Tesaro's Zejula (niraparib) 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.

- According to the National Cancer Institute, approximately 22,280 new cases of ovarian cancer were diagnosed in 2016 and an estimated 14,240 women died of this disease.

    — Despite high response rates to platinum-based chemotherapy in the second-line advanced treatment setting, approximately 85% of patients will experience recurrence within 2 years.

- Zejula is an orally available poly (ADP-ribose) polymerase (PARP) inhibitor that blocks an enzyme involved in repairing damaged DNA. Inhibition of PARP activity results in DNA damage, apoptosis and cell death.

    — Unlike other currently marketed PARP inhibitors, Zejula does not require BRCA mutation or other biomarker testing.

- Other currently available PARP inhibitors include Lynparza™ (olaparib) and Rubraca™ (rucaparib). Both are approved for use in patients with certain types of BRCA mutations associated with advanced ovarian cancer. Refer to the drug labels for specific indication information.

- The safety and efficacy of Zejula were based on data from a placebo-controlled trial of 553 patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who had received at least two prior treatments of platinum-based chemotherapy and achieved a complete or partial response with their most recent chemotherapy treatment. The primary outcome measure was progression free survival (PFS).

    — The trial demonstrated a statistically significant improvement in PFS in patients with or without germline BRCA (gBRCA) mutations randomized to Zejula vs. placebo.
    — The median PFS for those taking Zejula with deleterious or suspected deleterious gBRCA mutations was 21 months vs. 5.5 months for those with gBRCA mutations receiving placebo (HR = 0.26 [95% CI: 0.17, 0.41]; $p < 0.0001$).
    — The median PFS for those taking Zejula who did not have gBRCA mutations was 9.3 vs. 3.9 months for those patients without gBRCA mutations receiving placebo (HR = 0.45 [95% CI: 0.34, 0.61]; $p < 0.0001$).

- Warnings and precautions of Zejula include myelodysplastic syndrome/acute myeloid leukemia, bone marrow suppression, cardiovascular effects, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 10%) with Zejula use were thrombocytopenia, anemia, neutropenia, leukopenia, palpitations, nausea, constipation, vomiting, abdominal pain/distention, mucositis/stomatitis, diarrhea, dyspepsia, dry mouth, fatigue/asthenia, decreased appetite, urinary tract infection, aspartate aminotransferase/alanine aminotransferase elevation, myalgia, back pain, arthralgia, headache, dizziness, dysgeusia, insomnia, anxiety, nasopharyngitis, dyspnea, cough, rash, and hypertension.

- The recommended dose of Zejula as monotherapy is 300 mg (three 100 mg capsules) taken orally once daily.

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    - Patients should start treatment with Zejula no later than 8 weeks after their most recent platinum-containing regimen.
    - Zejula treatment should be continued until disease progression or unacceptable toxicity.

- Tesaro plans to launch Zejula as 100 mg capsules in late April 2017.