Important Safety Information on ZEJULA® (niraparib) - Update on the Maintenance Treatment in Recurrent Ovarian, Fallopian Tube, or Primary Peritoneal Cancer in the Second or Later Line Setting

2023/02/16

Audience
Healthcare professionals in Canada including medical oncologists, gynaecologic oncologists, chiefs of medicine in hospitals, pharmacists/pharmacies, nursing staff, and clinical investigators.

Key messages

- **Currently available data from the ENGOT-OV16/NOVA (NOVA) study is suggesting that median overall survival (OS) of patients treated with ZEJULA may be lower than expected in the non-g*BRCA*mut patient population.**
- **GlaxoSmithKline (GSK) has notified Health Canada that the company will be submitting updated OS data up to March 31, 2021. Health Canada will review all available OS data and further communicate if any actions are needed.**
- **At this time, there are no changes to the ZEJULA Product Monograph nor its approved indications in Canada. However, healthcare professionals are advised to:**
  - **Consider the information currently available before initiating ZEJULA for maintenance treatment in patients with non-g*BRCA*mut recurrent ovarian, fallopian tube, or primary peritoneal cancer in the second or later line setting.**
  - **Share this information with patients who may be affected to allow them to make an informed decision regarding their treatment plan.**

What is the issue?
Currently available data from the NOVA study, based on a data cut-off date of October 1, 2020, shows that the median OS may be lower with ZEJULA compared to placebo for patients in the overall non-g*BRCA*mut cohort and the non-g*BRCA*mut/ Homologous Recombinant Deficient (HRd) subgroup. GSK has notified Health Canada of additional OS data that will be submitted. Health Canada will review all available OS data and further communicate if any actions are needed.

Products affected
ZEJULA (niraparib), 100 mg capsules, 100 mg tablets

Background information
ZEJULA (niraparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor used as monotherapy for the maintenance treatment of adult patients with recurrent or advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

NOVA is a Phase III study conducted to evaluate the efficacy and safety of ZEJULA as maintenance treatment for patients with platinum-sensitive, recurrent ovarian cancer.

The primary endpoint of progression free survival in the NOVA study was evaluated as two independent cohorts (g*BRCA*mut and non-g*BRCA*mut) and demonstrated the benefit of ZEJULA over placebo in delaying disease progression in all populations studied.

The OS results, a secondary efficacy endpoint, based on the data cut-off date of October 1, 2020, are included below:

- In the g*BRCA*mut cohort (n=203), the median OS was 43.6 months for patients treated with ZEJULA compared to 41.6 months for patients on placebo (HR = 0.93 [95% CI 0.63, 1.36]).
- In the non-g*BRCA*mut cohort (n=350), the median OS was 31.1 months for patients treated with ZEJULA compared to 36.5 months for patients on placebo (HR = 1.10 [95% CI 0.83, 1.46]).

Additionally, within the non-g*BRCA*mut cohort, an exploratory analysis of OS was performed for patients who were HRd, Homologous Recombinant Proficient (HRp) and patients whose homologous recombination status was not determined (HRnd). These results are summarized below:

- In the non-g*BRCA*mut/HRd subgroup (n=162), the median OS was 37.3 months for patients treated with ZEJULA compared to 41.4 months for patients on placebo (HR = 1.32 [95% CI 0.84, 2.06]).
- In the non-g*BRCA*mut/HRp subgroup (n=134) had a median OS of 27.9 months for patients treated with ZEJULA or placebo (HR = 1.06 [95% CI 0.67, 1.66]).
- In the non-g*BRCA*mut/HRnd subgroup (n=54) had a median OS of 30.7 months for patients treated with ZEJULA compared to 20.2 months for patients on placebo (HR = 0.60 [95% CI 0.26, 1.41]).

The median OS may be lower with ZEJULA compared to placebo for patients in the overall non-g*BRCA*mut cohort and the non-g*BRCA*mut/HRd subgroup, suggesting a potential negative trend in survival in these populations. GSK has conducted a

thorough review of the OS data from the NOVA study and, to date, no clear underlying reason has been identified to explain the observed results in this patient population.

The analyses were initially conducted based on a data cut-off date of October 1, 2020. GSK has notified Health Canada that additional OS data up to March 31, 2021 will be submitted.

Information for consumers
ZEJULA is a type of drug called a PARP inhibitor. PARP inhibitors block a protein called poly [adenosine diphosphate-ribose] polymerase (PARP). This protein helps cells to repair their damaged DNA. Blocking PARP activity prevents the repair of damaged DNA in cancer cells, therefore, leading to cancer cell death.

ZEJULA is indicated for the maintenance treatment of ovarian cancer, fallopian tube cancer, or primary peritoneal cancer (the membrane that lines the inside of the abdomen), including cases where the cancer has come back, in patients who have responded to platinum-based chemotherapy.

Patients currently taking ZEJULA for these indications should contact their healthcare professional for more information.

Information for healthcare professionals
At this time, there are no changes to the ZEJULA Product Monograph nor its approved indications in Canada. However, healthcare professionals are advised to:

- Consider the information currently available before initiating ZEJULA for maintenance treatment in patients with non-g*BRCA*mut recurrent ovarian, fallopian tube, or primary peritoneal cancer in the second or later line setting.
- Share this information with patients who may be affected to allow them to make an informed decision regarding their treatment plan.

Action taken by Health Canada
Health Canada will review all available information that will be submitted by GSK and further communicate if any action is needed.

Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site. This communication will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns
Health Canada's ability to monitor the safety of marketed health products depends on healthcare professionals and consumers reporting adverse reactions and medical device incidents. Any serious or unexpected side effects in patients receiving ZEJULA should be reported to GlaxoSmithKline Inc. or Health Canada.

GlaxoSmithKline Inc.
100 Milverton Drive
Suite 800
Mississauga, Ontario
L5R 4H1
Tel: 1-800-387-7374

For more information, to correct your mailing address or fax number, contact GlaxoSmithKline Inc. 1-800-387-7374

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Pharmaceutical Drugs Directorate
E-mail: pharma_drug_enquiries-renseignements_medicaments_pharma@hc-sc.gc.ca
Telephone: 613-957-0368
Fax: 613-952-7756

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