[Pr]LYNPARZA® (olaparib): Risk of medication errors with new pharmaceutical form

May 4, 2018

Dear Health Care Professional(s):

AstraZeneca Canada Inc. (AstraZeneca), in agreement with Health Canada, would like to inform you of the following:

Summary

- A tablet formulation of LYNPARZA (olaparib) was approved by Health Canada on May 4, 2018. LYNPARZA capsules and tablets are NOT bioequivalent and are NOT interchangeable. The two formulations must NOT be substituted on a milligram-to-milligram basis due to differences in dosing and bioavailability of each formulation.

- There is a risk of medication error if the wrong formulation or dosage is prescribed, or if capsules and tablets are used interchangeably. The effects of overdose with olaparib are not known.

- To avoid medication errors, prescribers should specify the formulation AND dosage of LYNPARZA on each prescription and pharmacists should ensure that the correct formulation and dose is dispensed to patients

- Instruct patients on the correct dose they should take for their capsules or tablets. For any patients switching from capsules to tablets (or vice-versa), explain how the doses in milligrams for the two forms are different

Background on the safety concern

LYNPARZA (olaparib) tablet formulation is indicated as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed (PSR) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy.

- Marketing authorization **with conditions** issued for ovarian cancer patients with *BRCA* wild type status was based on promising evidence of superior benefit in prolonging progression-free survival (PFS) of olaparib capsule versus placebo in a phase II trial (Study 19) in patients with *BRCA* wild type status, as assessed by investigator using RECIST 1.0.
- Marketing authorization **without conditions** issued for ovarian cancer patients with *BRCA* mutation was based on results from a randomized, placebo-controlled phase III trial (SOLO2) demonstrating that olaparib tablet is superior to placebo in prolonging PFS in patients with *BRCA* mutation, as assessed by investigator using RECIST 1.0.

LYNPARZA (olaparib) capsule formulation is indicated as monotherapy for the maintenance treatment of adult patients with PSR *BRCA*-mutated (germline or somatic) high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy.

LYNPARZA capsules and tablets are not bioequivalent and are not interchangeable. The posology for tablets and capsules is different (see table below) and the two formulations should not be substituted on a milligram-to-milligram basis; there is a risk of overdose and increased adverse events if the capsule posology is used for the tablets or decreased efficacy if the tablet posology is used for the capsules.

Information regarding the reporting mechanisms for adverse events, including medication errors and near misses, is provided at the end of this letter.

Dosage Formulation, Strength, and Packaging	**Capsules 50 mg** Available in 190 ml bottles, supplied in a carton of four bottles.	**Tablets 150 mg**	**Tablets 100 mg**
		Available in 110 ml and 190 ml bottles.	
Recommended Dosage*	400 mg twice daily Morning: 8 x  Evening: 8 x  Total Daily Dosage: 800 mg	300 mg twice daily Morning: 2 x  Evening: 2 x  Total Daily Dosage: 600 mg	**Only to be used for tablet dose reductions** 
Dose adjustments	Dose reductions are achieved using fewer 50 mg capsules	Dose reductions are achieved using 100 mg and 150 mg tablets	
Adverse reactions	**Initial reduced dosage:** 200 mg BID (total daily dosage: 400 mg) **For further reductions use:** 100 mg BID (total daily dosage: 200 mg)	**Initial reduced dosage:** 250 mg BID (total daily dosage: 500 mg) **For further reductions use:** 200 mg BID (total daily dosage: 400 mg)	
Co-administration with CYP3A4 inhibitors	**Strong inhibitor:** 150 mg BID (total daily dosage: 300 mg) **Moderate inhibitor:** 200 mg BID (total daily dosage: 400 mg)	**Strong inhibitor:** 100 mg BID (total daily dosage: 200 mg) **Moderate inhibitor:** 150 mg BID (total daily dosage: 300 mg)	
Moderate renal impairment	300 mg BID (total daily dosage: 600 mg)	200 mg BID (total daily dosage: 400 mg)	

* Images of the formulations are representations only and are not to scale
BID twice daily

The Product Monographs, package inserts and packaging for both formulations of LYNPARZA include information that the two formulations are not bioequivalent or interchangeable, and must not be substituted on a milligram-to-milligram basis.

Access to LYNPARZA

LYNPARZA tablets are supplied through the standard distribution channels for prescription pharmaceuticals.

LYNPARZA capsules are only supplied through a controlled distribution program, and patients should be enrolled in the AstraZeneca Oncology Patient Support Program to receive LYNPARZA capsules. For more information, please call toll free 1-877-280-6208.

For the complete prescribing information and information available for patients/caregivers, please consult the LYNPARZA Product Monographs at: www.astrazeneca.ca. If you have medical enquiries regarding LYNPARZA, contact our Medical Information Department at 1-800-668-6000 (English) and/or 1-800-461-3787 (French).

Original Signed by:

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For adverse event reporting, contact our Medical Information Department at 1- 800-668-6000 (English) and/or 1-800-461-3787 (French)

Reporting Suspected Side Effects
Canada Vigilance Program
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Tunney's Pasture
Address Locator: 0701C
Ottawa, Ontario
K1A 0K9
Telephone: 613-957-0337 or Fax: 613-957-0335

To report an Adverse Reaction, consumers and health professionals may call toll free:
Telephone: 1-866-234-2345
Fax: 1-866-678-6789
Email: CanadaVigilance@hc-sc.gc.ca

The Adverse Reaction Reporting Form and the Adverse Reaction Guidelines can be found on the Health Canada website (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) or in *The Canadian Compendium of Pharmaceuticals and Specialties* (https://www.pharmacists.ca/products-services/compendium-of-pharmaceuticals-and-specialties/)

For other inquiries related to this communication, please contact Health Canada at:
Bureau of Metabolism, Oncology and Reproductive Sciences (BMORS)
E-mail: bmors_enquiries@hc-sc.gc.ca
Telephone: 613-941-3171
Fax: 613-941-1365