Dear Healthcare Professionals,

**Niraparib (Zejula▼): reports of severe hypertension and posterior reversible encephalopathy syndrome (PRES), particularly in early treatment**

Your attention is drawn to the United Kingdom Medicines and Healthcare products Regulatory Agency’s (MHRA) announcement on recent reports of onset of severe hypertension (including rare cases of hypertensive crisis) and rare cases of posterior reversible encephalopathy syndrome (PRES) within the first month of niraparib treatment.

A recent European review of the safety data for niraparib identified worldwide reports of patients who developed severe hypertension, including rare cases of hypertensive crisis (may affect up to 1 in 1000 patients), as early as within the first month of treatment with niraparib. The review also identified rare reports of PRES (may affect up to 1 in 1000 patients). Of 5 cases worldwide, 4 patients presented with severe hypertension and 3 reported that PRES occurred during the first month of therapy. Three reports originated from post-marketing sources and 2 from clinical trials.

Hypertension was identified as an important risk with niraparib in clinical trials. The product information for niraparib had an existing warning for hypertension, including hypertensive crisis, and recommended that blood pressure should be monitored monthly in the first year. Based on the new information identified in the European review, safety warnings have been updated and hypertensive crisis and PRES both added into the product information as rare reactions. The product information has been amended to recommend more frequent blood pressure measurement, especially at the start of treatment. Increase the frequency of blood pressure monitoring to at least weekly for the first 2 months, and then monitor monthly for the first year and periodically thereafter during treatment. For appropriate patients, home blood pressure monitoring can be considered with instruction for patients to contact their healthcare professional in case of rise in blood pressure. Adequate instructions should be provided to patients or caregivers on how to monitor blood pressure at home.

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In the United Kingdom, up to 30 Jul 2020, the Yellow Card Scheme received 6 reports associated with hypertension for niraparib. However, limited information is available for the details of the hypertension, including time of onset. No United Kingdom Yellow Card reports have been received for PRES associated with niraparib. Caution should be exercised in interpreting these data since there may be under-reporting and use of niraparib in the United Kingdom may be relatively low.

Hypertension, including hypertensive crisis, has been reported with the use of niraparib including in the first month of treatment. PRES is a rare, reversible, neurological disorder. The presenting signs and symptoms of PRES include seizures, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). The safety of reinitiating niraparib therapy in patients who have previously experienced PRES is not known.

Advice for healthcare professionals:
- There have been reports of severe hypertension (including rare cases of hypertensive crisis) with niraparib, including some with onset in the first month of treatment.
- Rare cases of posterior reversible encephalopathy syndrome (PRES) have also been reported, many associated with hypertension and within the first month of treatment.
- Before treatment, control pre-existing hypertension adequately before starting a patient on niraparib.
- Monitor blood pressure at least weekly for 2 months from initiation and then monthly afterwards for the first year and periodically thereafter during treatment.
- Consider home blood pressure monitoring for appropriate patients; provide adequate training and instruct them to contact their doctor in case of a rise in blood pressure.
- During treatment, manage hypertension with antihypertensives and if necessary, consider treatment interruption and subsequent adjustment of the niraparib dose as advised in product information.
- Discontinue niraparib in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy.
- In cases of PRES, discontinue niraparib and treat specific symptoms including hypertension.

Please refer to the following website in MHRA for details:

In Hong Kong, Zejula Capsules 100mg (HK-65945) is a pharmaceutical product containing niraparib. The product is registered by Zai Lab (Hong Kong) Limited, and is a prescription-only medicine. So far, the Department of Health (DH) has received 7 cases of adverse drug reaction related to niraparib, but

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these cases are not related to severe hypertension and posterior reversible encephalopathy syndrome. In light of the above MHRA’s announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under “ADR Reporting”: http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)