Important Safety Information
FASLODEX® (fulvestrant) – Risk of Unnecessary Therapy Modification due to Falsely Elevated Estradiol Levels

2016/10/18

Audience
Healthcare professionals involved in the management of breast cancer (medical oncologists, radiation oncologists, surgical oncologists, gynecologists, oncology nurses, laboratory directors), cancer clinics and cancer associations.

Key messages

- **FASLODEX (fulvestrant) can interfere with antibody based estradiol measurement by immunoassay due to structural similarity of fulvestrant and estradiol. This can result in falsely elevated estradiol levels.**
- **False estradiol positive assays may lead to misinterpretation of the menopausal status of women which can put patients at risk for unnecessary surgery or endocrine therapy modification.**
- **Healthcare professionals should consider reassessing the menopausal status of patients on FASLODEX by alternative methods where necessary. When requesting blood tests that include estradiol, indicate if the patient is on FASLODEX.**
- **New warnings have been added to the Canadian Product Monograph for FASLODEX advising of this safety risk.**

What is the issue?
Medical and scientific literature as well as post marketing reports suggest that fulvestrant can cross react with estradiol (E2) immunoassays due to structural similarity with estradiol. The false E2 positive assays may lead to misinterpretation of the menopausal status of women therefore putting patients at risk for unnecessary surgery or endocrine therapy modification.

Products affected
FASLODEX® (fulvestrant) 50 mg/mL injection

Background information
FASLODEX is indicated for the hormonal treatment of locally advanced or metastatic

breast cancer in postmenopausal women, regardless of age, who have disease progression following prior anti-estrogen therapy.

Rare international cases of false positive increased estradiol levels have been reported in patients receiving FASLODEX, resulting in unnecessary surgery being performed. It could also potentially result in modification of endocrine therapy being initiated.

The measurement of low estradiol levels is challenging because of the lack of standardization at low levels in postmenopausal women and the variation in sensitivity/specificity among different immunoassays. Studies suggest that direct immunoassay kits from different manufacturers provide different results and are not always reliable to measure estradiol levels in patients receiving fulvestrant therapy. It is therefore important to recognize the limitations of individual estradiol tests and choose an alternative test method (such as liquid chromatography-mass spectrometry).

Information for consumers

FASLODEX is used to treat breast cancer in postmenopausal women. In hormone sensitive breast cancer, estrogen (female sex hormone) promotes tumour growth. By stopping some of the actions of estrogen, FASLODEX reduces the amount that is in the body, which has an effect in reducing breast cancer tumour growth.

Blood tests to check levels of estradiol (a hormone) may be used during FASLODEX treatment to confirm menopausal status as, with breast cancer patients, this can sometimes change.

There have been reports that FASLODEX can interfere with estradiol blood tests and produce incorrect results. Incorrect test results could potentially lead to beneficial therapy being changed or stopped unnecessarily. In rare cases, misinterpreting a patient as premenopausal can lead to unnecessary surgery.

Patients should contact their healthcare professional for more information.

Information for healthcare professionals

When requesting blood tests that include estradiol, indicate if the patient is on FASLODEX. Caution should be exercised when performing antibody-based estradiol assays for patients taking FASLODEX. Healthcare professionals should consider the need to carry out a review of the previously reported test results.

Healthcare professionals should continue to use estradiol immunoassays for patients not on FASLODEX. If measuring estradiol levels in patients on FASLODEX, alternative methods such as liquid chromatography-mass spectrometry should be considered.

Action taken by Health Canada

Health Canada in collaboration with AstraZeneca Canada Inc. has updated the FASLODEX Canadian Product Monograph. Health Canada is communicating this important safety information to healthcare professionals and to the public through

its Healthy Canadians Web site (www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php) and MedEffect™ e-Notice.

Health Canada in collaboration with the manufacturers of estradiol assays has reviewed and updated the package inserts to include warnings about the risks on the use of such tests in FASLODEX patient populations.

Report health or safety concerns

Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any case of an unnecessary surgery or endocrine therapy modification due to falsely elevated estradiol levels or other serious or unexpected side effects in patients receiving FASLODEX should be reported to AstraZeneca or Health Canada.

AstraZeneca Canada Inc.
1004 Middlegate Road, Suite 5000
Mississauga, ON, L4Y 1M4
Tel: 1-800-668-6000
Email: medinfo.canada@astrazeneca.com

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:

Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

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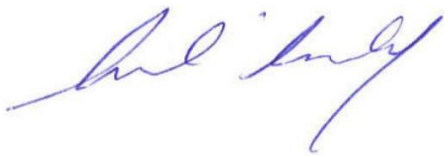

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