PLEASE READ

IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

22 September 2025

Xtandi (enzalutamide) and Lanoxin (digoxin): enzalutamide laboratory test interference leading to falsely elevated digoxin plasma levels

Dear Healthcare Professional,

Astellas Pharma Europe and Aspen Pharma Trading Limited in agreement with the Health Products Regulatory Authority (HPRA) would like to inform you of the following:

Summary:

- **Falsely elevated serum digoxin levels detected using chemiluminescent microparticle immunoassay (CMIA) have been identified in patients treated with enzalutamide, even in the absence of digoxin treatment.**
  - **Therefore, results of serum digoxin levels obtained by CMIA should be interpreted with caution in patients taking enzalutamide.**
  - **Confirmation by another type of assay before determining the need for any discontinuation of or decrease in dose of digoxin is recommended.**

- **Healthcare professionals are reminded that enzalutamide may additionally inhibit the efflux transporter P-glycoprotein (P-gp) which could lead to increased serum levels of digoxin, a P-gp substrate.**
  - **Digoxin should therefore be used with caution when administered concomitantly with enzalutamide and may require dose adjustment to maintain optimal plasma concentrations.**

Background on the safety concern

Xtandi (enzalutamide) is an androgen receptor inhibitor indicated for prostate cancer. Lanoxin (digoxin) is a cardiac glycoside used as an inotrope to improve systolic dysfunction in patients with congestive heart failure, and in the management of certain supraventricular arrhythmias, particularly chronic atrial flutter and fibrillation.

Based on a review of the available information from the individual case safety reports sourced from safety databases, along with a review of scientific literature, it has been concluded that enzalutamide

may interfere with the CMIA laboratory test method, leading to falsely elevated digoxin plasma level results in patients taking enzalutamide, regardless of whether the patient is taking digoxin or not. In case of doubtful results, it is recommended that confirmation of serum digoxin levels is obtained by another type of assay without known interference before determining the need for any discontinuation of or decrease in dose of digoxin in patients taking enzalutamide.

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) has recommended that the laboratory test interference by enzalutamide leading to falsely elevated digoxin levels should be reflected in the product information for both enzalutamide and digoxin products.

Separately, healthcare professionals are reminded that the current product information for enzalutamide highlights that enzalutamide may be an inhibitor of the efflux transporter P-glycoprotein (P-gp), which may lead to increased serum levels of medicines that are substrates of P-gp. Medicinal products with a narrow therapeutic range that are substrates for P-gp, including digoxin, should be used with caution when administered concomitantly with enzalutamide and may require dose adjustment to maintain optimal plasma concentrations.

Recommendation for sharing

This communication should be shared with relevant colleagues to ensure all laboratory professionals are informed of this safety information.

Call for reporting

Healthcare professionals are asked to report any suspected adverse drug reactions via HPRA Pharmacovigilance, website: www.hpra.ie.

Company contact points

Should you have any questions regarding the contents of this letter or the use of these medicines, please contact

Astellas (Xtandi (enzalutamide)
Tel: +353 1 467 1555
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Aspen Drug Safety (Lanoxin (digoxin))
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Email: DUB-GM-Drugsafety@ie.aspenpharma.com

Sincerely,

Philip Maddison

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17 Sep 2025 14:26:019+0000
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EU-QPPV and UK-QPPV

Astellas Pharma Europe

Paula Flanagan

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Head of Pharmacovigilance/ Deputy EU-QPPV

Aspen Pharma Trading Limited

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