Leuprorelin depot medicines: new measures to avoid handling errors

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Information on Leuprorelin medicines

- Depot formulations of leuprorelin medicines include implants as well as powders and solvents for the preparation of injections. They are given as subcutaneous injection (injection under the skin) or intramuscular injection (injection into a muscle). The active substance is gradually released over 1 to 6 months
- Leuprorelin depot medicines are used to treat prostate cancer, breast cancer, conditions that affect the female reproductive system (endometriosis and uterine fibroids), and early puberty
- Leuprorelin medicines are also available as daily injections but this formulation is not included in the review as there have been no reports of handling errors with daily use injections.

The following products are authorised in Malta through different procedures

Active Ingredients	Product Name	Pharmaceutical Form	Classification	Authorisation Number	MAH/license holder
ELIGARD 7.5mg powder and solvent for solution for injection	Leuprorelin acetate 7.5 milligram(s)	Powder and solvent for solution for injection	POM	AA067/01101	Astellas Pharma Europe B.V.
ELIGARD 22.5mg powder and solvent for solution for injection	Leuprorelin acetate 22.5 milligram(s)	Powder and solvent for solution for injection	POM	AA067/01102	Astellas Pharma Europe B.V.
ELIGARD 45mg powder and solvent for solution for injection	Leuprorelin acetate 45 milligram(s)	Powder and solvent for solution for injection	POM	AA067/01103	Astellas Pharma Europe B.V.
Prostap SR DCS 3.75mg Powder and Solvent for Prolonged-release Suspension for Injection	Leuprorelin acetate 3.75 milligram(s)	Powder and solvent for suspension for injection	POM	AA565/27501	Central Procurement & Supplies Unit
Lutrate 1 month Depot 3.75mg Powder & Solvent for prolonged-release Suspension for Injection	Leuprorelin acetate 3.75 milligram(s)	Powder and solvent for prolonged-release suspension for injection	POM	AA565/42901	Central Procurement & Supplies Unit

Active Ingredients	Product Name	Pharmaceutical Form	Classification	Authorisation Number	MAH/license holder
Prostap SR DCS 3.75mg Pdr & solv for prolonged-release susp for injection in pre-filled syringee	Leuprorelin acetate 3.75 milligram(s)	Powder and suspension for suspension for injection	POM	AA1369/00401	Health House Pharma Ltd T/As P&D Pharmaceuticals Ltd

Information from the EMA on new measures to avoid handling errors

The Pharmacovigilance Risk Assessment Committee (PRAC) carried out a review on leuprorelin depot medicines following request of Germany.

The review showed that handling errors included incorrect use of the needle or syringe, causing the medicine to leak from the syringe, and failure to inject leuprorelin properly. As a result, some patients did not receive sufficient amount of their medicine. PRAC's recommendations were as follows:

- Leuprorelin depot medicines should be prepared and administered to patients only by healthcare professionals familiar with the preparation steps. Patients should not prepare or inject these medicines themselves
- For the medicine Eligard, the product information is to be updated with warnings to strictly follow the instructions for preparation and administration and to monitor patients if a handling error occurs. In addition, the company marketing Eligard must replace the current device used to administer the medicine with one that is easier to handle. The regulatory application for this modification should be submitted by October 2021
- For the medicine Lutrate Depot, the instructions for handling the medicine must be revised to make them easier to follow and its packaging changed so the instructions are easier to find.

The PRAC recommendations were adopted by the CMDh[1] by consensus and will be implemented directly at national level.

In Malta

For Healthcare Professionals

- The following recommendations are the results of a review of reports of handling errors with depot formulations of leuprorelin medicines, which could result in underdosing and a lack of efficacy
- Leuprorelin depot medicines should be prepared and administered to patients only by healthcare professionals familiar with the preparation steps. Patients should not prepare or inject these medicines themselves
- The complex reconstruction process, which involves multiple steps for some leuprorelin depot formulations can cause handling errors. Reported handling errors include incorrect use of

[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.

syringe or needle (causing the medicine to leak from the syringe), inadequate reconstitution, and incorrect injection of the leuprorelin implant

- For Eligard, used to treat advanced hormone-dependent prostate cancer, warnings will be included in the summary of product characteristics to inform healthcare professionals about cases of handling errors and to remind them to strictly follow the instructions for preparation and administration of the medicine. In case of suspected or known handling error with the medicine, patients should be monitored appropriately. The company that markets Eligard has been asked to modify the device to reduce the high number of preparation steps. The regulatory application for this modification should be submitted within 18 months
- Instructions for handling Lutrate Depot will be revised to make them easier to follow and the packaging will be changed to facilitate access to these instructions.

A DHPC letter will be disseminated to HCPs in Malta in due course. Archived DHPC letters are available online at http://www.medicinesauthority.gov.mt/dhpc

Advice for Patients

- Errors in using leuprorelin depot medicines (which are designed to work over a long period) may make treatment less effective
- Leuprorelin depot medicines should only be prepared and given by a doctor or nurse with experience in using them. You should not prepare or inject these medicines yourself
- If you have concerns about your treatment, please discuss these with your doctor or pharmacist

For more information, visit the European Medicines Agency's Leuprorelin-containing depot medicinal products referral page

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Leuprorelin- containing depot medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

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Pharmacovigilance Section

Post-Licensing Directorate

Medicines Authority

Sir Temi Żammit Buildings

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