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Leuprorelin depot medicines: PRAC recommends new measures to avoid handling errors

EMA's safety committee (PRAC) is recommending measures to avoid handling errors in the preparation and administration of leuprorelin depot medicines.

A review by the PRAC found that handling errors resulted in some patients receiving insufficient amounts of their medicine. The errors reported included incorrect use of the needle or syringe, causing the medicine to leak from the syringe, and failure to inject leuprorelin properly.

The Committee is therefore recommending that only healthcare professionals familiar with the preparation steps for leuprorelin depot medicines should prepare and administer the medicines to patients. Patients should not prepare or inject these medicines themselves.

The Committee also made recommendations for particular leuprorelin depot medicines. 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.[1]

For another medicine, Lutrate Depot, the PRAC recommended that instructions for handling the medicine be revised to make them easier to follow and its packaging changed so the instructions are easier to find.

Depot formulations of leuprorelin are used to treat prostate cancer, breast cancer, certain conditions that affect the female reproductive system, and early puberty. Several formulations require complex steps to prepare the injection.

Information for patients

- Errors in using leuprorelin depot medicines (which are designed to work over a long period) may make treatment less effective.
- These 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.

[1] The text was updated on 20 May 2020 to clarify that the deadline of October 2021 applies to the submission of the application to modify the device.

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- If you have concerns about your treatment, please discuss these with your doctor or pharmacist.

Information for healthcare professionals

- Leuprorelin depot medicines should only be prepared and given by healthcare professionals who are familiar with the procedures. Patients should not inject the medicine themselves.
- These recommendations follow a review of reports of handling errors with depot formulations of leuprorelin medicines, which could result in underdosing and a lack of efficacy.
- Handling errors are related to the complexity of the reconstitution process, which involves multiple steps for some leuprorelin depot formulations. Reported handling errors include incorrect use of 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.[1]
- 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 direct healthcare professional communication (DHPC) will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC will also be published on a dedicated page on the EMA website.

More about the medicines

Depot formulations of leuprorelin medicines are given by injection under the skin or into a muscle and they release the active substance gradually over 1 to 6 months. These medicines are used to treat prostate cancer, breast cancer, conditions that affect the female reproductive system (endometriosis and uterine fibroids), and early puberty. They include implants as well as powders and solvents for the preparation of injections.

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.

Leuprorelin medicines have been authorised via national procedures. They are marketed in many EU countries and are available under several brand names, including Eligard, Eliprogel, Enantone, Ginecrin, Lupron, Lutrate, Politrate and Procren.

[1] The text was updated on 20 May 2020 to clarify that the deadline of October 2021 applies to the submission of the application to modify the device.

More about the procedure

The review of leuprorelin depot medicines was initiated at the request of Germany, under Article 31 of Directive 2001/83/EC.

The review was carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has issued a set of recommendations. As all leuprorelin medicines are authorised nationally, the PRAC recommendations will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.