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Review of hydroxyprogesterone started

EMA has started a review of medicines containing hydroxyprogesterone following concerns about the safety and effectiveness of these medicines. In the EU, these medicines are available as hydroxyprogesterone caproate and are given as injections to prevent pregnancy loss or premature birth in pregnant women. In some countries they are also authorised for the treatment of various gynaecological disorders, including disorders caused by a lack of a hormone called progesterone.

EMA's safety committee (PRAC) started this review due to concerns about results from a study[1] which suggested that people who were exposed to hydroxyprogesterone caproate in the womb may have an increased risk of cancer compared with those who were not. The risk seemed to increase when the medicine was used during the first trimester of pregnancy and with the number of injections given. The use of hydroxyprogesterone caproate during the second or third trimester appeared to further increase the risk of cancer for males but not for females.

In addition, results from a second study[2] suggested that hydroxyprogesterone caproate is no more effective than placebo in preventing recurrent premature birth or medical complications due to prematurity in the newborn infant.

As a result of these concerns, the French medicines agency (ANSM) requested the PRAC to review the risks and benefits of these medicines in all their approved uses and to issue a recommendation on whether their marketing authorisations should be maintained, varied, suspended or withdrawn across the EU.

EMA will communicate PRAC's recommendations once the review has concluded.

[1] Murphy CC, et al. In utero exposure to 17α-hydroxyprogesterone caproate and risk of cancer in offspring. Am J Obstet Gynecol. 2022 Jan;226(1):132.e1-132.e14. doi:10.1016/j.ajog.2021.10.035

[2] Blackwell, S. C. et al. 17-OHPC to prevent recurrent preterm birth in singleton gestations (PROLONG Study): A multicenter, international, randomized double-blind trial. Am J Perinatol. 2020 Jan;37(2):127-136. doi:10.1055/s-0039-3400227.

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More about the medicine

Hydroxyprogesterone caproate is a synthetic form of the naturally occurring hydroxyprogesterone which is formed in the body from progesterone. Progesterone is involved in preparing the endometrium (womb lining) for pregnancy and maintaining it during pregnancy. Hydroxyprogesterone caproate is thought to attach to receptors (targets) on cells that normally attach to progesterone. This is expected to reduce the risk of pregnancy loss or premature labour in pregnant women and help treat certain gynaecological disorders related to a lack of progesterone such as menstrual irregularities.

Hydroxyprogesterone caproate is available as a solution for injection. Within the EU, the medicine is currently available in Austria, France, and Italy under the trade names Proluton Depot, Progesterone Retard Pharlon and Lentogest.

More about the procedure

The review of hydroxyprogesterone has been initiated at the request of France, under Article 31 of Directive 2001/83/EC.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As hydroxyprogesterone-containing medicines are all 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.