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Updated restrictions for Gilenya: multiple sclerosis medicine not to be used in pregnancy

EMA has recommended that the multiple sclerosis medicine Gilenya (fingolimod) must not be used in pregnant women and in women able to have children who are not using effective contraception. If a woman becomes pregnant while using Gilenya, the medicine must be stopped and the pregnancy will have to be closely monitored. This is because the active substance in Gilenya, fingolimod, can harm the unborn baby and may cause birth defects.

To minimise this risk, women able to have children must have a pregnancy test before starting treatment with Gilenya to ensure they are not pregnant, and must use effective contraception during treatment and for two months after stopping the medicine.

These recommendations follow a review triggered by reports suggesting that the risk of birth defects in infants who have been exposed to Gilenya during pregnancy is twice as high as the 2 to 3% risk observed in the general population. The most frequently reported birth defects in infants exposed to Gilenya were those affecting the heart, kidneys, bones and muscles.

Doctors, patients and carers will receive updated educational materials with information about this risk and what actions and precautions need to be taken to ensure the safe use of Gilenya.

Information for patients

- You must not take the multiple sclerosis medicine Gilenya if you are pregnant or if you are able to have children but are not using effective contraception.
- This is because Gilenya may harm the unborn baby if used during pregnancy. If you use Gilenya during pregnancy, your child could be at higher risk of birth defects, in particular those affecting the heart, kidneys, bones and muscles.
- You must use effective contraception while taking Gilenya. If you are taking Gilenya and are planning to have a baby, talk to your doctor first. Before trying for a baby, you must stop taking Gilenya and wait for at least two months. During these two months, you must still use contraception.
- If you do become pregnant while taking Gilenya, tell your doctor straight away. Your doctor will stop your Gilenya treatment and carry out extra tests to monitor your pregnancy.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

- Your doctor will talk to you about this risk before starting and during treatment with Gilenya, and will give you a card with information on why you should not become pregnant while taking Gilenya, and what you should do to avoid becoming pregnant while you are taking this medicine.
- If you are a female patient able to have children and just starting treatment with Gilenya, you will first need to have a pregnancy test to make sure that you are not pregnant.
- If you have any questions about Gilenya or the risks it poses to the unborn child, talk to your doctor, nurse or pharmacist.

Information for healthcare professionals

- Due to the risk of congenital malformations in fetuses exposed to fingolimod *in utero*, Gilenya is now contraindicated in pregnant women and in women of childbearing potential not using effective contraception.
- For women of childbearing potential, ensure that:
  - patients are informed of the risk of harmful effects to the fetus associated with fingolimod treatment;
  - a negative pregnancy test result is available before treatment initiation;
  - effective contraception is used during treatment and for 2 months after treatment discontinuation;
  - fingolimod treatment is stopped 2 months before planning a pregnancy.
- If a woman becomes pregnant during treatment, Gilenya must be discontinued and the patient should be given medical advice about the risk of harmful effects to the fetus. The pregnancy should be closely monitored, and ultrasonography examinations should be performed.

These updated recommendations follow a review of available data triggered by post-marketing reports suggesting that infants born to mothers treated with fingolimod during pregnancy have a two-fold increased risk of major congenital malformations compared with the rate observed in the general population (which is 2-3 %, according to EUROCAT - the European network of population-based registries for the epidemiological surveillance of congenital anomalies[1]).

The most frequently reported major malformations in infants exposed to fingolimod *in utero* are congenital heart diseases (such as atrial and ventricular septal defects, tetralogy of Fallot), renal abnormalities and musculoskeletal abnormalities.

Updated educational materials to help counsel patients about the risk of reproductive toxicity will be made available and will include a physician's checklist, a guide for patients, parents and caregivers and a pregnancy-specific patient reminder card.

More about the medicine

Gilenya is a type of medicine known as a 'disease-modifying therapy' that is used to treat adults and children over 10 years of age with highly active relapsing-remitting multiple sclerosis (MS), a disease

[1] http://www.eurocat-network.eu

in which inflammation destroys the protective sheath surrounding the nerve cells. 'Relapsing-remitting' means that the patient has flare-ups of symptoms (relapses) followed by periods of recovery (remissions). Gilenya is used when the disease remains active despite appropriate treatment with at least one other disease-modifying therapy, or is severe and getting worse rapidly. Gilenya contains the active substance fingolimod.

More information on Gilenya can be found on the EMA website.

More about the procedure

The review of Gilenya was conducted by EMA's safety committee (PRAC) and its human medicines committee (CHMP) in the context of a procedure known as a 'type II variation'.

The European Commission will issue a legally binding decision valid throughout the EU in due course.