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Our Ref: HSS(MD)24/2022
Date: 17 May 2022

HSS(MD)24/2022

FOR ACTION

Chief Executives HSC Trusts (*for onward cascade to Medical Directors)*
Chief Executives, Public Health Agency/Strategic Planning and Performance Group (SPPG)
GP Medical Advisers, SPPG
All General Practitioners and GP Locums *(for onward distribution to practice staff)*
Director of Pharmacy at SPPG *(for cascade to prescribing advisers and community pharmacies)*

PLEASE SEE ATTACHED FULL CIRCULATION LIST

Dear Colleague

SAFETY OF PREGABALIN (LYRICA) IN PREGNANCY: MHRA DRUG SAFETY UPDATE AND FINDINGS OF SAFETY STUDY ON RISKS DURING PREGNANCY

A new study has suggested pregabalin may slightly increase the risk of major congenital malformations if used in pregnancy. Patients should continue to use effective contraception during treatment and avoid use in pregnancy unless clearly necessary. The Medicines and Healthcare products Regulatory Agency (MHRA) have published a Drug Safety Update for Pregabalin (Lyrica): findings of a safety study on risks during pregnancy[1]

Actions for Healthcare professionals who prescribe or dispense pregabalin[1]

- continue to provide counselling to patients using pregabalin on:
  - the potential risks to an unborn baby (see separate patient safety leaflet[2])
  - the need to use effective contraception during treatment
- continue to avoid use of pregabalin during pregnancy unless clearly necessary and only if the benefit to the patient clearly outweighs the potential risk to the fetus – ensure the patient has a full understanding of the benefits, risks, and alternatives, and is part of the decision-making process
- advise patients planning a pregnancy or who become pregnant during treatment to make an appointment to discuss their health condition and any medicines they are taking

- in cases where the benefit outweighs the risk, and it is clearly necessary that pregabalin should be used during pregnancy, it is recommended to:
    - use the lowest effective dose
    - report any suspected adverse drug reactions, including for the baby, via the Yellow Card scheme[3]

Reminder for prescribers of ANY antiepileptic drug:

- at initiation and as part of the recommended annual review for patients with epilepsy, discuss the risks associated with antiepileptic drugs and with untreated epilepsy during pregnancy and review their treatment according to clinical condition and circumstances – see advice for antiepileptic drugs in pregnancy[4]
- urgently refer anyone planning a pregnancy or who is suspected to be pregnant for specialist advice on their antiepileptic treatment
- if a patient is planning to have a baby, offer 5mg per day of folic acid before any possibility of pregnancy

The Strategic Planning and Performance Group is asked to work with the Business Services Organisation to monitor the impact of this updated guidance through the examination of prescribing and dispensing data, focusing on trends in use of antiepileptic drugs in women of childbearing potential.

Overview

Pregabalin is indicated for the treatment of peripheral and central neuropathic pain in adults, as adjunctive therapy in adults with partial seizures with or without secondary generalisation, and for generalised anxiety disorder in adults.

An observational study of more than 2,700 pregnancies exposed to pregabalin has shown use in the first trimester to be associated with a slightly increased risk of major congenital malformations compared with exposure to no antiepileptic drugs or to lamotrigine or to duloxetine.

The advice in this letter is relevant for patients taking pregabalin who are pregnant or may become pregnant. Patients who are taking pregabalin should continue to use effective contraception during treatment and avoid use in pregnancy unless advised by a doctor.

If patients are planning a pregnancy or if think they may be pregnant, they should see their doctor to jointly decide the best course of action in their individual situation. It is important that patients talk to their doctor before stopping pregabalin or making any changes to their usual medicines. Untreated pain, anxiety, or epilepsy could be harmful to them and their unborn baby.

The MHRA will be actively maintaining the patient guidance and will review the need for any updates at 1 month, 6 months and 18 months (as is routine). If you have any further feedback, please send this to info@mhra.gov.uk where it will be reviewed by the assessment team.

Previous reviews of pregabalin in pregnancy

Following a national review into the safety of antiepileptic drugs in pregnancy, including pregabalin, in January 2021 the MHRA published new safety advice which was highlighted in HSS(MD) 14/2021.

At the time of publication, it was noted that due to conflicting data, no firm conclusions could be drawn on the potential teratogenic effect of pregabalin. This review included one US cohort study of 477 infants exposed to pregabalin in the first trimester, which did not show an increased risk after adjustment, but was unable to rule out a small effect on the rate of congenital malformations.[5] The review considered preliminary data from a study, from which further information and analyses have become available and evaluated.

At the time, the product information noted that the potential risk for humans in pregnancy was unknown. As such, patients were advised to use effective contraception and avoid pregabalin in pregnancy unless necessary.

New review of study of pregabalin in pregnancy

Fuller data is now available from a Nordic observational study of more than 2,700 pregnancies exposed to pregabalin in the first trimester.

The MHRA have carefully reviewed the results of the study alongside a recent European review of the same findings. The review concluded that pregabalin use during the first trimester of pregnancy may cause a slightly increased risk of major congenital malformations in the unborn child.

The MHRA has considered the recommendations of the European review, together with the other limited safety data available regarding pregabalin safety in pregnancy, and agreed that the product information should be updated to include information from this study. The Summary of Product Characteristics and Patient Information Leaflet for Pregabalin (Lyrica) has now been updated.

The product information continues to advise that effective contraception should be used during treatment and that use in pregnancy avoided unless clearly necessary.

Healthcare professionals are advised to consider MHRA guidance on contraceptive methods, and take into account the patient's personal circumstances when advising on contraception.

Detailed information on study and outcomes data is available at MHRA Drug Safety Update Pregabalin (Lyrica)

Antiepileptic medicines in pregnancy: new registry

The antiepileptic medicines in pregnancy registry has recently become operational in England. Consideration will be given to how this could be extended to the devolved nations in future phases of the project.

Further resources for prescribers

Clinicians should continue to use resources for prescribers about medicines of potential teratogenic effects. The UK Teratology Information Service provides independent advice about the risks and benefits of medicines use in pregnancy.

Report suspected reactions on a Yellow Card

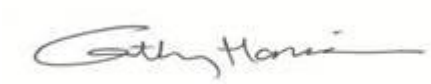
Please continue to report any suspected adverse drug reactions (ADRs) associated with pregabalin or any other medicines via the Yellow Card scheme.

Please report any suspected ADRs associated with medicines taken during pregnancy or breastfeeding, including any suspected effects on the baby or child.

All patients, caregivers, and healthcare professionals can report via the Yellow Card when they suspect a medication used during pregnancy has caused an adverse reaction or adverse pregnancy outcome.

Yours sincerely

Prof Sir Michael McBride
Chief Medical Officer



Mrs Cathy Harrison
Chief Pharmaceutical Officer

1. Medicines and Healthcare products Regulatory Agency 2022 2022. Drug Safety Update. Pregabalin (Lyrica): findings of safety study on risks during pregnancy. Available at: https://www.gov.uk/drug-safety-update/pregabalin-lyrica-findings-of-safety-study-on-risks-during-pregnancy
2. Medicines and Healthcare products Regulatory Agency 2022. Patient safety advice leaflet. Pregabalin and risks in pregnancy. Available at:https://www.gov.uk/government/publications/pregabalin-and-risks-in-pregnancy
3. Medicines and Healthcare products Regulatory Agency 2022. Yellow Card. Available at: https://yellowcard.mhra.gov.uk/
4. Department of Health 2021. HSS(MD) 14/2021 Safety of Antiepileptic drugs in pregnancy: Updated advice following comprensive safety review. Available at: https://www.health-ni.gov.uk/sites/default/files/publications/health/doh-hss-md-14-2021.pdf
5. Patorno E *et al*.2017. Neurology volume 88, p2020 to 2025. Pregabalin use early in pregnancy and the risk of major congenital malformations.

Circulation List

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