SAFETY ALERT

DRAP SAFTEY ALERT NO. 27

Risk of Major Congenital Malformations with Pregabalin

Date: 29th of November, 2022.

Target Audience:

- Manufacturers and importers of Pregabalin;
- Healthcare Professionals; and
- Patients, consumers or caregivers.

Background:

The Medicine and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom on 19th April, 2022 announced that the product information for pregabalin will be updated to include information from a new study which has suggested pregabalin may slightly increase the risk of major congenital malformations if used in pregnancy. The MHRA reviewed the results of a Nordic observational study that consisted of 2,700 pregnancies exposed to pregabalin in the first trimester, alongside a recent European review which had the same conclusions. The study showed a higher prevalence of major congenital malformations in the babies (live or stillborn) exposed to pregabalin in the first trimester of pregnancy compared with those not exposed to pregabalin or any other antiepileptic drug.

The review concluded that pregabalin's use during the first trimester of pregnancy may cause a slight increase in the risk of major congenital malformations in the unborn child. Furthermore, the Health Products Regulatory Authority (HPRA) of Ireland back in February 2022 also recommended that product information of Pregabalin along with other anti-epileptic drugs be updated based on the evidence of risks associated with in-utero exposure to these drugs. The product information of pregabalin continues to advise that effective contraception should be used

during treatment and that use in pregnancy should be avoided unless it is necessary.

Action in Pakistan:

Accordingly, the case of the risk of major congenital malformations with Pregabalin was discussed in the 1st meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the National Pharmacovigilance Centre (NPC), Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP). The PRAEC after detailed deliberation and discussion decided as per Rule 10 (1) (h) (iv) and (vi) of Pharmacovigilance Rules, 2022 (reliance mechanism) to update prescribing information of Pregabalin to include information from a new study that pregabalin may slightly increase the risk of major congenital malformations if used in pregnancy and include advise on effective contraception during treatment in pregnancy.

Therapeutic Goods Affected:

Name: **Pregabalin**

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 generalization, and for generalized anxiety disorder in adults.

Advice for patients:

Patients are advised to talk to their doctors before initiation of treatment with Pregabalin and discuss the benefit-risk of the medicine, particularly related to their case. Patients are also advised to talk with their healthcare professionals and use an appropriate contraception method during the treatment with Pregabalin to avoid pregnancy.

Advice for healthcare professionals:

A new study has demonstrated that pregabalin may slightly increase the risk of major congenital malformations if used in first trimester of pregnancy. Therefore, healthcare professionals should provide counselling to the patients on potential risks to an unborn baby with pregabalin and also on the need to use effective contraception during the treatment. Healthcare professionals are also advised to continue to avoid the use of pregabalin during pregnancy unless clearly necessary and only if the benefit to the patient clearly outweigh the potential risk to the fetus. In case where the benefit outweighs the risk, and it is clearly necessary that pregabalin has to used during the pregnancy, then the lowest effective dose should be used.

Guidelines for reporting of Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with Pregabalin to the National Pharmacovigilance Centre, Drug Regulatory Authority of Pakistan through Med Vigilance E-Reporting system available on the DRAP website. Similarly, ADRs can also be reported through MedSafety App which is available for download from App store (for iOS devices) and Google Play (for Android devices).

References:

1. Minutes of 1st meeting of Pharmacovigilance Risk Assessment Expert Committee of the DRAP.
2. Pregabalin (Lyrica): findings of safety study on risks during pregnancy of MHRA.

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