HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Updated Recommendations on the Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) During Pregnancy

Key Messages

The EMAs Pharmacovigilance Risk Assessment Committee (PRAC) has issued updated recommendations following a review of recently available data that indicates that from the 20th week of pregnancy onward, prolonged use of systemic NSAIDs may lead to oligohydramnios due to foetal renal dysfunction. Additionally, there have been reports of ductus arteriosus constriction following NSAID treatment during the second trimester, with most cases resolving after treatment cessation.

Systemic NSAIDs

- During the first and second trimesters of pregnancy, systemic NSAIDs (including fixed-dose combinations) should not be administered unless deemed clearly necessary.
- For women attempting to conceive or during the first and second trimesters, the dose should be kept as low as possible, and treatment duration should be minimised.
- Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to NSAIDs for several days from gestational week 20 onward. If oligohydramnios or ductus arteriosus constriction is detected, NSAID treatment should be discontinued promptly.
- If the product information already contains stricter advice regarding the use of NSAIDs during pregnancy, the stricter advice should be followed.
- Healthcare professionals are reminded that currently, the used of systemic NSAIDs is contraindicated in the last pregnancy trimester.

Topical NSAIDs

- The PRAC has recommended that the same precautions regarding the use, dosage, and duration of treatment for systemic NSAIDs be observed for topical NSAIDs.

Acetylsalicylic acid

- The PRAC has not issued these recommendations for acetylsalicylic acid-containing products at this time.

Background information

The EMA's PRAC has recommended that the approved product information* for systemic (i.e. oral and injectable) NSAID-containing medicinal products, including fixed-dose combinations, should be updated with regard to the use of these products during pregnancy. The updates follow the review of available data which concluded that the use from the 20th week of pregnancy onward may cause oligohydramnios resulting from foetal renal dysfunction. It was observed that this may occur shortly after treatment initiation and was usually reversible upon treatment discontinuation. Additionally, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation.

The PRAC recommendations for systemic NSAIDs during pregnancy

During the first and second pregnancy trimesters, systemic NSAIDs should not be given unless deemed clearly necessary. If the NSAID is deemed necessary, the dose should be kept as low and the duration of treatment as short as possible. This recommendation also applies to a woman attempting to conceive.

Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to NSAIDs for several days from gestational week 20 onward. The NSAID should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

While the product information for NSAIDs will be amended to include updated advice for use during pregnancy, when stricter advice on use in pregnancy already exists, the stricter advice will remain.

These new recommendations primarily concern the first and second pregnancy trimesters; currently, the use of systemic NSAIDs is contraindicated in the last trimester of pregnancy as they may induce foetal cardiopulmonary and renal toxicity, inhibit uterine contraction, leading to delayed or prolonged labour and possibly extend the bleeding time for mothers and neonates due to anti-aggregating effects that may occur even at very low doses.

New recommendations for topical NSAIDs in pregnancy

Following several routine reviews of available data concerning medicines within the same therapeutic class, the PRAC concluded that although systemic exposure with the use of topical NSAIDs (including oromucosal formulations and transdermal patches) is typically lower compared to oral administration, it could not definitively exclude the potential risk of oligohydramnios and ductus arteriosus to the embryo/foetus.

Consequently, to date the PRAC recommended updating the product information for several topical NSAIDs, including naproxen, ketoprofen, ibuprofen and flurbiprofen products. It is recommended to avoid the use of topical NSAID products during the first and second pregnancy trimesters unless deemed clearly necessary. If deemed necessary, the dosage should be kept as low and the treatment duration as short as possible. As is the case for systemic NSAIDs, use of topical NSAIDs is contraindicated during the last trimester of pregnancy.

Healthcare professionals are advised to check relevant product information when considering the use of topical NSAIDs during pregnancy, as it is already recommended to avoid certain topical NSAIDs, like ibuprofen, during pregnancy.

Implication for Acetylsalicylic Acid-containing Products

Due to the different clinical applications and dosages of acetylsalicylic acid-containing products, and the need to evaluate the available data and the implications of the NSAID recommendations, acetylsalicylic acid-containing products are currently excluded from the implementation of PRAC recommendations to date.

* The approved product information comprises the Summary of Product Characteristics (SmPC) and Package Leaflet (PL) and is available at www.hpra.ie.