Date: 11-12-2022

Direct Healthcare Professional Communication

Topiramate (IPRAMAX): Increased risk of neurodevelopmental disorders in infants whose mothers used topiramate during pregnancy

Dear Healthcare professional,

Tabuk Pharmaceuticals in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform About risk of neurodevelopmental disabilities in children whose mothers took Topiramate during pregnancy.

Summary:

- A large observational study that found a link between prenatal exposure to Topiramate and an increased risk of autism spectrum disorders, intellectual disability, and neurodevelopmental disorders.
- Pregnancy testing should be done prior to starting Topiramate in a woman of childbearing potential, and the patient should be fully informed of the hazards of using the Topiramate during Pregnancy.

Background on the safety concern:

Topiramate is used:

- Monotherapy in adults, adolescents and children over 6 years of age with partial seizures with or without secondary generalised seizures, and primary generalised tonic-clonic seizures.
- Adjunctive therapy in children aged 2 years and above, adolescents and adults with partial onset seizures with or without secondary generalization or primary generalized tonic-clonic seizures and for the treatment of seizures associated with Lennox-Gastaut syndrome.
- Ipramax is indicated in adults for the prophylaxis of migraine headache after careful evaluation of possible alternative treatment options. Topiramate is not intended for acute treatment.

The Nordic register-based study of antiepileptic drugs in pregnancy (SCAN-AED) is a population-based cohort including 4.5 million mother child pairs, the most important findings were robust and dose dependent associations between prenatal topiramate exposure and neurodevelopmental disorders. These associations persisted after accounting for potential confounding factors.

The results further demonstrated that prenatal exposure to several common antiseizure medication (ASM) dual therapies was associated with an increased risk of neurodevelopmental disorders within the same range as prenatal topiramate exposure, even without these ASMs being one of the drugs used. The population based cohort found a clear risk of adverse neurodevelopment in children exposed to topiramate, particularly at doses of 100 mg or more per day. Prenatal topiramate exposure is associated with an increased risk of being born small for gestational age, and with an increased risk of congenital malformations. High risks for congenital malformations have been associated with daily doses more than 100 mg. Few studies have assessed cognitive and behavioural child outcomes after prenatal topiramate exposure.

When appropriate, counsel pregnant women and women of childbearing potential about alternative therapeutic options is advisable. Women of childbearing potential who are not planning a pregnancy to use effective contraception while using topiramate, keeping in mind that there is a potential for decreased contraceptive efficacy when using estrogen-containing birth control with topiramate.

Please refer to Ipramax® Patient information leaflet for complete prescribing information,

The information in this letter has been approved by the Saudi Food and Drug Authority (SFDA).

References:

- https://jamanetwork.com/journals/jamaneurology/fullarticle/2793003
- Nationwide cohort study in France. Sci Rep. 2020;10(1):17362. doi:10.1038/s41598-020-74409-x
- https://www.ema.europa.eu/en/news/prac-starts-review-topiramate-usepregnancy-women-childbearing-potential

Call for reporting for adverse reactions:

Reporting suspected adverse reactions is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

Saudi Food and Drug Authority, National Pharmacovigilance Center:
Unified Contact Center: 19999
Toll Free Number: 80024900000
Email: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

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