This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Topiramate

February 15, 2024

Non-proprietary name

Topiramate

Brand name (marketing authorization holder)

Topina Tablets 25 mg, 50 mg, 100 mg, Topina Fine Granules 10% (Kyowa Kirin Co., Ltd.), and the others

Japanese market launch

Tablets 25 mg: October 2010

Tablets 50mg, 100 mg: September 2007

Fine Granules 10%: May 2014

Indications

Concomitant therapy with other antiepileptic drugs for partial seizures (including secondary generalized seizures) in epileptic patients who are not sufficiently responsive to other antiepileptic drugs

Summary of revisions

1. The Patients with Reproductive Potential section of PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS should be newly added, and a precautionary statement should be added that the patients should be fully informed of the risks that may occur in infants/children born to topiramate-exposed mothers when this drug is used in women of child-bearing potential.
2. The following precautions should be added to the Pregnant Women section of PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS.

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1) When this drug is used during pregnancy, or when the women become pregnant while on treatment with this drug, the patients should be fully informed of the risks that may occur in infants/children born to topiramate-exposed mothers.
2) There may be a possible relationship between the infants/children born to topiramate-exposed mothers and the occurrence of neurodevelopmental disorder (autism spectrum disorder, intellectual development disorder, and attention deficit hyperactivity disorder).

Investigation results and background of the revision

The overseas epidemiological literature concerning neurodevelopmental disorder in infants/children born to topiramate-exposed mothers during pregnancy was evaluated. Overseas observational studies (JAMA Neurol. 2022;79:672-681, JAMA Neurol. 2023;80:568-577) suggested the possible occurrence of neurodevelopmental disorder in infants/children born to topiramate-exposed mothers during pregnancy. As a result of consultation with expert advisors regarding the relevant literature and the necessity of revision of PRECAUTIONS, taking into account the possible occurrence suggested in the studies, the MHLW/PMDA concluded that revising PRECAUTIONS was appropriate since it is necessary to issue precautions that the patients should be fully informed of the risks in infants/children born to topiramate-exposed mothers, including precautions for the occurrence of neurodevelopmental disorder (autism spectrum disorder, intellectual development disorder, and attention deficit hyperactivity disorder) and precautions for teratogenicity that had already been included in the PRECAUTIONS.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).