European Medicines Agency

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Questions and answers on the referral for Topamax and associated names topiramate tablets and capsules

The European Medicines Agency has completed a review of Topamax and associated names. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that there is a need to harmonise the prescribing information for Topamax and associated names in the European Union (EU) and the European Economic Area (EEA).
The review was carried out under an 'Article 30' referral[1].

What is Topamax?

Topamax is an antiepileptic medicine. It is used as monotherapy (on its own) or as adjunctive therapy (together with other medicines) to prevent seizures (epileptic fits). Topamax is also used to prevent migraine headaches.
The exact way in which topiramate, the active substance in Topamax, works is unknown but it is thought to act by interfering with the activity of receptors on nerve cells, which leads to a reduction in electrical transmission. Because these cells are involved in causing seizures and in migraines, reducing their electrical activity helps to reduce the chance of having a seizure or developing a migraine.
Topamax is also available in the EU under other trade names: Topimax, Epitomax, Topiramat-Cilag, Topiramat-Janssen, Topamax Migräne and Topamac. It is available as tablets (25 mg, 50 mg, 100 mg and 200 mg) and capsules (15 mg, 25 mg and 50 mg).
The company that markets Topamax is Johnson & Johnson Pharma R & D.

Why was Topamax reviewed?

Topamax and associated names have been authorised in the EU via national procedures. This has led to divergences across Member States in the way the medicine can be used, as seen in the differences in the Summaries of Product Characteristics (SPCs), labelling and package leaflets in the different countries where the product is marketed. Topamax has been identified as needing harmonisation by the Co-ordination Group on the Mutual Recognition and Decentralised Procedures – Human (CMD(h)). On 8 May 2008, the European Commission referred the matter to the CHMP in order to harmonise the marketing authorisations for Topamax and associated names in the EU and the EEA.

What are the conclusions of the CHMP?

The CHMP, in the light of the data submitted and the scientific discussion within the Committee, was of the opinion that the SPCs, labelling and package leaflets should be harmonised across the EU.

The areas harmonised include:

4.1 Therapeutic indications

The CHMP agreed on a harmonised wording for the indications:

[1] Article 30 of Directive 2001/83/EC as amended, referral on the grounds of divergent decisions adopted by Member States

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- '*monotherapy in adults, adolescents and children over six 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 for 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;*
- *in adults for the prophylaxis of migraine headache after careful evaluation of possible alternative treatment options. Topiramate is not intended for acute treatment.*'

The CHMP had considered all available evidence and the various indications already authorised in different Member States. The main differences concerned the age of children that can be given Topamax, and the medicine's use in monotherapy and conversion to monotherapy. The CHMP removed a restriction that was present in some Member States that Topamax monotherapy be used for only newly diagnosed epilepsy.

4.2 Posology and method of administration

Epilepsy
For monotherapy in adults the CHMP recommended 100 mg to 200 mg a day as the initial dose and a maximum daily dose of 500 mg a day, divided into two doses. The Committee also recommended the initial dose of 100 mg in children aged six years and above.
For adjunctive therapy, the Committee endorsed a dose range for adults of 200 to 400 mg a day, divided into two doses. For children aged two years and above, the Committee recommended a dose of 5 to 9 mg per kilogram body weight a day, divided into two doses.

Migraine
For prevention of migraine in adults, the Committee recommended a total daily dose of 100 mg, divided into two doses. The initial dose should be of 25 mg a day for one week followed by weekly increases of 25 mg until a beneficial dose is reached.

4.3 Contra-indications

The CHMP agreed on a harmonised wording for the contra-indications. Patients who may be hypersensitive (allergic) to the active substance or to any of the other ingredients should not take Topamax.
The Committee did not include a contraindication for the use of Topamax for treating epilepsy in pregnant women or women of childbearing potential who are not using effective methods of contraception. Advice was included in section 4.6 of the SPC about the risks to the mother and the unborn baby of treatment with Topamax.

Other changes

The CHMP harmonised the SPC section on special warnings and included warnings about mood disturbances and depression, suicide and suicidal ideation, and metabolic acidosis (increased acid levels in the body).
The Committee also harmonised the SPC section on the interactions of Topamax with other medicines. The new wording highlights the possibility of reduced effectiveness of oral contraceptives in patients taking Topamax.
The amended information to doctors and patients is available here.

The European Commission issued a decision on 1 October 2009.

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