
Part VI: Summary of the risk management plan

Summary of risk management plan for Topiramate (Topiramate)

This is a summary of the risk management plan (RMP) for Topiramate. The RMP details important risks of Topiramate, how these risks can be minimised, and how more information will be obtained about Topiramate's risks and uncertainties (missing information).

Topiramate 's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Topiramate should be used.

Important new concerns or changes to the current ones will be included in updates of Topiramate 's RMP.

I. The medicine and what it is used for

Topiramate is authorised for

- partial seizures with or without secondary generalised seizures and primary generalised tonic-clonic seizures.
- partial onset seizures with or without secondary generalization or primary generalised tonic-clonic seizures and for the treatment of seizures associated with Lennox-Gastaut Syndrome
- the prophylaxis of migraine headache after careful evaluation of possible alternative treatment options (see SmPC for the full indication).

It contains Topiramate as the active substance and it is given by oral route of administration.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Topiramate, together with measures to minimise such risks and the proposed studies for learning more about Topiramate 's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Topiramate, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of important risks and missing information

Important risks of Topiramate are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Topiramate. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	<ul style="list-style-type: none"> • Acute myopia and secondary angle-closure glaucoma • Metabolic acidosis • Suicide/suicide ideation • Major congenital malformations with use during pregnancy • Foetal growth restrictions
Important potential risks	<ul style="list-style-type: none"> • Neurodevelopmental disorders in children exposed to topiramate in utero
Missing information	<ul style="list-style-type: none"> • None

II.B Summary of important risks

Important identified risk: Major congenital malformations with use in pregnancy	
Risk minimisation measures	<p>Routine risk minimisation measures:</p> <p>SmPC section 4.2, 4.3, 4.4, 4.5, 4.6, and 4.8.</p> <p>PL section 2</p> <p>Visible warning on outer packaging</p> <p>Legal status: medicinal product restricted to medical prescription only</p> <p>Additional risk minimisation measures:</p> <p>– Educational materials</p>

Important identified risk: Major congenital malformations with use in pregnancy	
	<ul style="list-style-type: none"> - Healthcare Professional Guide Including a Risk Awareness Form - Patient Guide • Patient Card • Direct Healthcare Professional Communication (DHPC) with Communication Plan
Additional pharmacovigilance activities	<p>Additional pharmacovigilance activities:</p> <p>Short study name:</p> <ul style="list-style-type: none"> - PCSESPA0008 - PCSESPA0009 <p>See section II.C of this summary for an overview of the post-authorisation development plan.</p>

Important identified risk: Fetal growth restrictions	
Risk minimisation measures	<p>Routine risk minimisation measures:</p> <p>SmPC sections 4.2, 4.3, 4.4, 4.5 and 4.6</p> <p>PL Section 2</p> <p>Visible warning on outer packaging</p> <p>Legal status: medicinal product restricted to medical prescription only</p> <p>Additional risk minimisation measures:</p> <ul style="list-style-type: none"> - Educational materials - Healthcare Professional Guide Including a Risk Awareness Form - Patient Guide

Important identified risk: Fetal growth restrictions	
	<ul style="list-style-type: none"> • Patient Card • Direct Healthcare Professional <p>Communication (DHPC) with Communication Plan</p>
Additional pharmacovigilance activities	<p>Additional pharmacovigilance activities:</p> <p>Short study name:</p> <ul style="list-style-type: none"> – PCSESPA0008 – PCSESPA0009 <p>See section II.C of this summary for an overview of the post-authorisation development plan.</p>

Important potential risk: Neurodevelopmental disorders (NDDs) associated with in utero exposure to topiramate	
Risk minimisation measures	<p>Routine risk minimisation measures:</p> <p>SmPC sections 4.2, 4.3, 4.4, 4.5 and 4.6</p> <p>PL Section 2 Visible warning on outer packaging</p> <p>Legal status: medicinal product restricted to medical prescription only</p> <p>Additional risk minimisation measures:</p> <ul style="list-style-type: none"> – Educational materials - Healthcare Professional Guide Including a Risk Awareness Form - Patient Guide • Patient Card • Direct Healthcare Professional <p>Communication (DHPC) with Communication Plan</p>
Additional pharmacovigilance activities	<p>Additional pharmacovigilance activities:</p> <p>Short study name:</p> <ul style="list-style-type: none"> – PCSESPA0008

Important potential risk: Neurodevelopmental disorders (NDDs) associated with in utero exposure to topiramate	
	<p>– PCSESPA0009</p> <p>See section II.C of this summary for an overview of the post-authorisation development plan.</p>

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

The following two joint Post-Authorization Safety Studies studies are conditions of the marketing authorisation:

Study short name and title:

Protocol PCSESPA0009: Post-Authorization Safety Study to Assess the Effectiveness of the Newly Implemented Risk Minimization Measures for Topiramate: Drug Utilization Study.

Purpose of the study: The study aims to describe the prevalence and the incidence of topiramate use among WOCBP with epilepsy or migraine during the pre- and post-implementation of the newly implemented RMMs. In addition, the study aims to quantify exposure to topiramate during pregnancy among incident users of topiramate at two critical points: (1) being pregnant at treatment initiation, and (2) becoming pregnant during treatment. In addition, the study aims to determine the effectiveness of the newly implemented risk minimization measures to reduce exposure to topiramate during pregnancy and for at least 4 weeks after discontinuing treatment with topiramate.

Study short name and title:

PCSESPA0008: Post-Authorization Safety Study to Assess the Effectiveness of the Newly Implemented Risk Minimization Measures for Topiramate: HCP and Patient Knowledge and Behavior Survey.

Purpose of the study: This cross-sectional, multinational, non-interventional survey aims to evaluate the effectiveness of additional risk minimisation measures (RMMs) for topiramate mono-component products in five European countries. The study assesses awareness, knowledge, and self-reported behaviours among women of childbearing potential (WOCBP) treated with topiramate and healthcare professionals (HCPs), including prescribers, pharmacists, and obstetric/gynecological care providers. Specifically, it evaluates receipt of educational materials and Direct Healthcare Professional Communications, understanding of the teratogenic risks associated with topiramate use during pregnancy, and implementation of measures to prevent exposed pregnancies. The findings will inform the adequacy of current RMMs and identify potential gaps in risk communication and adherence.

II.C.2 Other studies in post-authorisation development plan

Not applicable.