Summary of risk management plan for Topiramat Orion 25 mg, 50 mg, 100 mg, 200 mg film-coated tablet (Topiramate)

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

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

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

I. The medicine and what it is used for

Topiramat Orion is authorized for the following indications:

• 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 as monotherapy.

• In children aged 2 years and above, adolescents and adults with 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 as adjunctive therapy.

• In adults for the prophylaxis of migraine headache after careful evaluation of possible alternative treatment options. Topiramate is not intended for acute treatment.

It contains topiramate as the active substance and it is given by mouth.

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

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

Measures to minimise the risks identified for Topiramat Orion are:

- Specific information, such as warnings, precautions, and advice on correct use, in the SmPC and PL addressed to healthcare professionals (HCP) and patients;
- Visual text warning on the outer packaging and in certain countries also pictogram may be added on the outer packaging;
- The medicine's legal status — the way a medicine is supplied to the patient

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

In the case of Topiramat Orion, 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 Topiramat Orion 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 Topiramat Orion. 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);

Summary of safety concerns	
Important identified risks	Major congenital malformations with use during pregnancy Fetal growth restriction with use during pregnancy
Important potential risks	Neurodevelopmental disorders in children exposed to topiramate in utero
Missing information	None

II.B Summary of important risks

The safety information in the proposed product information is aligned to the originator/reference medicinal product.

Important identified risk: Major congenital malformations with use during pregnancy	
Evidence for linking the risk to the medicine	Pharmacovigilance data (clinical and postmarketing data), and worldwide scientific literature.
Risk factors and risk groups	<u>Population at risk:</u> Pregant women and women of childbearing potential exposed to topiramate
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Information in SmPC sections 4.2, 4.3, 4.4, 4.5, 4.6 and 4.8. A text warning on the outer package including a text warning and in certain countries also a pictogram. Prescription only medicine. <u>Additional risk minimisation measures:</u> A Pregnancy Prevention Programme (PPP) which combines the use of educational tools with interventions to minimize pregnancy exposure during treatment with topiramate. The educational materials: • Guide for HCPs including a risk awareness form • Guide for Patients • Patient Card
Additional pharmacovigilance activities	<u>Additional pharmacovigilance activities:</u> Drug Utilization Study to evaluate the effectiveness of the risk minimisation measures with a particular focus on preventing pregnancies and on further characterising the prescribing patterns for topiramate in the target populations for pregnancy prevention. Survey among HCPs to assess the knowledge and behaviour of HCPs with regard to the measures to be taken to prevent pregnancies as well as receipt/use of DHPC and educational materials. Survey among patients to assess the knowledge of patients with regard to the risks of topiramate use during pregnancy and the measures implemented to prevent pregnancy as well as receipt/use of educational materials.

Important identified risk: Fetal growth restriction with use during pregnancy	
Evidence for linking the risk to the medicine	Pharmacovigilance data (clinical and postmarketing data), and worldwide scientific literature.
Risk factors and risk groups	<u>Population at risk:</u> Pregant women and women of childbearing potential exposed to topiramate
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Information in SmPC sections 4.2, 4.3, 4.4, 4.5, 4.6 and 4.8. A text warning on the outer package including a text warning and in certain countries also a pictogram. Prescription only medicine. <u>Additional risk minimisation measures:</u> A Pregnancy Prevention Programme (PPP) which combines the use of educational tools with interventions to minimize pregnancy exposure during treatment with topiramate. The educational materials: • Guide for HCPs including a risk awareness form • Guide for Patients • Patient Card
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Important potential risk: Neurodevelopmental disorders in children exposed to topiramate in utero	
Evidence for linking the risk to the medicine	Pharmacovigilance data (clinical and postmarketing data) and worldwide scientific literature.
Risk factors and risk groups	<u>Population at risk:</u> Pregant women and women of childbearing potential exposed to topiramate
Risk minimisation measures	<u>Routine risk minimisation measures:</u> Information in SmPC sections 4.2, 4.3, 4.4, 4.5 and 4.6. A text warning on the outer package. Prescription only medicine <u>Additional risk minimisation measures:</u> A Pregnancy Prevention Programme (PPP). It combines the use of educational tools with interventions to minimize pregnancy exposure during treatment with topiramate. The educational materials: • Guide for HCPs including a risk awareness form • Guide for Patients • Patient Card
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II.C Post-authorisation development plan

The following studies are conditions of the marketing authorization:

Drug utilization study
Purpose of the study To evaluate the effectiveness of the risk minimisation measures with a particular focus on preventing pregnancies and on further characterising the prescribing patterns for topiramate in the target populations for pregnancy prevention.
Survey among heathcare professionals
Purpose of the study To assess the knowledge and behaviour of healthcare professionals (HCPs) with regard to the measures to be taken to prevent pregnancies as well as receipt/use of DHPC and educational materials.
Survey among patients
Purpose of the study To assess the knowledge of patients with regard to the risks of topiramate use during pregnancy and the measures implemented to prevent pregnancy as well as receipt/use of educational materials.