Summary of Risk Management Plan for Sativex® (Delta-9-tetrahydrocannabinol [THC] and cannabidiol [CBD])

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Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of Sativex is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Sativex in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic.

Almirall AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Sativex.

Summary of Risk Management Plan for Sativex (Delta-9-tetrahydrocannabinol [THC] and cannabidiol [CBD])

This is a summary of the Risk Management Plan (RMP) for Sativex. The RMP details important risks of Sativex, risk minimisation measures, and how more information will be obtained about Sativex's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Sativex is authorised for treatment of moderate to severe spasticity due to multiple sclerosis (MS) (see SmPC for the full indication). Sativex is a complex botanical drug product for oromucosal use. The drug substance in Sativex is a mixture of cannabinoids, the most abundant being THC and CBD derived from *Cannabis sativa* L plants.

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

Important risks of Sativex, together with measures to minimise such risks and the proposed studies for learning more about Sativex'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 (PL) 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 (eg, with or without prescription) can help to minimise its risks.

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

If important information that may affect the safe use of Sativex is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Sativex 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 Sativex. 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 (eg, on the long-term use of the medicine).

Important identified risks	Suicide and suicidal behaviour
Important potential risks	Misuse for illegal purposes, abuse liability, addiction, tolerance, and withdrawal syndromes
Missing information	Limited experience of the effect of Sativex on human pregnancy and lactation

II.B Summary of important risks

Important Identified Risk 1: Suicide and Suicidal Behaviour	
Evidence for linking the risk to the medicine	There is very limited if any evidence within the available clinical trial and post-marketing data to suggest that Sativex increases the risk of suicide in patients with MS when compared to the co-morbidity already present in the MS population.
Risk factors and risk groups	Patients with major depression and history of pre-existing suicide attempt or suicidal thoughts. Patients with more disability from the MS symptoms are at higher risk of suicidality than patients with less disability.
Risk minimisation measures	Routine risk minimisation measures: Information for Professionals section 'Dosage/Administration' Information for Professionals section 'Contraindications' Information for Professionals section 'Warnings and Precautions' Specific clinical measures: Information for Professionals section 'Dosage/Administration', advises that treatment must be initiated and supervised by a physician with specialist expertise in treating this patient population. Information for Professionals section 'Warnings and Precautions', recommends to stop Sativex immediately and monitor patient until the suicidal ideation has completely resolved Pack size: None Legal status: Restricted medical prescription Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None See Section II.C of this summary for an overview of the post-authorisation development plan.

Important Potential Risk 1: Misuse for Illegal Purposes, Abuse Liability, Addiction, Tolerance, and Withdrawal Syndromes	
Evidence for linking the risk to the medicine	This risk was identified in the clinical trial setting in a specifically designed trial to study the abuse potential of Sativex. This showed some abuse potential evidence at high doses, but Sativex was not taken how it is recommended in the SmPC and package leaflet.
Risk factors and risk groups	Patients who have a history of substance abuse, may be more prone to abuse Sativex.
Risk minimisation measures	Routine risk minimisation measures: Information for Professionals section 'Dosage/Administration' Information for Professionals section 'Warnings and Precautions' Specific clinical measures: Information for Professionals section 'Dosage/Administration', advises that treatment must be initiated and supervised by a physician with specialist expertise in treating this patient population Pack size: None Legal status: Restricted medical prescription Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing Information: Limited Experience of the Effect of Sativex on Human Pregnancy and Lactation	
Risk minimisation measures	Routine risk minimization measures: Information for Professionals section 'Contraindications' Information for Professionals section 'Pregnancy, lactation' Information for Professionals section 'Preclinical data' Specific clinical measures: Information for Professionals section 'Pregnancy, lactation', advises that men and women of child-bearing potential should take reliable contraceptive precautions for the duration of the therapy and for three months after discontinuation of therapy. Patients on hormonal contraceptives are advised to use an additional alternative, non-hormonal/reliable barrier method of birth control during Sativex therapy. Pack size: None Legal status: Restricted medical prescription Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None See Section II.C of this summary for an overview of the post-authorisation development plan.

Abbreviations: MS = multiple sclerosis; PL = package leaflet; SmPC = summary of product characteristics.

II.C Post-authorisation development plan

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

There are no studies which are conditions of the marketing authorisation or specific obligation of Sativex.

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

There are no other studies in the post-authorisation development plan for Sativex.