Saphnelo®

Concentrate for solution for infusion
300 mg/2 ml (150 mg/ml)

Summary of the Risk Management Plan (RMP) for Saphnelo® (anifrolumab)

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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 Saphnelo® 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 Saphnelo® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. AstraZeneca AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Saphnelo®.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR ANIFROLUMAB

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

Anifrolumab's SmPC give essential information to healthcare professionals and patients on how anifrolumab should be used.

This summary of the RMP for anifrolumab should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report.

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

I.1 THE MEDICINE AND WHAT IT IS USED FOR

The indication of anifrolumab is as an add-on therapy for the treatment of adult patients with moderate to severe systemic lupus erythematosus, in addition to standard therapy (see SmPC for full indication). It contains anifrolumab as the active substance and is administered as an IV infusion.

I.2 RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of anifrolumab, together with measures to minimise such risks and the proposed studies for learning more about anifrolumab'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 SmPC addressed to 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.

Information about adverse reactions is collected continuously and regularly analysed, including in the Periodic Safety Update Report, 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 anifrolumab is not yet available, it is listed under 'missing information' below.

I.2.1 List of important risks and missing information

Important risks of anifrolumab are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 anifrolumab. 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).

Table 1 List of important risks and missing information

Important Potential Risks	Malignancy Serious infection
Missing Information	Use in pregnant and breastfeeding women
	Effects on responses to inactivated vaccines

I.2.2 Summary of important risks

Table 2 Important potential risk: Malignancy

Evidence for linking the risk to the medicine	There is a plausible mechanism of action for how anifrolumab may increase the risk of developing malignancy.
Risk factors and risk groups	Patients with SLE are reported to have an increased risk of haematologic malignancies, particularly non-Hodgkin's lymphoma and leukaemia. In addition, increased risks of cancer of the vulva, lung, thyroid, and possibly liver were suggested (**Fehler! Verweisquelle konnte nicht gefunden werden.**). Female patients with SLE also have an increased risk of developing abnormal cervical cytology and squamous intraepithelial lesions.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section Warnings and precautions
Additional pharmacovigilance activities	Study D3461R00046 - A non-interventional multi-country post-authorisation safety study (PASS) to assess the incidence of serious infections & malignancies in systemic lupus erythematosus (SLE) patients exposed to anifrolumab.

SLE Systemic lupus erythematosus; SmPC Summary of Product Characteristics.

Table 3 Important potential risk: Serious infection

Evidence for linking the risk to the medicine	Due to the mechanism of action of anifrolumab, it is plausible that anifrolumab may increase the risk of developing certain serious infections. However, the incidence of serious infection was similar between treatment groups in the controlled Phase II and Phase III clinical studies.
Risk factors and risk groups	The risk factors for serious infection in patients treated with anifrolumab are unknown. Infection is a risk of prolonged immunosuppression and high-dose corticosteroid therapy in patients with SLE, even in the absence of other impairments of host defences. Infection is one of the most common causes of morbidity and mortality among patients with SLE and may contribute to disease exacerbations (**Fehler! Verweisquelle konnte nicht gefunden werden.**). The probability of developing a given disease depends on the risk for exposure to potential pathogens, the virulence of the pathogen, and the level of immunosuppression of the patient.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section Warnings and precautions
Additional pharmacovigilance activities	Study D3461R00046 - A non-interventional multi-country post-authorisation safety study (PASS) to assess the incidence of serious infections & malignancies in systemic lupus erythematosus (SLE) patients exposed to anifrolumab.

SLE Systemic lupus erythematosus; SmPC Summary of Product Characteristics.

Table 4 Missing information: Use in pregnant and breastfeeding women

Risk minimisation measures	Routine risk minimisation measures: SmPC Section Pregnancy, lactation
Additional pharmacovigilance activities	D3461R00028 - A Non-Interventional Multi-Database Post Authorisation Study to Assess Pregnancy-Related Safety Data from Women with SLE Exposed to Anifrolumab

SLE Systemic lupus erythematosus; SmPC Summary of Product Characteristics.

Table 5 Missing information: Effects on responses to inactivated vaccines

Risk minimisation measures	Routine risk minimisation measures: SmPC Sections Warnings and precautions and Interactions
Additional pharmacovigilance activities	D3461C00023 - Nature of anifrolumab impact on vaccine-emergent immunity in patients with moderately to severely active systemic lupus erythematosus: A multi-centre open label parallel group trial: The NAÏVE study.

SmPC Summary of Product Characteristics.

I.2.3 Post-authorisation development plan

I.2.3.1 Studies that are conditions of the marketing authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of anifrolumab.

I.2.3.2 Other studies in post-authorisation development plan

Anifrolumab pregnancy study (D3461R00028)

Study title: Retrospective Pregnancy Study, A Non-Interventional Multi-Database Post Authorisation Study to Assess Pregnancy-Related Safety Data from Women with SLE Exposed to Anifrolumab.

Purpose of the study: Systemic lupus erythematosus affects a high proportion of women of child-bearing potential age. However, there is limited information on pregnancy and birth outcomes in women who are exposed to anifrolumab during pregnancy.

The aim of this study is to describe the congenital malformations, adverse pregnancy and birth outcomes in pregnancies/offspring from women with moderate/severe SLE exposed to anifrolumab during pregnancy and to compare with outcomes in women with moderate/severe SLE who are exposed to other SOC but not anifrolumab. Adverse outcomes related to infant growth up to one year of age will also be investigated.

Anifrolumab serious infections and malignancy study (D3461R00046)

Study title: A non-interventional multi-country post-authorisation safety study (PASS) to assess the incidence of serious infections & malignancies in systemic lupus erythematosus (SLE) patients exposed to anifrolumab.

Purpose of the study: In the absence of sufficient data from clinical studies to determine the risk of malignancy and serious infections among moderate/severe SLE patients exposed to anifrolumab, AstraZeneca will conduct a PASS to compare the risk of serious infections and malignancies, separately, in a population of patients receiving treatment with anifrolumab and a comparable population of SLE patients receiving standard therapy.

This is an observational study, in which the main research question is to evaluate the risk of malignancies and serious infections among moderate/severe SLE patients who receive anifrolumab compared with a comparable population of moderate/severe SLE patients on SOC who do not initiate anifrolumab. To address this research question, 2 study cohorts will be defined - one for the evaluation of malignancy outcomes and the other for the evaluation of serious infection outcomes.

The NAÏVE study (D3461C00023)

Study title: Nature of anifrolumab impact on vaccine-emergent immunity in patients with moderately to severely active Systemic Lupus Erythematosus: A multi-centre open label parallel group trial.

Purpose of the study: To better understand the impact of anifrolumab on vaccination responses, including measuring antibody concentrations; an external partner (Oklahoma Medical Research Foundation) is conducting a study.

The study has the following objectives:

- To compare induction of influenza immunity after receipt of a currently recommended quadrivalent flu shot in 2 groups of patients who enter the trial with moderately to severely active SLE, 10 having initiated anifrolumab at baseline in addition to standard of care, and 10 receiving only standard of care.
- To evaluate the safety and tolerability of influenza vaccine given with or without anifrolumab treatment.