Swiss Summary of the Risk Management Plan (RMP)

Lyfnua®

(Gefapixant Tablet)

Active substance(s): Gefapixant

Product(s) concerned: LYFNUA®

Based on EU-RMP V0.3 and Swiss RMP Annex V1.0

Version 1.0 (June 2022)

Marketing Authorisation Holder: MSD Merck Sharp & Dohme AG, Lucerne

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 Lyfnua® 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 Lyfnua® in Switzerland is the «Arzneimittelinformation/ Information sur le médicament» (see www.swissmedic.ch) approved and authorized by Swissmedic. MSD Merck Sharp and Dohme AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Lyfnua®.

Summary of risk management plan for LYFNUA®

This is a summary of the RMP for LYFNUA. The RMP details important risks of LYFNUA, how these risks can be minimised, and how more information will be obtained about risks and uncertainties (missing information) of LYFNUA. The SmPC for LYFNUA and its package leaflet give essential information to healthcare professionals and patients on how gefapixant should be used.

This summary of the RMP for LYFNUA 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 (EPAR).

Important new concerns or changes to the current ones, will be included in updates of the RMP for LYFNUA.

I. The Medicine and What it is Used For

LYFNUA is authorised for the treatment of refractory or unexplained chronic cough (see SmPC for the full indication). It contains gefapixant as the active substance and it is given by oral administration.

Further information about the evaluation of benefits of LYFNUA can be found in the EPAR for LYFNUA, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of LYFNUA, together with measures to minimise such risks and the proposed studies for learning more about the risk of LYFNUA, 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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) assessment 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 LYFNUA 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 gefapixant. 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).

Table II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	Progression of respiratory tract infections and risk of development of pneumonia Sensory neuropathies and trophic disturbances
Missing information	Use in patients with comorbid obstructive sleep apnoea Use in pregnancy and lactation Long-term safety

II.B Summary of Important Risks

Table II.B.1: Progression of respiratory tract infections and risk of development of pneumonia

Evidence for linking the risk to the medicine	Gefapixant is a first in class molecule for the treatment of RCC and UCC in adults. The indications for use, warnings and precautions, and the safety profile of LYFNUA are well described in the SmPC. While there is no mechanistic or clinical evidence indicating a risk of progression of respiratory tract infections and risk of development of pneumonia, this risk is included as potentially important recognizing that gefapixant is a first in class molecule and that further characterization of this important potential risk would be helpful.
Risk factors and risk groups	Individuals with chronic cough experience a higher incidence of pneumonia, as well as, upper and lower respiratory infections, than individuals without chronic cough.
Risk minimisation measures	Routine risk minimisation measures

Table II.B.2: Sensory neuropathies and trophic disturbances

Evidence for linking the risk to the medicine	Gefapixant is a first in class molecule for the treatment of RCC and UCC in adults. The indications for use, warnings and precautions, and the safety profile of LYFNUA are well described in the SmPC. It is the opinion of Swissmedic, that based on the postulated mechanism of action by ATP inhibition and the observed safety profile in the clinical trial

	program with taste-related AEs, oral hypoesthesia, oral paraesthesia and dry mouth, that sensory neuropathies and trophic disturbances are potential safety concerns and that further characterization is needed.
Risk factors and risk groups	Taste-related AEs (dysgeusia, ageusia, hypogeusia, taste disorder, and hypergeusia) are the most frequently reported adverse events (65.4%) reported in patients treated with gefapixant 45 mg BID. However, there is no evidence of a postulated mechanism that gefapixant inhibits all ATP-mediated danger signals of sensory neurons, and no risk factors or risk groups have been identified.
Risk minimisation measures	Routine risk minimisation measures

II.C Summary of Missing Information

Table II.C.1: Use in patients with obstructive sleep apnoea

Risk minimisation measures	Routine risk minimsation measures

Table II.C.2: Use in pregnancy and lactation

Risk minimisation measures	Routine risk minimisation measures

Table II.C.3: Long-term safety

Risk minimisation measures	Routine risk minimisation measures

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 LYFNUA.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for LYFNUA.