Summary of Risk Management Plan for Lumykras™ (Sotorasib)

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

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

This summary of the RMP for Lumykras should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of 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 Lumykras's RMP.

I. The medicine and what it is used for

Lumykras is authorized as monotherapy for the treatment of adult patients with previously treated Kirsten rat sarcoma viral oncogene homolog *(KRAS) G12C*-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC)] (see SmPC for the full indication). It contains sotorasib as the active substance and it is given orally.

Further information about the evaluation of Lumykras's benefits can be found in Lumykras's EPAR, including in its plain-language summary, available on the EMA webpage:

https://www.ema.europa.eu/en/medicines/human/EPAR/lumykras

II. Risks associated with the medicine and activities to minimize or further characterize the risks

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

Measures to minimize 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 authorized 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 public (eg, with or without prescription) can help to minimize its risks.

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

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed including PSUR assessment 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 Lumykras is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Lumykras are risks that need special risk management activities to further investigate or minimize 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 Lumykras. 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).

List of important risks and missing information	
Important identified risks	None
Important potential risks	None
Missing information	Use in patients with hepatic impairment

II.B. Summary of Important Risks

Important Missing information: Use in patients with hepatic impairment	
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.2 • SmPC Section 5.2 • PL Section 2 • PL Section 4 Routine risk minimization activities recommending specific clinical measures to address the risk: • None Other risk minimization measures beyond the Product Information (PI): • Medicine's legal status: Medicinal product subject to restricted medical prescription Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Study 20200362 See Section II.C of this summary for an overview of the postauthorization development plan.

II.C. Postauthorization Development Plan

II.C.1. Studies Which Are Conditions of the Marketing Authorization

The following studies are conditions of the marketing authorization.

Study Short Name	Purpose of the Study
Study 20190009 A phase 3, multicenter, randomized, open-label, active-controlled study of AMG 510 versus docetaxel for the treatment of previously treated locally advanced and unresectable or metastatic NSCLC subjects with mutated *KRAS p.G12C*	Primary Objectives: • To compare the efficacy of AMG 510 versus docetaxel as assessed by progression-free survival (PFS) in previously treated subjects with *KRAS p.G12C* mutated non-small cell lung cancer (NSCLC) Key Secondary Objectives: • To compare the efficacy of AMG 510 versus docetaxel as assessed by: – Overall Survival (OS) – Objective response rate (ORR) • To compare patient reported outcomes (PRO) as assessed by: – European Organization for Research and Treatment of Cancer Quality-of-life Questionnaire Core 13 (EORTC QLQ-LC13) – European Organization for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORTC QLQ-C30)

II.C.2. Other Studies in Postauthorization Development Plan

Study Short Name	Purpose of the Study
Study 20200362 An open label study to evaluate the pharmacokinetics of AMG 510 in healthy subjects with normal hepatic function and subjects with moderate and severe hepatic impairment Category 3	Primary objectives: • To evaluate the PK of a single 960 mg oral dose of AMG 510 administered in subjects with normal hepatic function and subjects with moderate and severe hepatic impairment Secondary objectives: • To evaluate the safety and tolerability of AMG 510 administered in subjects with normal hepatic function and subjects with moderate and severe hepatic impairment Safety concerns addressed: • Use in patients with hepatic impairment