EU Risk Management Plan

for

Sorafenib Accord 200 mg film-coated tablets

(Sorafenib)

RMP version to be assessed as part of this application:

RMP Version number	2.1
Data lock point for this RMP	25-Aug-2025
Date of final sign off	15-Sep-2025

Rationale for submitting an updated RMP: This RMP has been updated in line with Request for Supplementary Information (RfSI) for Sorafenib Accord (EMA/VR/0000287524) Type IB variation report, dated 25-Aug-2025.

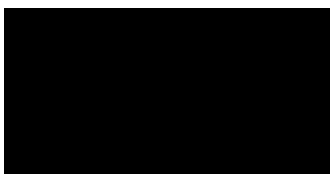
Summary of significant changes in this RMP: Significant changes have been made in following sections of RMP: Part I, Part II (Module SVII and SVIII), Part III (III.I), Part VI and Part VII (Annex 4, Annex 7 and Annex 8).

Other RMP versions under evaluation: Not applicable

Details of the currently approved RMP:

Version	Approved with Procedure	Approval date
1.1	Centralised Procedure (EMEA/H/C/0005921)	15-Sep-2022

QPPV name: Arletta Werynska

QPPV signature: 

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Part I: Product(s) Overview

Table 1: Product Overview

Active substance(s) **(INN or common name)**	Sorafenib
Pharmacotherapeutic group(s)(ATC Code)	**Pharmacotherapeutic group(s):** Antineoplastic agents, protein kinase inhibitors **ATC Code**: L01XE02
Marketing Authorisation Holder	Accord Healthcare S.L.U., Spain
Medicinal products to which this RMP refers	01
Invented name(s) in the European Economic Area (EEA)	Sorafenib Accord 200 mg film-coated tablets
Marketing authorisation procedure	Centralised Procedure: EMEA/H/C/0005921
Brief description of the product	*Chemical Class:* Sorafenib is an oral multi-kinase inhibitor that is used in the therapy of advanced renal cell, liver and thyroid cancer.
	Summary of mode of action: Sorafenib is a multikinase inhibitor that decreases tumour cell proliferation *in vitro*. Sorafenib inhibits tumour growth of a broad spectrum of human tumour xenografts in athymic mice accompanied by a reduction of tumour angiogenesis. Sorafenib inhibits the activity of targets present in the tumour cell (CRAF, BRAF, V600E BRAF, c-KIT, and FLT-3) and in the tumour vasculature (CRAF, VEGFR-2, VEGFR-3, and PDGFR-ß). RAF kinases are serine/threonine

	kinases, whereas c-KIT, FLT-3, VEGFR-2, VEGFR-3, and PDGFR-ß are receptor tyrosine kinases.
	Important information about its composition: Each film-coated tablet contains 200 mg of sorafenib (as tosilate).
Hyperlink to the Product Information	Refer Module 1.3.1 for Product Information
Indication(s) in the EEA	*Current:* Hepatocellular carcinoma Sorafenib Accord is indicated for the treatment of hepatocellular carcinoma. Renal cell carcinoma Sorafenib Accord is indicated for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy. Differentiated thyroid carcinoma Sorafenib Accord is indicated for the treatment of patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine.
Dosage in the EEA	*Current:* Sorafenib Accord treatment should be supervised by a physician experienced in the use of anticancer therapies. Posology The recommended dose of Sorafenib Accord in adults is 400 mg sorafenib (two tablets of 200 mg) twice daily (equivalent to a total daily dose of 800 mg).

	Treatment should continue as long as clinical benefit is observed or until unacceptable toxicity occurs. Posology adjustments Management of suspected adverse drug reactions may require temporary interruption or dose reduction of sorafenib therapy. When dose reduction is necessary during the treatment of hepatocellular carcinoma (HCC) and advanced renal cell carcinoma (RCC), the Sorafenib Accord dose should be reduced to two tablets of 200 mg sorafenib once daily. After improvement of non-haematological adverse reactions, the dose of Sorafenib Accord may be increased. When dose reduction is necessary during the treatment of differentiated thyroid carcinoma (DTC), the Sorafenib Accord dose should be reduced to 600 mg sorafenib daily in divided doses (two tablets of 200 mg and one tablet of 200 mg twelve hours apart). If additional dose reduction is necessary, Sorafenib Accord may be reduced to 400 mg sorafenib daily in divided doses (two tablets of 200 mg twelve hours apart), and if necessary further reduced to one tablet of 200 mg once daily. Method of Administration For oral use. It is recommended that sorafenib should be administered without food or with a low or moderate fat meal. If the patient intends to have a high-fat meal, sorafenib tablets should be taken at least 1 hour before or 2 hours after the meal. The tablets should be swallowed with a glass of water.
Pharmaceutical form(s) and strengths	*Current:* **Pharmaceutical form(s):** Film-coated tablet

[redacted]

	Strength: 200 mg
Is the product subject to additional monitoring in the EU?	No

Part II: Safety specification

Module SI – Epidemiology of the indication(s) and target population(s)

Not applicable

Module SII – Non-clinical part of the safety specification

Not applicable

Module SIII – Clinical trial exposure

Not applicable

Module SIV – Populations not studied in clinical trials

SIV.1 Exclusion criteria in pivotal clinical studies within the development programme

Not applicable

SIV.2 Limitations to detect adverse reactions in clinical trial development programmes

Not applicable

SIV.3 Limitations in respect to populations typically under-represented in clinical trial development programmes

Not applicable

Module SV – Post-authorisation experience

SV.1 Post-authorisation exposure

Not applicable

Module SVI – Additional EU requirements for the safety specification

Potential for misuse for illegal purposes

Not applicable

Module SVII – Identified and potential risks

SVII.1 Identification of safety concerns in the initial RMP submission

SVII.1.1 Risks not considered important for inclusion in the list of safety concerns in the RMP

Not applicable

SVII.1.2 Risks considered important for inclusion in the list of safety concerns in the RMP

Not applicable

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

Not applicable

SVII.3 Details of important identified risks, important potential risks, and missing information

SVII.3.1 Presentation of important identified risks and important potential risks

Not applicable

SVII.3.2 Presentation of the missing information

Not applicable

Module SVIII – Summary of the safety concerns

Table 2: Summary of safety concerns

Important identified risks	• None
Important potential risks	• None
Missing information	• None

[redacted]

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file are sufficient for the well characterised safety concerns.

III.2 Additional pharmacovigilance activities

None proposed

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable

Part IV: Plans for post-authorisation efficacy studies

Not applicable

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

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

V.1 Routine Risk Minimisation Measures

Not applicable

V.2 Additional Risk Minimisation Measures

None proposed

V.3 Summary of risk minimisation measures

Not applicable

Part VI: Summary of the risk management plan

Summary of risk management plan for Sorafenib Accord 200 mg film-coated tablets (Sorafenib)

This is a summary of the risk management plan (RMP) for Sorafenib Accord 200 mg film-coated tablets. The RMP details important risks of Sorafenib Accord 200 mg film-coated tablets, how these risks can be minimised, and how more information will be obtained about Sorafenib Accord 200 mg film-coated tablets' risks and uncertainties (missing information).

Sorafenib Accord 200 mg film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Sorafenib Accord 200 mg film-coated tablets should be used.

This summary of the RMP for Sorafenib Accord 200 mg film-coated tablets 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 Sorafenib Accord 200 mg film-coated tablets' RMP.

I. The medicine and what it is used for

Sorafenib Accord is indicated for following indications:

Hepatocellular carcinoma

Sorafenib Accord is indicated for the treatment of hepatocellular carcinoma.

Renal cell carcinoma

Sorafenib Accord is indicated for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.

Differentiated thyroid carcinoma

Sorafenib Accord is indicated for the treatment of patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine.

It contains sorafenib as the active substance and it is given by oral route.

[redacted]

Further information about the evaluation of Sorafenib Accord 200 mg film-coated tablets' benefits can be found in Sorafenib Accord 200 mg film-coated tablets' EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/sorafenib-accord

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

Important risks of Sorafenib Accord 200 mg film-coated tablets together with measures to minimise such risks and the proposed studies for learning more about Sorafenib Accord 200 mg film-coated tablets' 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 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, 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 Sorafenib Accord 200 mg film-coated tablets 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 Sorafenib Accord 200 mg film-coated tablets. 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).

[redacted]

Important identified risks	• None
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

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 Sorafenib Accord 200 mg film-coated tablets.

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

There are no studies required for Sorafenib Accord 200 mg film-coated tablets.