EU/UK Risk Management Plan

for

Abiraterone Accord 250 mg tablets
Abiraterone Accord 500 mg film-coated tablets
(Abiraterone)

RMP version to be assessed as part of this application:

RMP Version number	2.0
Data lock point for this RMP	30-Dec-2023
Date of final sign off	07-Mar-2024

Rationale for submitting an updated RMP: The Risk Management Plan (RMP) has been updated in line with EPAR-RMP of Zytiga® (Abiraterone), published by EMA on 06-Dec-2023.

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

Other RMP versions under evaluation: Not applicable

Details of the currently approved RMP:

RMP Version number	Approved with procedure	Date of approval (opinion date)
1.1	Centralised Procedure EMEA/H/C/005408	25-Feb-2021

QPPV name: Agata Gesiewicz

[redacted]

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Part I: Product(s) Overview

Table 1: Product Overview

Active substance(s) (INN or common name)	Abiraterone acetate
Pharmacotherapeutic group(s)(ATC Code)	Endocrine therapy, other hormone antagonists and related agents (L02BX03)
Marketing Authorisation Holder	Accord Healthcare S.L.U., Spain
Medicinal products to which this RMP refers	02
Invented name(s) in the European Economic Area (EEA)/United Kingdom (UK)	Abiraterone Accord 250 mg tablets Abiraterone Accord 500 mg film-coated tablets
Marketing authorisation procedure	Centralised Procedure (EMEA/H/C/005408) [redacted]
Brief description of the product	*Chemical Class:* Abiraterone is a 3beta-sterol, a member of pyridines and a 3beta-hydroxy-Delta(5)-steroid. It is a potent, irreversible, and selective inhibitor of 17 αhydroxylase/C17,20-lyase (CYP17), an enzyme expressed in testicular, adrenal, and prostatic tumour tissues, to regulate androgen biosynthesis.
	<u>Summary of mode of action:</u> Abiraterone acetate (Abiraterone Accord) is converted in vivo to abiraterone, an androgen biosynthesis inhibitor. Specifically, abiraterone selectively inhibits the enzyme 17α-hydroxylase/C17, 20-lyase (CYP17). This enzyme is expressed in and is required for androgen biosynthesis in testicular, adrenal and prostatic tumour tissues. CYP17 catalyses the conversion of pregnenolone and progesterone into testosterone precursors, DHEA and

	androstenedione, respectively, by 17α-hydroxylation and cleavage of the C17, 20 bond. CYP17 inhibition also results in increased mineralocorticoid production by the adrenals. Androgen-sensitive prostatic carcinoma responds to treatment that decreases androgen levels. Androgen deprivation therapies, such as treatment with LHRH analogues or orchiectomy, decrease androgen production in the testes but do not affect androgen production by the adrenals or in the tumour. Treatment with Abiraterone Accord decreases serum testosterone to undetectable levels (using commercial assays) when given with LHRH analogues (or orchiectomy).
	Important information about its composition: **Abiraterone Accord 250 mg tablets** Each tablet contains 250 mg of abiraterone acetate. Excipients with known effect: Each tablet contains 189 mg of lactose monohydrate. **Abiraterone Accord 500 mg film-coated tablets** Each film-coated tablet contains 500 mg of abiraterone acetate. Excipients with known effect Each film-coated tablet contains 253.2 mg of lactose monohydrate and 12 mg of sodium.
Hyperlink to the Product Information	Refer Module 1.3.1 for Product Information
Indication(s) in the EEA/UK	*Current*: Abiraterone Accord is indicated with prednisone or prednisolone for:

	• the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer (mHSPC) in adult men in combination with androgen deprivation therapy (ADT) • the treatment of metastatic castration resistant prostate cancer (mCRPC) in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated • the treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.
Dosage in the EEA/UK	*Current:* **Posology** Abiraterone Accord 250 mg tablets The recommended dose is 1,000 mg (four 250 mg tablets) as a single daily dose that must not be taken with food. Taking the tablets with food increases systemic exposure to abiraterone. Abiraterone Accord 500 mg film-coated tablets The recommended dose is 1,000 mg (two 500 mg tablets) as a single daily dose that must not be taken with food. Taking the tablets with food increases systemic exposure to abiraterone. Abiraterone Accord 250 mg tablets and Abiraterone Accord 500 mg film-coated tablets *Dosage of prednisone or prednisolone* For mHSPC, Abiraterone Accord is used with 5 mg prednisone or prednisolone daily. For mCRPC, Abiraterone Accord is used with 10 mg prednisone or prednisolone daily.

	Medical castration with luteinising hormone releasing hormone (LHRH) analogue should be continued during treatment in patients not surgically castrated. <u>Method of Administration</u> Abiraterone Accord is for oral use. The tablets should be taken at least one hour before or at least two hours after eating. These should be swallowed whole with water.
Pharmaceutical form(s) and strengths	*Current:* Tablet, 250 mg Film-coated tablet, 500 mg
Is the product subject to additional monitoring in the EU/UK?	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

The safety concerns of this RMP have been considered as per European Public Assessment Report (EPAR) – RMP available for the reference product Zytiga (abiraterone acetate) (Procedure No. EMEA/H/C/002321/II/0072), published by EMA on 06-Dec-2023. There is no change proposed by MAH in these safety concerns mentioned in Module SVIII which is in-line with RMP summary of reference product (Zytiga).

Hence this section remains "Not applicable".

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

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 safety concerns mentioned in "Module SVIII – Summary of the 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 Abiraterone Accord 250 mg tablets and Abiraterone Accord 500 mg film-coated tablets (abiraterone)

This is a summary of the risk management plan (RMP) for Abiraterone Accord 250 mg tablets and Abiraterone Accord 500 mg film-coated tablets (Throughout this section, product name is referred to as Abiraterone Accord). The RMP details important risks of Abiraterone Accord, how these risks can be minimised, and how more information will be obtained about Abiraterone Accord's risks and uncertainties (missing information).

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

This summary of the RMP for Abiraterone Accord 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 Abiraterone Accord's RMP.

I. The medicine and what it is used for

Abiraterone Accord is indicated with prednisone or prednisolone for:

- the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer (mHSPC) in adult men in combination with androgen deprivation therapy (ADT)
- the treatment of metastatic castration resistant prostate cancer (mCRPC) in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated
- the treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.

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

Further information about the evaluation of Abiraterone Accord's benefits can be found in Abiraterone Accord's 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/abiraterone-accord

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

Important risks of Abiraterone Accord together with measures to minimise such risks and the proposed studies for learning more about Abiraterone Accord'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 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 Abiraterone Accord 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 Abiraterone Accord. 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).

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 Abiraterone Accord.

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

There are no studies required for Abiraterone Accord.