Part VI: Summary of the risk management plan

Summary of risk management plan for Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets (Ivermectin/Albendazole)

This is a summary of the Risk Management Plan (RMP) for Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets. The RMP details important risks of Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets, how these risks can be minimised, and how more information will be obtained about Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets' risks and uncertainties (missing information).

Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets' Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets should be used.

This summary of the RMP for Ivermectin/Albendazole 9 mg/400 mg orodispersible 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 Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets' RMP.

I. The medicine and what it is used for

Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets is authorised in adults, adolescents and children ≥5 years of age with a body weight of ≥15 kg for the treatment of soil-transmitted helminths infections, caused by one or more of the following parasites: Hookworm (*Ancylostoma duodenale, Necator americanus*), Roundworm (*Ascaris lumbricoides*), Whipworm (*Trichuris trichiura*) and *Strongyloides stercoralis*; and for the treatment of proven or suspected microfilaraemia in patients with lymphatic filariasis caused by *Wuchereria bancrofti* (see SmPC for the full indication). It contains ivermectin and albendazole as active substances and it is given by oral route of administration.

Further information about the evaluation of Ivermectin/Albendazole 9 mg/400 mg orodispersible tablet' benefits can be found in Ivermectin/Albendazole 9 mg/400 mg orodispersible 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.

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

Important risks of Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets, together with measures to minimise such risks and the proposed studies for learning more about Ivermectin/Albendazole 9 mg/400 mg orodispersible 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, including 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 Ivermectin/Albendazole 9 mg/400 mg orodispersible 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 Ivermectin/Albendazole 9 mg/400 mg orodispersible 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);

List of important risks and missing information	
Important identified risks	• Encephalopathy following treatment in patients with heavy Loa loa co-infection (ivermectin)
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

Encephalopathy following treatment in patients with heavy Loa loa co-infection (ivermectin)	
Risk minimisation measures	Routine risk minimisation measures *SmPC section 4.8.* *PL section 4.* *According to section 4.3 of the SmPC, treatment with Ivermectin/Albendazole orodispersible tablets is contraindicated in patients with high Loa loa microfilaria and for MDA settings in Loa loa endemic regions, unless a feasible and validated risk mitigation strategy can be put in place which should follow WHO recommendations or relevant national guidelines for safe use in these settings.* *According to section 4.4 of the SmPC, for individual treatment (outside the scope of a mass drug administration) in Loa loa endemic areas, special measures (e.g. pre-treatment diagnostic tests such as Giemsa-stained thin or thick blood*

Encephalopathy following treatment in patients with heavy Loa loa co-infection (ivermectin)	
	smears, any validated quantifiable Loa loa diagnostic test available in the country, knowledge of regional Loa loa prevalence, monitoring of patients for serious CNS adverse events) should be taken before any treatment with ivermectin. Generally, patients with a high Loa loa microfilaria must not be given ivermectin unless feasible and validated risk mitigation strategies are put in place. Given the limited access to diagnostic tests in MDA settings, MDA treatment with ivermectin in Loa loa endemic areas is contraindicated. In these cases, alternative treatment strategies are necessary. Overall, monitoring patients for serious CNS symptoms is essential to prevent adverse effects and affected patients should be referred and managed appropriately. Additional risk minimisation measures *None.*

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 Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets.

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

There are no studies required for Ivermectin/Albendazole 9 mg/400 mg orodispersible tablets.

Summary of risk management plan for Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets (Ivermectin/Albendazole)

This is a summary of the Risk Management Plan (RMP) for Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets. The RMP details important risks of Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets, how these risks can be minimised, and how more information will be obtained about Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets' risks and uncertainties (missing information).

Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets' Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets should be used.

This summary of the RMP for Ivermectin/Albendazole 18 mg/400 mg orodispersible 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 Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets' RMP.

I. The medicine and what it is used for

Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets is authorised in adults, adolescents and children ≥5 years of age for the treatment of soil-transmitted helminth infections, caused by one or more of the following parasites: Hookworm (*Ancylostoma duodenale, Necator americanus*), Roundworm (*Ascaris lumbricoides*), Whipworm (*Trichuris trichiura*) and *Strongyloides stercoralis*; and for the treatment of proven or suspected microfilaraemia in patients with lymphatic filariasis caused by *Wuchereria bancrofti* (see SmPC for the full indication). It contains ivermectin and albendazole as active substances and it is given by oral route of administration.

Further information about the evaluation of Ivermectin/Albendazole 18 mg/400 mg orodispersible tablet' benefits can be found in Ivermectin/Albendazole 18 mg/400 mg orodispersible 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.

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

Important risks of Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets, together with measures to minimise such risks and the proposed studies for learning more about Ivermectin/Albendazole 18 mg/400 mg orodispersible 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, including 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 Ivermectin/Albendazole 18 mg/400 mg orodispersible 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 Ivermectin/Albendazole 18 mg/400 mg orodispersible 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);

List of important risks and missing information	
Important identified risks	• Encephalopathy following treatment in patients with heavy Loa loa co-infection (ivermectin)
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

Encephalopathy following treatment in patients with heavy Loa loa co-infection (ivermectin)	
Risk minimisation measures	Routine risk minimisation measures *SmPC section 4.8.* *PL section 4.* *According to section 4.3 of the SmPC, treatment with Ivermectin/Albendazole orodispersible tablets is contraindicated in patients with high Loa loa microfilaria and for MDA settings in Loa loa endemic regions, unless a feasible and validated risk mitigation strategy can be put in place which should follow WHO recommendations or relevant national guidelines for safe use in these settings.* *According to section 4.4 of the SmPC, for individual treatment (outside the scope of a mass drug administration) in Loa loa endemic areas, special measures (e.g. pre-treatment diagnostic tests such as Giemsa-stained thin or thick blood smears, any validated quantifiable Loa loa diagnostic test available in the country, knowledge of regional Loa loa prevalence, monitoring of patients for serious CNS adverse events) should be taken before any treatment with ivermectin.*

Encephalopathy following treatment in patients with heavy Loa loa co-infection (ivermectin)	
	Generally, patients with a high Loa loa microfilaria must not be given ivermectin unless feasible and validated risk mitigation strategies are put in place. Given the limited access to diagnostic tests in MDA settings, MDA treatment with ivermectin in Loa loa endemic areas is contraindicated. In these cases, alternative treatment strategies are necessary. Overall, monitoring patients for serious CNS symptoms is essential to prevent adverse effects and affected patients should be referred and managed appropriately. Additional risk minimisation measures *None.*

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 Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets.

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

There are no studies required for Ivermectin/Albendazole 18 mg/400 mg orodispersible tablets.

Part VII: Annexes

Table of contents

Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme

Not applicable.

Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan

Not applicable.

Annex 4 - Specific adverse drug reaction follow-up forms

Day 0 (dd/mm/yyyy):

Filled by (name, signature and date):

1. **Parent information**

Mother ☐ Father ☐

Date of birth:

Age:

Race:

Weight:

Height:

2. **Pregnancy history (for former pregnancies)**

Pregnancy no.	**Year**	**Outcome**

3. **Relevant medical history**

4. Suspected Drug(s)

Drug	Dose/frequency/route of administration	Start date	End date	Batch no.	Indication	Exposed quarter	Action taken

5. Concomitant medication

Drug	Dose/frequency/route of administration	Start date	End date	Batch no.	Indication	Exposed quarter	Action taken

6. Adverse reaction (s)

Adverse reaction	Start date	End date	Duration

7. Description of the case including lab test and other procedures performed.

8. Seriousness.

Serious ☐ Not serious ☐

Please select seriousness criteria:

☐ Death

☐ Requires inpatient hospitalisation or prolongation of existing hospitalisation,

☐ Life-threatening

☐ Persistent or significant disability or incapacity

☐ Congenital anomaly/birth defect

☐ Medically significant

9. Outcome.

☐ Recovered

☐ Recovered with sequels

☐ Not recovered

☐ Death

☐ Unknown

10. Pregnancy information.

Use of contraceptives: Yes ☐ Specify:_____

No ☐

Last menstruation date:

Delivery estimated date:

Delivery outcome:

Date of delivery:

Type of delivery:

Comments:

11. Neonate Information.

Child nº:

APGAR:

Weight (kg):

Height (cm):

Sex:

Date of birth:

Gestation week:

Outcome:

Comments:

12. Breast-feeding information.

Breast-feeding: Yes ☐ No ☐

Start date:

Did the patient notice any issue during lactation? (lack of milk, medical condition…)

13. Reporter contact data.

Name:

Address:

Telephone number:

Email:

Annex 5 - Protocols for proposed and on-going studies in RMP part IV

Not applicable.

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Not applicable.

Annex 7 - Other supporting data (including referenced material)

Not applicable.

Annex 8 – Summary of changes to the risk management plan over time

Version	Approval date Procedure	Change
1.0	Approval date: pending Procedure:	First Marketing Authorisation Application
0.2	Approval date: not approved Procedure: Centralised	Updated according to Day 120 Comments Assessment Report
0.3	Approval date: not approved Procedure: Centralised	Updated some SmPC sections and RMP's references to them. **Summary of significant changes in this RMP:** Part I: Product(s) Overview - Indications and Dosage updated. Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities) – SmPCs references updated with new information. Part VI: Summary of the risk management plan - SmPCs references updated with new information.
0.4	Approval date: not approved Procedure: Centralised	Updated according last updates on the SmPC. **Summary of significant changes in this RMP:** Part I: Product(s) Overview - Indications and Dosage updated. Part V: V.1. Routine Risk Minimisation Measures Part V: V.3 Summary of risk minimisation measures Part VI: II.B Summary of important risks
0.5	Approval date: not approved Procedure: Centralised	Updated according an EMA request during the Assessment. **Summary of significant changes in this RMP:** Annex 4 - Specific adverse drug reaction follow-up forms:

		Included a drug exposure during pregnancy follow-up questionnaire.