PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TIORFAN 4 MG/ML INFANTS AND CHILDREN ORAL SUSPENSION

This is a summary of the risk management plan (RMP) for Tiorfan 4 mg/ml infants and children oral suspension. The RMP details important risks of Tiorfan 4 mg/ml infants and children oral suspension, how these risks can be minimised, and how more information will be obtained about Tiorfan 4 mg/ml infants and children oral suspension's risks and uncertainties (missing information).

Tiorfan 4 mg/ml infants and children oral suspension's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfan 4 mg/ml infants and children oral suspension should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfan 4 mg/ml infants and children oral suspension is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfan 4 mg/ml infants and children oral suspension, together with measures to minimise such risks and the proposed studies for learning more about Tiorfan 4 mg/ml infants and children oral suspension'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.

If important information that may affect the safe use of Tiorfan 4 mg/ml infants and children oral suspension is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfan 4 mg/ml infants and children oral suspension 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 Tiorfan 4 mg/ml infants and children oral suspension. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 35: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfan 4 mg/ml infants and children oral suspension

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

There are no studies required for Tiorfan 4 mg/ml infants and children oral suspension

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR - TIORFAN® 100 MG CAPSULE

This is a summary of the risk management plan (RMP) for Tiorfan 100 mg Capsule. The RMP details important risks of Tiorfan 100 mg Capsule, how these risks can be minimised, and how more information will be obtained about Tiorfan 100 mg Capsule's risks and uncertainties (missing information).

Tiorfan 100 mg Capsule's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfan 100 mg Capsule should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfan 100 mg Capsule is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfan 100 mg Capsule, together with measures to minimise such risks and the proposed studies for learning more about Tiorfan 100 mg Capsule'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.

If important information that may affect the safe use of Tiorfan 100 mg Capsule is not yet available, it is listed under 'missing information' below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfan 100 mg Capsule 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 Tiorfan 100 mg

Capsule. 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

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 36: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfan 100 mg Capsule

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

There are no studies required for Tiorfan 100 mg Capsule

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR HIDRASEC 100 MG CAPSULE

This is a summary of the risk management plan (RMP) for Hidrasec 100 mg Capsule. The RMP details important risks of Hidrasec 100 mg Capsule, how these risks can be minimised, and how more information will be obtained about Hidrasec 100 mg Capsule's risks and uncertainties (missing information).

Hidrasec 100 mg Capsule's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Hidrasec 100 mg Capsule should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Hidrasec 100 mg Capsule is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Hidrasec 100 mg Capsule, together with measures to minimise such risks and the proposed studies for learning more about Hidrasec 100 mg Capsule'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.

If important information that may affect the safe use of Hidrasec 100 mg Capsule is not yet available, it is listed under 'missing information' below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Hidrasec 100 mg Capsule 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 Hidrasec 100 mg

Capsule. 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

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 37: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Hidrasec 100 mg Capsule

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

There are no studies required for Hidrasec 100 mg Capsule

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TIORFIX ® 100 MG CAPSULE

This is a summary of the risk management plan (RMP) for Tiorfix 100 mg Capsule. The RMP details important risks of Tiorfix 100 mg Capsule, how these risks can be minimised, and how more information will be obtained about Tiorfix 100 mg Capsule's risks and uncertainties (missing information).

Tiorfix 100 mg Capsule's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfix 100 mg Capsule should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfix 100 mg Capsule is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfix 100 mg Capsule, together with measures to minimise such risks and the proposed studies for learning more about Tiorfix 100 mg Capsule'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.

If important information that may affect the safe use of Tiorfix 100 mg Capsule is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfix 100 mg Capsule 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 Tiorfix 100 mg

Capsule. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 38: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfix 100 mg Capsule

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

There are no studies required for Tiorfix 100 mg Capsule

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TIORFAST 100 MG CAPSULE

This is a summary of the risk management plan (RMP) for Tiorfast 100 mg Capsule. The RMP details important risks of Tiorfast 100 mg Capsule, how these risks can be minimised, and how more information will be obtained about Tiorfast 100 mg Capsule's risks and uncertainties (missing information).

Tiorfast 100 mg Capsule's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfast 100 mg Capsule should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfast 100 mg Capsule is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfast 100 mg Capsule, together with measures to minimise such risks and the proposed studies for learning more about Tiorfast 100 mg Capsule'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.

If important information that may affect the safe use of Tiorfast 100 mg Capsule is not yet available, it is listed under 'missing information' below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfast 100 mg Capsule 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 Tiorfast 100 mg

Capsule. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 39: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfast 100 mg Capsule

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

There are no studies required for Tiorfast 100 mg Capsule

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR DIARFIX® 100 MG CAPSULE

This is a summary of the risk management plan (RMP) for Diarfix 100 mg Capsule. The RMP details important risks of Diarfix 100 mg Capsule, how these risks can be minimised, and how more information will be obtained about Diarfix 100 mg Capsule's risks and uncertainties (missing information).

Diarfix 100 mg Capsule's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Diarfix 100 mg Capsule should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Diarfix 100 mg Capsule is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Diarfix 100 mg Capsule, together with measures to minimise such risks and the proposed studies for learning more about Diarfix 100 mg Capsule'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.

If important information that may affect the safe use of Diarfix 100 mg Capsule is not yet available, it is listed under 'missing information' below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Diarfix 100 mg Capsule 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 Diarfix 100 mg

Capsule. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 40: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Diarfix 100 mg Capsule

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

There are no studies required for Diarfix 100 mg Capsule

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TIORFANOR 175 MG TABLET

This is a summary of the risk management plan (RMP) for Tiorfanor 175 mg Tablet. The RMP details important risks of Tiorfanor 175 mg Tablet, how these risks can be minimised, and how more information will be obtained about Tiorfanor 175 mg Tablet's risks and uncertainties (missing information).

Tiorfanor 175 mg Tablet's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfanor 175 mg Tablet should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfanor 175 mg Tablet is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfanor 175 mg Tablet, together with measures to minimise such risks and the proposed studies for learning more about Tiorfanor 175 mg Tablet'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.

If important information that may affect the safe use of Tiorfanor 175 mg Tablet is not yet available, it is listed under 'missing information' below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfanor 175 mmg tablet 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 Tiorfanor 175 mmg

tablet. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 41: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfanor 175 mg Tablet

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

There are no studies required for Tiorfanor 175 mg Tablet

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TIORFAN® INFANTS 10 MG GRANULES, AND TIORFAN® CHILDREN 30 MG GRANULES

This is a summary of the risk management plan (RMP) for Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules. The RMP details important risks of Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules, how these risks can be minimised, and how more information will be obtained about Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules's risks and uncertainties (missing information).

Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules, together with measures to minimise such risks and the proposed studies for learning more about Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules'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.

If important information that may affect the safe use of Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules 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 Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 42: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules

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

There are no studies required for Tiorfan® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR HIDRASEC® INFANTS 10 MG GRANULES, AND TIORFAN® CHILDREN 30 MG GRANULES

This is a summary of the risk management plan (RMP) for Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules. The RMP details important risks of Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules, how these risks can be minimised, and how more information will be obtained about Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules's risks and uncertainties (missing information).

Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules, together with measures to minimise such risks and the proposed studies for learning more about Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules'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.

If important information that may affect the safe use of Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules 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 Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 43: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules

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

There are no studies required for Hidrasec® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TIORFIX® INFANTS 10 MG GRANULES, AND TIORFAN® CHILDREN 30 MG GRANULES

This is a summary of the risk management plan (RMP) for Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules. The RMP details important risks of Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules, how these risks can be minimised, and how more information will be obtained about Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules's risks and uncertainties (missing information).

Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules, together with measures to minimise such risks and the proposed studies for learning more about Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules'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.

If important information that may affect the safe use of Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules 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 Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 44: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules

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

There are no studies required for Tiorfix® Infants 10 mg Granules, and Tiorfan® Children 30 mg Granules

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR VAPRINO GEGEN AKUTEN DURCHFALL

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

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

I. THE MEDICINE AND WHAT IT IS USED FOR

Vaprino gegen akuten durchfall is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Vaprino gegen akuten durchfall, together with measures to minimise such risks and the proposed studies for learning more about Vaprino gegen akuten durchfall'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.

If important information that may affect the safe use of Vaprino gegen akuten durchfall is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Vaprino gegen akuten durchfall 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

Vaprino gegen akuten durchfall. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 45: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Vaprino gegen akuten durchfall

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

There are no studies required for Vaprino gegen akuten durchfall

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR VAPRINO GEGEN AKUTEN DURCHFALL JUNIOR

This is a summary of the risk management plan (RMP) for Vaprino gegen akuten durchfall junior. The RMP details important risks of Vaprino gegen akuten durchfall junior, how these risks can be minimised, and how more information will be obtained about Vaprino gegen akuten durchfall junior's risks and uncertainties (missing information).

Vaprino gegen akuten durchfall junior's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Vaprino gegen akuten durchfall junior should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Vaprino gegen akuten durchfall junior is authorised for symptomatic treatment of acute diarrhoea (see SmPC for the full indication). It contains racecadotril as the active substance and it is given by oral route.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Vaprino gegen akuten durchfall junior, together with measures to minimise such risks and the proposed studies for learning more about Vaprino gegen akuten durchfall junior'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.

If important information that may affect the safe use of Vaprino gegen akuten durchfall junior is not yet available, it is listed under ‘missing information’ below.

II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of Vaprino gegen akuten durchfall junior 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

Vaprino gegen akuten durchfall junior. 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.

Summary of safety concerns	
Important identified risks	Skin reactions (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue) Interaction with angiotensin converting enzyme inhibitors (ACEIs) (angiodema, tongue and lip oedema; oedema mouth; eyelid oedema; face oedema, swollen tongue, lymphoedema, peripheral oedema)
Important potential risks	SCARs (Stevens-Johnson syndrome, toxic epidermal necrolysis, skin exfoliation, DRESS) Anaphylactic/hypersensitivity reactions Off label use in chronic diarrhoea Treatment of diarrhoea induced by invasive bacteria
Missing information	Patients with renal and hepatic insufficiency Pregnant or breast-feeding women

II.B SUMMARY OF IMPORTANT RISKS

Important identified Risk

Table 46: Important identified risk: Skin reactions (angioedema)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Low but potentially comedication known to induce skin reactions
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important identified risk: Interaction with angiotensin converting enzyme inhibitors ACEIs	
Evidence source	Post-authorisation experience
Risk group or risk factor	Unknown but potentially comedication with ACEis
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3, 4.4., 4.5 and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Important Potential Risks

severe cutaneous adverse reactions (SCARs)	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

anaphylactic/hypersensitivity reactions	
Evidence source	Post-authorisation experience
Risk group or risk factor	Not evaluable
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.3 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

off-label use in chronic diarrhoea	
Evidence source	Clinical trials experience: 753 patients were treated with Racecadotril in clinical trials performed in chronic diarrhoea including irritable bowel syndrome
Risk groups and risk factors	No risks related to a chronic treatment (above 7 days duration) were identified during the pre-authorisation phase during which 734 patients were treated for chronic diarrhoea
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

treatment of diarrhoea induced by invasive bacteria	
Evidence source	No source
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this clinical indication. Therefore the efficacy was not assessed and the risk could be an aggravation of the pathology because of the inefficacy of Racecadotril
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1, 4.4 Additional risk minimisation measures None
Additional pharmacovigilance activities	None

Paediatric population below 3-month old	
Safety concern	Application for treating patients below 3 months
Evidence source	Clinical trials and routine pharmacovigilance
Risk groups and risk factors	Racecadotril has not been sufficiently studied in this population. Therefore the safety was not assessed
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.1 and 4.2 (Paediatric formulations), 4.4 (Paediatric formulation Sanofi-Aventis), 4.4 (Paediatric formulation Bioprojet) and 4.2 (Adult formulation) Additional risk minimisation measures None
Additional pharmacovigilance activities	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 Vaprino gegen akuten durchfall junior

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

There are no studies required for Vaprino gegen akuten durchfall junior

Part VI: Summary of the risk management plan for Vaprino 100 mg Hartkapseln -