PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

CIBINQO (Abrocitinib)

Marketing Authorization Number 68174

Film-coated tablet, 50mg and 100mg

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LIST OF ABBREVIATIONS

AD	Atopic Dermatitis
AE	Adverse Event
BMI	Body Mass Index
CBC	Complete blood count
DHCP	Dear Health Care Professional
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
GI	Gastrointestinal
HCP	Health Care Professional
JAK	Janus kinase
MAH	Marketing Authorization Holder
MACE	Major adverse cardiovascular events
MRI	Magnetic resonance imaging
PASS	Post-Authorisation Safety Study
PL	Patient Leaflet
PSUR	Periodic Safety Update Report
QD	Once daily
RMM	Risk minimisation measures
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics (Europe)
TB	Tuberculosis
VTE	Venous Thrombotic Events

OVERVIEW

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary for Cibinqo is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g., by mentioning risks occurring in populations or indications not included in the Swiss marketing authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Cibinqo in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of Cibinqo.

SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Cibinqo (Abrocitinib)

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

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

This summary of the RMP for Cibinqo 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 Cibinqo's RMP.

I. The Medicine and What It Is Used For

Cibinqo is indicated for the treatment of moderate-to-severe atopic dermatitis in adults who are candidates for systemic therapy (see SmPC for the full indication). It contains Abrocitinib as the active substance and it is given by oral route of administration.

Further information about the evaluation of Cibinqo's benefits can be found in Cibinqo's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

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

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

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

In the case of Cibinqo, these measures are supplemented with *additional risk minimisation* measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse events will be collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

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

II.A List of Important Risks and Missing Information

Important risks of Cibinqo 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 Cibinqo. 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);

Table 1. List of Important Risks and Missing Information

Important identified risks	Venous thromboembolism
	Herpes zoster
Important potential risks	Serious and opportunistic infections
	Malignancy (excluding NMSC)
	Non-melanoma skin cancer
	MACE
	Myopathies (including rhabdomyolysis)
	Gastrointestinal perforation
	Embryofoetal toxicity following exposure in utero
	Impaired bone growth and development if used off-label in paediatric patients <12 years-of-age
	Fractures
Missing information	Long-term safety[a]
	Long-term safety in adolescents[b]

a. For ≥18 years of age.
b. Adolescent defined as ≥12 years of age and <18 years of age.

II.B Summary of Important Risks

Table 2. Important Identified Risk - Venous Thromboembolism

Evidence for linking the risk to the medicine	Abrocitinib and other approved JAK inhibitors clinical trial data.
Risk factors and risk groups	There was an insufficient number of events in the Abrocitinib development program for formal risk factor or subgroup analysis. Risk factors that should be considered in prescribing include previous VTE, patients undergoing major surgery, immobilization, myocardial infarction (within the previous 3 months), heart failure, use of combined hormonal contraceptives or hormone replacement therapy, inherited coagulation disorder, and malignancy. Age, obesity (BMI ≥30), diabetes, hypertension, and smoking status should also be considered.

Table 2. Important Identified Risk - Venous Thromboembolism

Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects PL Sections 2 and 4 Additional risk minimisation measures: Prescriber Brochure Patient Card Direct Healthcare Professional Communication
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 3. Important Identified Risk - Herpes zoster

Evidence for linking the risk to the medicine	Clinical study data with Abrocitinib and understanding of JAK mechanisms based on data from the JAK class of therapies.
Risk factors and risk groups	For all herpes zoster events (regardless of adjudication as an opportunistic), age ≥65 years, a dose of 200 mg, a history of herpes zoster, severe AD at baseline, and an ALC $<0.5\times10^3/mm^3$ were identified as risk factors.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.3 Contraindications SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects PL Sections 2 and 4 Additional risk minimisation measures: Prescriber Brochure Patient Card Direct Healthcare Professional Communication
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 4. Important Potential Risk – Serious and Opportunistic Infections

Evidence for linking the risk to the medicine	Abrocitinib and other approved JAK inhibitors clinical trial data.
Risk factors and risk groups	Elderly age and diabetes are general risk factors for serious infections.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.3 Contraindications SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects PL Sections 2 and 4 Additional risk minimisation measures: Prescriber Brochure Patient Card Direct Healthcare Professional Communication
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 5. Important Potential Risk – Malignancy (excluding NMSC)

Evidence for linking the risk to the medicine	Abrocitinib and other approved JAK inhibitors clinical trial data.
Risk factors and risk groups	There was an insufficient number of events in the Abrocitinib development program for risk factor or subgroup analysis. Like with other JAK inhibitors, age ≥65 years, current or past smoking history, and a history of malignancy (excluding basal cell carcinoma) are risk factors for malignancy.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects PL Section 2 Additional risk minimisation measures: Prescriber Brochure Patient Card Direct Healthcare Professional Communication

Table 5. Important Potential Risk – Malignancy (excluding NMSC)

Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 6. Important Potential Risk – Non-Melanoma Skin Cancer

Evidence for linking the risk to the medicine	Abrocitinib and other approved JAK inhibitors clinical trial data.
Risk factors and risk groups	There was an insufficient number of events in the Abrocitinib development program for risk factor or subgroup analysis. Like with other JAK inhibitors, age ≥65 years, current or past smoking history, and a history of malignancy (excluding basal cell carcinoma) are risk factors for malignancy.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects PL Section 2 Additional risk minimisation measures: Prescriber Brochure Patient Card Direct Healthcare Professional Communication
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 7. Important Potential Risk – MACE

Evidence for linking the risk to the medicine	Clinical study data and data other approved JAK inhibitors.

Table 7. Important Potential Risk – MACE

Risk factors and risk groups	There was an insufficient number of events in the Abrocitinib development program for formal risk factor or subgroup analysis. Like with other JAK inhibitors, age ≥65 years, current or past smoking history, and a history of atherosclerotic disease are risk factors for MACE.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.4 Special warnings and precautions for use SmPC Section 4.8 Undesirable effects PL Section 2 and 4 Additional risk minimisation measures: Prescriber Brochure Patient Care Direct Healthcare Professional Communication
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 8. Important Potential Risk – Myopathies (including Rhabdomyolysis)

Evidence for linking the risk to the medicine	Clinical trial data and based on the data from the JAK class. Approved JAK inhibitors are being investigated for potential risk of myopathy (including rhabdomyolysis).
Risk factors and risk groups	There were insufficient events to establish risk factors.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration SmPC Section 4.8 Undesirable effects (Blood creatine phosphokinase increase) Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 9. Important Potential Risk – Gastrointestinal Perforation

Evidence for linking the risk to the medicine	Approved JAK inhibitors are being investigated for potential risk of GI perforation.
Risk factors and risk groups	There was an insufficient number of events to establish risk factors. The subject with the serious event of duodenal ulcer haemorrhage and non-serious event of gastritis erosive was 83 years old.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 10. Important Potential Risk – Embryofoetal Toxicity Following Exposure in Utero

Evidence for linking the risk to the medicine	Abrocitinib did not cause skeletal malformations in pregnant rats or rabbits. Approved therapies in the JAK inhibitor class are being investigated for potential risk of foetal variations or malformation following exposure in utero.
Risk factors and risk groups	Risk of foetal malformation pertains only to women of childbearing potential who become pregnant while receiving Abrocitinib or and for at least 4 weeks after treatment.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.3 Contraindications SmPC Section 4.6 Fertility, Pregnancy and Lactation Additional risk minimisation measures: Prescriber Brochure Patient Card
Additional pharmacovigilance activities	Additional pharmacovigilance activities: B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 11. Important Potential Risk – Impaired Bone Growth and Development if Used Off-label in Paediatric Patients <12 Years-of-Age

Evidence for linking the risk to the medicine	Administration of Abrocitinib to juvenile rats beginning on postnatal Day 21 and older (comparable to a 2-year-old human and older) was not associated with microscopic or macroscopic bone findings. Administration of Abrocitinib to juvenile rats beginning on postnatal Day 10 (comparable to a 3-month-old human infant) resulted in adverse microscopic and macroscopic bone findings, including malrotated paws, fractures, and/or femoral head abnormalities.

Table 11. Important Potential Risk – Impaired Bone Growth and Development if Used Off-label in Paediatric Patients <12 Years-of-Age

Risk factors and risk groups	There is a potential risk for patients <12 years-of-age.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.2 Posology and method of administration PL Section 2 Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: B7451085: A Drug Utilization Study to Evaluate the Effectiveness of RMMs for Abrocitinib in EU using Electronic Healthcare Data See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 12. Important Potential Risk – Fractures

Evidence for linking the risk to the medicine	Nonclinical data and data from other JAK inhibitors.
Risk factors and risk groups	There was an insufficient number of events to establish risk factors.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 5.3 Preclinical safety data SmPC Section 4.2 Posology and method of administration (starting dose of 100 mg once a day is recommended in adolescents weighing <59 kg) Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451015: Long-term Extension Study B7451120: A Prospective Active Surveillance Study to Monitor Growth, Development, and Maturation Among Adolescents with Atopic Dermatitis Exposed to Abrocitinib See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 13. Missing Information – Long-Term Safety[a]

Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451015: Long-term Extension Study See Section II.C of this summary for an overview of the post-authorisation development plan.

a. For ≥18 years of age.

Table 14. Missing Information – Long-Term Safety in Adolescents[a]

Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU B7451015: Long-term Extension Study B7451015: Adolescent Imaging Substudy B7451120: A Prospective Active Surveillance Study to Monitor Growth, Development, and Maturation Among Adolescents with Atopic Dermatitis Exposed to Abrocitinib See Section II.C of this summary for an overview of the post-authorisation development plan.

a. Adolescent defined as ≥12 years of age and <18 years of age.

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 Abrocitinib-Pfizer Europe MA EEIG.

II.C.2 Other Studies in Post-Authorisation Development Plan

Study B7451084: An Active Surveillance Study to Monitor the Real-World Safety of Abrocitinib among Patients with Atopic Dermatitis in the EU

Purpose of the study:

Based on data from Cibinqo clinical program, it is of MAH's opinion that it is important to monitor the real-world safety of Cibinqo following its authorization in the EU. An active safety surveillance study will assess safety endpoints of interest with Cibinqo in the post-approval setting.

The study objective is to estimate incidence rates of safety events of interest among patients with AD receiving Abrocitinib and patients with AD receiving biologic and/or non-biologic (non- Janus Kinase inhibitor [non-JAKi]) chronic systemic treatments for AD (comparator treatments) in the real-world setting.

The following are the primary safety endpoints of interest:

- VTE,
- Herpes zoster,
- Serious infections and opportunistic infections,
- Rhabdomyolysis,
- Gastrointestinal perforation,
- MACE,
- Fractures,
- Malignancy (excluding NMSC),
- NMSC,
- All-cause mortality, and
- Height as a measure for impaired bone growth in adolescents (Denmark only).

Study B7451085: A Drug Utilization Study to Evaluate the Effectiveness of Risk Minimisation Measures for Abrocitinib in the EU Using Electronic Healthcare Data

Purpose of the study:

To mitigate the risks associated with Abrocitinib, required routine RMMs including the SmPC and package leaflet are being employed. In order to minimise important risks with the use of Cibinqo, the MAH has also implemented additional RMMs: an educational program intended to enhance the communication of the risk and risk minimisation practices to HCPs and patients. The program includes a Prescriber Brochure, a DHPC and a Patient Card.

The MAH plans to evaluate the effectiveness of RMMs being implemented for Abrocitinib. The proposed study will be designated as a PASS.

Research question: Does routinely collected data in the EU indicate adherence to the recommendations for the use of Abrocitinib described in the SmPC, prescriber brochure and DHPC?

The study objectives are to evaluate, to the extent measurable in the available routinely collected data, indicators of HCPs' adherence to the prescribing information in accordance with the Abrocitinib SmPC, prescriber brochure, and DHPC specifically:

- Indicators of adherence to performing laboratory tests of complete blood count (CBC), lipid panel, hepatitis B/C and tuberculosis (TB) screening prior to initiation of Abrocitinib treatment,
- Indicators of adherence to performing laboratory tests of CBC and lipid panel at Week 4 (± 2 weeks) from initiation of Abrocitinib treatment,
- Indicators of adherence to consideration of risk factors for VTE, MACE, malignancy excluding NSMC, NMSC and serious infection prior to treatment with Abrocitinib,
- Indicators of adherence to avoid live attenuated vaccine immediately prior to and during treatment with Abrocitinib,
- Indicators of adherence to contraindications for use during pregnancy,
- Indicators of adherence to contraindications for use among patients with severe hepatic impairment,
- Indicators of adherence to not use in patients aged <12 years-of-age, and
- Indicators of adherence to recommended posology (estimated average daily dose).

Study B7451015: A Phase 3 Multi-Center, Long-Term Extension Study Investigating the Efficacy and Safety of Abrocitinib, With or Without Topical Medications, Administered to Subjects Aged 12 Years and Older with Moderate to Severe Atopic Dermatitis

Purpose of the Study:

The objective of this study is to assess the long-term safety of 100 mg and 200 mg once daily of Abrocitinib with or without topical treatments in adult and adolescent subjects who previously participated in qualifying Abrocitinib AD trials.

The study objectives will be to assess safety by the spontaneous reporting of AEs, physical examinations and clinical laboratory results in all subjects who receive at least one dose of the investigational product. This study will continue to describe safety data to include:

- VTE,
- Serious and opportunistic infections,
- Herpes zoster,
- Malignancy (excluding NMSC),
- NMSC,
- Fractures, including in adolescents,
- Myopathy (including rhabdomyolysis),
- Gastrointestinal perforation,

- MACE,
- Height in adolescents,
- Development in adolescents,
- Pregnancy outcomes, and
- All-cause mortality.

Study B7451015: Adolescent Imaging Substudy

Purpose of the Substudy:

The objective of this substudy is to evaluate the potential effects of Abrocitinib in terms of abnormal bone findings in knee MRI in subjects enrolled as adolescents (12 to <18 years-of-age) in the Abrocitinib development program. The substudy will evaluate the proportion of abnormal bone finding in knee MRI in adolescent subjects exposed to Abrocitinib 100 mg and 200 mg QD.

Study B7451120: A Prospective Active Surveillance Study to Monitor Growth, Development and Maturation Among Adolescents with Atopic Dermatitis Exposed to Abrocitinib.

Purpose and objectives: As part of the Abrocitinib pharmacovigilance plan, a long-term follow-up study is being proposed to actively monitor growth, development (including bone development), and maturation (including pubertal development) in adolescents aged 12-17 years in the post-approval setting.

The objectives are to:

- Describe growth, development (including bone development), and maturation (including pubertal maturation) metrics among adolescent patients with atopic dermatitis (AD) treated with Abrocitinib and, separately, among adolescent patients with AD unexposed to Abrocitinib and receiving systemic treatments;
- Describe the risk of fractures stratified by Abrocitinib dose (100 mg and 200 mg).

Additionally, an exploratory objective is to compare adolescent patients treated with Abrocitinib with adolescent patients unexposed to Abrocitinib and treated with comparators for select outcomes, depending on the sample size.