PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

ATGAM (HORSE ANTI-HUMAN T LYMPHOCYTE IMMUNOGLOBULIN (eATG))

Marketing Authorization Number 68824

Concentrate for solution for infusion, 250mg/5mL

Document Version: 2.0

Document Date: 02 April 2024

Based on Part VI of EU RMP version 3.1, dated 01 June 2023

Pfizer AG, Schärenmoosstrasse 99, CH-8052 Zürich

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

AA	Aplastic Anaemia
AEs	Adverse Events
eATG	Horse anti-human T lymphocyte immunoglobulin
EMA	European Medicines Agency
EPAR	European Public Assessment Report
HCP	Healthcare Professional
HSCT	Haematopoietic Stem Cell Transplantation
LAIV	Live Attenuated Influenza Vaccine
MMR	Measles, Mumps, Rubella
MMRV	Measles, Mumps, Rubella and Varicella
NSAID	Non Steroidal Anti-Inflammatory Drug
OPV	Oral Polio Vaccine
PL	Package Leaflet
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SAA	Severe Aplastic Anaemia
SmPC	Summary of Product Characteristics (European Union)

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 Atgam 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 Atgam 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 Atgam.

SUMMARY OF RISK MANAGEMENT PLAN FOR ATGAM

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

Atgam's SmPC and its Package Leaflet (PL) give essential information to Healthcare Professionals (HCPs) and patients on how Atgam should be used.

I. The Medicine and What It Is Used For

Atgam is indicated for use in adults and in children aged 2 years and older for the treatment of acquired moderate to Severe Aplastic Anaemia (SAA) of known or suspected immunologic aetiology as part of standard immunosuppressive therapy in patients who are unsuitable for haematopoietic stem cell transplantation (HSCT) or for whom a suitable haematopoietic stem cell donor is not available. It contains Horse anti-human T lymphocyte immunoglobulin (eATG) as the active substance and it is given by infusion.

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

Important risks of Atgam, together with measures to minimise such risks and the proposed studies for learning more about Atgam'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 PL and SmPC addressed to patients and HCPs;
- 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 public (eg, with or without prescription) can help to minimise its risks.

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

In addition to these measures, information about AEs is collected continuously and regularly analysed, including assessment of Periodic Safety Update Report 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 Atgam is not yet available, it is listed under ‘missing information’ below.

II.A. List of Important Risks and Missing Information

Important risks of Atgam are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Atgam. 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 (eg, on the long-term use of the medicine).

Table 1. List of Important Risks and Missing Information

Important identified risks	Systemic anaphylaxis Infections
Important potential risks	Cytokine Release Syndrome Secondary immunodeficiency adversely impacting live-virus vaccination
Missing information	Use in pregnant and lactating women
	Use in paediatric patients

II.B. Summary of Important Risks

Table 2. Important Identified Risk 1: Systemic Anaphylaxis

Evidence for linking the risk to the medicine	Clinical trials, literature and post-marketing data.
Risk factors and risk groups	Patients with history of known reactions to the active substance or to any of the excipients or hypersensitivity to any other horse gamma globulin preparation are at risk. Studies reporting incidence of drug-induced anaphylaxis demonstrate that anaphylaxis is higher in female patients and in the younger population. Antibiotics and NSAID are the most commonly reported drugs that induce anaphylaxis.
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)

Table 3. Important Identified Risk 2: Infections

Evidence for linking the risk to the medicine	Clinical trials, literature and post-marketing data.
Risk factors and risk groups	Severe and prolonged neutropenia and treatment modalities lead to increasing the risk of infection in patients with AA. In addition, patients with moderate to SAA who are also being treated with additional immunosuppressive drugs such as ciclosporin, may be at increased risk for infections.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 (Special warnings and precautions for use) SmPC Section 4.8 (Undesirable effects)

Table 4. Important Potential Risk 1: Cytokine Release Syndrome

Evidence for linking the risk to the medicine	Literature and post-marketing data.
Risk factors and risk groups	Patients treated with polyclonal anti-thymocyte antibodies produced either in horses (Atgam®) or in rabbits (Thymoglobulin®).

Table 4. Important Potential Risk 1: Cytokine Release Syndrome

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)

Table 5. Important Potential Risk 2: Secondary immunodeficiency adversely impacting live-virus vaccination

Evidence for linking the risk to the medicine	Literature and post-marketing data.
Risk factors and risk groups	Immunocompromised patients such as patients treated with horse anti-human T lymphocyte immunoglobulin and ciclosporin or other immunosuppressant medication are at risk of being unable to control infection with live-virus or having a reduced immune response to live-virus vaccine. The following are live-virus vaccines: MMR; MMRV, OPV, LAIV, yellow fever, varicella, zoster, rotavirus, and vaccinia (smallpox).
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 (Special warnings and precautions for use)

Table 6. Missing information 1: Use in pregnant and lactating women

Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.6 (Fertility, pregnancy and lactation) and SmPC Section 5.3 (Pre-clinical safety data).

Table 7. Missing information 2: Use in paediatric patients

Risk minimisation measures	Routine risk minimisation measures: Section 4.2 (Posology and method of administration, SmPC Section 4.8 (Undesirable effects) and SmPC Section 5.1 (Pharmacodynamic properties).

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 Atgam.

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

There are no other study planned or ongoing in Post-Authorisation Development Plan.