RISK MANAGEMENT PLAN - PART VI

SUMMARY OF THE RISK MANAGEMENT PLAN

Active substance(s) (INN or common name)	**Yellow Fever Vaccine (live)**
Product's concerned (Brand name(s))	**STAMARIL** **Single dose and multidose presentation**
Name of Marketing Authorization Holder or Applicant	**Sanofi Pasteur** **14 Espace Henry Vallée,** **69007 Lyon, France** **Phone: +33 4 3737 0100** **Fax: +33 4 3737 7737**
Data lock point (DLP) for this module	**30-SEP-2019**
Version number of Risk Management Plan (RMP) when this module was last updated	**Version 3.1**

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ABBREVIATIONS

DLP	Data Lock Point
EPAR	European Public Assessment Report
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SmPC	Summary of Product Characteristic
YF	Yellow Fever
YEL-AND	Yellow fever vaccine Associated acute Neurotropic Disease
YEL-AVD	Yellow fever vaccine Associated acute Viscerotropic Disease

Summary of risk management plan for Stamaril (Yellow Fever Vaccine)

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

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

VI.1. THE MEDICINE AND WHAT IT IS USED FOR

Stamaril is authorised for active immunization against yellow fever in persons: travelling to, passing through or living in an area where there is a current or periodic risk of yellow fever transmission, travelling to any country that requires an International Certificate of Vaccination for entry (which may or may not depend on the previous itinerary) or handling potentially infectious materials (e.g. laboratory personnel) (see SmPC for the full indication). It contains live attenuated Yellow Fever virus as the active substance and it is given by injection.

VI.2. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Stamaril, together with measures to minimise such risks and the proposed studies for learning more about Stamaril's risks, are outlined in the next sections.

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

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;

- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

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

If important information that may affect the safe use of Stamaril is not yet available, it is listed under 'missing information' outlined in the next section.

VI.2.1. List of important risks and missing information

Important risks of Stamaril 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 Stamaril. 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	Anaphylactic reactions
	Yellow fever vaccine-associated viscerotropic disease (YEL-AVD)
	Yellow fever vaccine-associated neurotropic disease (YEL-AND)
Important potential risks	Potential transmission of vaccine virus through breastfeeding
Missing information	Use in pregnant women
	Use in immunocompromised individuals

VI.2.2. Summary of important risks

Table 2 – Important risks and missing information with corresponding risk minimisation activities and additional pharmacovigilance activities if any: Important identified risk: Anaphylactic reactions

Important identified risk: Anaphylactic reactions	
Evidence for linking the risk to the medicine	Literature, data from postmarketing individual case safety reports
Risk factors and risk groups	Hereditary predisposition, history of atopic or allergic conditions. Anaphylactic/allergic reaction following a previous immunization

Important identified risk: Anaphylactic reactions	
Risk minimization measures	**Routine risk minimisation measures:** Labelled in Sections 4.3, 4.4 and 4.8 of SmPC Legal status: Medical product subject to medical prescription. Restricted medical prescription in designated authorized Yellow Fever vaccination centres by qualified and trained healthcare professional with experience in benefit risk evaluation of yellow fever vaccine according to International Health Regulation 2005. Labelled in Sections 4.1 of SmPC **Additional risk minimisation measures:** None

Table 3- Important risks and missing information with corresponding risk minimisation activities and additional pharmacovigilance activities if any: Important identified risk: Yellow Fever Vaccine Associated Acute Viscerotropic disease

Important identified risk: Yellow Fever Vaccine Associated Acute Viscerotropic disease (YEL-AVD)	
Evidence for linking the risk to the medicine	Yellow Fever vaccine-associated acute viscerotropic disease was first described in 2001 Source of evidence include literature, data from postmarketing individual case safety reports and Working group review (European Union Working Group, Center for Disease Control, Yellow Fever Working Group)
Risk factors and risk groups	**Risk factors outweighing benefits (contraindication to vaccination)** Risk factors recognized to be strongly associated with YEL-AVD occurrence or increased severity includes: congenital or acquired immunodeficiency, history of thymus dysfunction (including myasthenia gravis, thymoma) and thymectomy (for any reason). **Potential risk factors (precaution)** The risk appears to be higher in those aged over 60 years although cases have also been reported in other age groups. However, based on available data, the risk of fatal YEL-AVD in an individual >60 years of age without any associated contraindications to vaccination is lower than the estimated risk of dying from wild Yellow Fever in an unvaccinated traveler visiting areas with Yellow Fever vaccine transmission. However, in up to 40% of YEL-AVD cases there have been no associated risk factors identified, and the occurrence of YEL-AVD is unpredictable. Each potential vaccinee should be informed on the risks associated with vaccination or with non-vaccination in the context of the Yellow Fever epidemiology in the visited area**.**

Important identified risk: Yellow Fever Vaccine Associated Acute Viscerotropic disease (YEL-AVD)	
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.3, 4.4 and 4.8 of SmPC (and corresponding Package Leaflet sections) Legal status: Medical product subject to medical prescription. Restricted medical prescription in designated authorized Yellow Fever vaccination centres by qualified and trained healthcare professional with experience in benefit risk evaluation of yellow fever vaccine according to International Health Regulation 2005. Labelled in Sections 4.1 of SmPC **Additional risk minimization measures:** Direct Healthcare Professional Communication (DHPC) letter and Check-list in United Kingdom.

Table 4 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any: Important identified risk: Yellow Fever Vaccine Associated Neurotropic disease

Important identified risk : Yellow Fever Vaccine Associated Neurotropic disease (YEL-AND)	
Evidence for linking the risk to the medicine	Literature, Center for Disease Control Publication, Working group from EU and Center for Disease Control Yellow Fever, and post-marketing setting
Risk factors and risk groups	Identified risk factors strongly associated with increased occurrence or increased severity of YEL-AND include immune deficiency and age <9 months of age. Other potential risk factors: Although YEL-AND can occur in all age group, the risk seems to be higher in those aged >60 as compared with other indicated age groups. However, in up to 50% of YEL-AVD cases there have been no associated risk factors identified, and the occurrence of YEL-AVD is unpredictable. Each potential vaccinee should be informed on the risks associated with vaccination or with non-vaccination in the context of the Yellow Fever epidemiology in the visited area.
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.3, 4.4 and 4.8 of SmPC (and corresponding Package Leaflet sections) Legal status: Medical product subject to medical prescription. Restricted medical prescription in designated authorized Yellow Fever vaccination centres by qualified and trained healthcare professional with experience in benefit risk evaluation of yellow fever vaccine according to International Health Regulation 2005. Labelled in Sections 4.1 of SmPC **Additional risk minimization measures**: None

Table 5 - Important risks and missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any : Important potential risk: Potential transmission of vaccine virus through breastfeeding

Important potential risk : Potential transmission of vaccine virus through breastfeeding	
Evidence for linking the risk to the medicine	Aggregate pharmacovigilance data and literature publication
Risk factors and risk groups	Children breastfed within 1 week from maternal Yellow Fever vaccination
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.4 and 4.6 of SmPC Legal status: Medical product subject to medical prescription. Restricted medical prescription in designated authorized Yellow Fever vaccination centres by qualified and trained healthcare professional with experience in benefit risk evaluation of yellow fever vaccine according to International Health Regulation 2005. Labelled in Sections 4.1 of SmPC **Additional risk minimization measures:** None

Table 6 - Missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any : Missing information: Use in pregnant women

Missing information : Use in pregnant women	
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.4 and 4.6 of SmPC Legal status: Medical product subject to medical prescription. Restricted medical prescription in designated authorized Yellow Fever vaccination centres by qualified and trained healthcare professional with experience in benefit risk evaluation of yellow fever vaccine according to International Health Regulation 2005. Labelled in Sections 4.1 of SmPC **Additional risk minimization measures:** None

Table 7- Missing information with corresponding risk minimization activities and additional pharmacovigilance activities if any : Missing information: Use in immunocompromised individuals

Missing information : Use in immunocompromised individuals	
Risk minimization measures	**Routine risk minimization measures:** Labelled in Sections 4.3 of SmPC Legal status: Medical product subject to medical prescription. Restricted medical prescription in designated authorized Yellow Fever vaccination centres by qualified and trained healthcare professional with experience in benefit risk evaluation of yellow fever vaccine according to International Health Regulation 2005. Labelled in Sections 4.1 of SmPC **Additional risk minimization measures:** None

VI.2.3. Post-authorisation development plan

VI.2.3.1.Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Stamaril.

VI.2.3.2.Other studies in post-authorisation development plan

Table 8 - Other studies in post-authorisation development plan

Cross sectional survey to evaluate HCPs and patients knowledge and understanding of UK additional risk minimization measures (e.g. chek-list). (category 3)
Purpose of the study: The objective is to assess the knowledge and understanding of Stamaril local minimization measures among 1) HCP from Yellow Fever Vaccination Centers and 2) patients having visited YFVC for Yellow Fever vaccination in UK

REFERENCES

Not applicable