PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Artiss

This is a summary of the Risk Management Plan (RMP) for Artiss. The RMP provides details on the risks of Artiss and how more information will be obtained about the risks.

The summary of product characteristics (SmPC) and package leaflet (PL) for Artiss provide essential information to healthcare professionals and patients on how Artiss should be used.

New safety concerns and/or changes to the current safety concerns will be included in future updates of the RMP.

I. The medicine and what it is used for

Artiss is authorized for use as a tissue glue to adhere/seal subcutaneous tissue in plastic, reconstructive, and burn surgery, as a replacement or an adjunct to sutures or staples. In addition, Artiss is indicated as an adjunct to hemostasis on subcutaneous tissue surfaces; refer to the SmPC for complete indication wording. It contains fibrinogen, thrombin, calcium chloride, aprotinin as the active substances, and is for epilesional use.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

The important risks of Artiss, together with measures to minimize such risks, are outlined below. Measures to minimize the risks identified for medicinal products may 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 authorized pack size – the amount of medicine in a pack is chosen so as 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 minimize its risks.

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

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

II.A List of important risks and missing information

Important risks of medicinal products are risks that need special risk management activities to further investigate or minimize 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 medicinal products. Potential risks are concerns for which an association with the use of the medicinal product is possible based on available data, but this association has not been established yet and needs to be further monitored. Missing information refers to information on the safety of the medicinal product that is currently missing and further information may need to be collected (e.g., on the long-term use of the medicine).

The important risks for Artiss are listed in the table below.

List of important risks and missing information	
Important identified risk	Air or gas embolism due to incorrect use of the device when applying Tisseel/Artiss
Important potential risk	Tissue adhesion and granuloma formation due to incorrect use of the product
Missing information	None

II.B Summary of important risks and missing information

Air or gas embolism due to incorrect use of the device when applying Tisseel/Artiss	
Evidence for linking the risk to the medicine	Evidence source: post-market reports and medical literature. Air or gas embolism due to incorrect use of the spray device when applying Tisseel or Artiss have been reported in the post-market setting. Air or gas embolism may occur with the use of spray devices employing a pressure regulator to administer fibrin sealants at higher than recommended pressure and in close proximity to the tissue (Felema 2013), which may be life-threatening and potentially fatal.
Risk factors and risk groups	Surgical patients who are administered fibrin sealants by a spray device.
Risk minimization measures	**Routine risk minimization measures:** Discussed in SmPC section 4.4, Special warnings and precautions for use. Listed in SmPC section 4.8, Undesirable effects. Discussed in SmPC section 6.6, Special precautions for disposal and other handling.

	Discussed in PL section 2, What you need to know before you use Tisseel/Artiss, Warnings and precautions. Discussed in PL section 3, How to use Artiss. Discussed in PL section 4, Possible side effects. **Additional risk minimization measures:** No additional risk minimization measures.
Tissue adhesion and granuloma formation due to incorrect use of the product	
Evidence for linking the risk to the medicine	Evidence source: medical literature. Application of fibrin sealants beyond the intended area of application may result in undesired tissue adherence if tissues come into contact with the sealant during onset of clotting. The impact of undesired tissue adhesion formation may range from negligible to significant depending on acuity and severity. Injury may occur if attempts are made to separate the undesired tissue adherence. If the granulation tissue forms in excessive amounts above the level of the epidermis, the wound will not heal, or defects in the skin or scar tissue may persist. Excess granulation tissue may interfere with the effectiveness of fibrin sealants and the wound healing process.
Risk factors and risk groups	Surgical patients who are administered fibrin sealants.
Risk minimization measures	**Routine risk minimization measures:** Discussed in SmPC section 4.2, Posology and method of administration Discussed in SmPC section 4.4, Special warnings and precautions for use. Discussed in PL section 2, What you need to know before you use Artiss, Warnings and precautions. **Additional risk minimization measures:** No additional risk minimization measures.

II.C Post-authorization development plan

II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligations of Artiss.

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

There are no studies required for Artiss.