6 PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

6.1 Summary of Risk Management Plan for Axumin

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

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

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

6.1.1 The Medicine and what it is Used for

Axumin is authorised for Positron Emission Tomography (PET) imaging to detect recurrence of prostate cancer in adult men with a suspected recurrence based on elevated blood prostate specific antigen (PSA) levels after primary curative treatment (see SmPC for the full indication). It contains fluciclovine (^{18}F) as the active substance and it is given by intravenous injection.

Further information about the evaluation of Axumin's benefits can be found in Axumin's EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004197/human_med_002100.jsp&mid=WC0b01ac058001d124

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

Important risks of Axumin, together with measures to minimise such risks and the proposed studies for learning more about Axumin'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 minimise the risk that the medicine is used incorrectly;
- 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 Axumin, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (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 Axumin is not yet available, it is listed under 'missing information' below.

6.1.2.1 List of Important Risks and Missing Information

Important risks of Axumin 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 Axumin. 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);

Important identified and potential risks, together with missing information, are summarised in Table 22.

Table 1: List of Important Risks and Missing Information

Important Identified Risks	Injection site reactions
Important Potential Risks	PET imaging interpretation errors Off-label use Risk due to contact with radiation (carcinogenic and hereditary risk)
Missing Information	Patients with impaired renal function Patients with impaired hepatic function

6.1.2.2 Summary of Important Risks

Important risks are summarised in Table 23 to Table 26.

Table 2: Important Identified Risk – Injection Site Reaction

Important Identified Risk – Injection Site Reaction	
Evidence for Linking the Risk to the Medicine	Clinical trial SAEs and post-marketing AEs on the global safety database for Axumin; published studies in the scientific and medical literature.
Risk Factors and Risk Groups	Not applicable – there do not appear to be any patient-related risk groups or risk factors for injection site reactions.
Risk Minimisation Measures	**Routine risk minimisation measures:** • Listed as an ADR in Section 4.8 of the SmPC. • Section 4.2 of the SmPC provides information on the correct method of administration. • Included in PL. **Additional risk minimisation measures:** None.

Table 3: Important Potential Risk – PET Imaging Interpretation Errors

Important Potential Risk – PET Imaging Interpretation Errors	
Evidence for Linking the Risk to the Medicine	Clinical trial SAEs and post-marketing AEs on the global safety database for Axumin; published studies in the scientific and medical literature.
Risk Factors and Risk Groups	There are no patient-specific risk groups or risk factors, but lack of familiarity or of complete training by image interpreters may be a risk factor for misinterpretation of imaging results. For example, normal biodistribution of fluciclovine (^{18}F) can result in uptake into muscle and the pancreas may be misinterpreted as an abnormal finding. Additionally, sub-optimal PSA levels may lead to false negative findings as the optimal performance of Axumin is linked to a PSA level of 1.05 ng/mL.
Risk Minimisation Measures	**Routine risk minimisation measures:** • Included as a warning in SmPC Section 4.4. • Section 4.2 of the SmPC provides information on the correct method of image acquisition. **Additional risk minimisation measures:** Provision of a self-training programme containing the following information: • Physiological distribution of fluciclovine. • Image interpretation guidelines. • Examples of incidental findings on PET-CT with fluciclovine. • Examples of positive and negative findings on PET-CT with fluciclovine • Demonstration cases with image interpretation provided by an expert.

Table 4: Important Potential Risk – Off-label Use

Important Potential Risk – Off-label Use	
Evidence for Linking the Risk to the Medicine	Clinical trial SAEs and post-marketing AEs on the global safety database for Axumin; published studies in the scientific and medical literature
Risk Factors and Risk Groups	There are no specific risk groups or risk factors. Any patient receiving Axumin for an off-label indication could be considered at risk.
Risk Minimisation Measures	**Routine risk minimisation measures:** • The indication for diagnostic use of the medicinal product is clearly stated in SmPC Section 4.1. • Included in PL. **Additional risk minimisation measures:** None.

Table 5: Important Potential Risk – Risk due to Contact with Radiation (Carcinogenic and Hereditary Risk)

Important Potential Risk – Risk due to Contact with Radiation (Carcinogenic and Hereditary Risk)	
Evidence for Linking the Risk to the Medicine	Clinical trial SAEs and post-marketing AEs on the global safety database for Axumin; published studies in the scientific and medical literature.
Risk Factors and Risk Groups	There are no specific risk groups or risk factors. Any patient receiving Axumin could be considered at risk.
Risk Minimisation Measures	**Routine risk minimisation measures:** • Included as a warning in SmPC Section 4.8. • SmPC Section 4.4: highlights that patients should be encouraged to drink sufficient amounts and void as often as possible during the first hours after the scan in order to reduce radiation exposure of the bladder. • Included in PL. **Additional risk minimisation measures:** None.

Missing information are summarised in Table 27 and Table 28.

Table 6: Missing Information – Patients with Impaired Renal Function

Missing Information – Patients with Impaired Renal Function	
Risk Minimisation Measures	**Routine risk minimisation measures:** • SmPC Sections 4.2 and 4.4: warning of possible increased radiation exposure. • Included in PL. **Additional risk minimisation measures:** None.

Table 7: Missing Information – Patients with Impaired Hepatic Function

Missing Information – Patients with Impaired Hepatic Function	
Risk Minimisation Measures	**Routine risk minimisation measures:** SmPC Section 4.2: warning of possible increased radiation exposure. **Additional risk minimisation measures:** None.

6.1.2.3 Postauthorisation Development Plan

6.1.2.3.1 Studies which are Conditions of the Marketing Authorisation

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

6.1.2.3.2 Other Studies in Postauthorisation Development Plan

There are no studies in the postauthorisation development plan.