Summary of risk management plan for Ivozall 1 mg/ml concentrate for solution for infusion (clofarabine)

This is a summary of the risk management plan (RMP) for Ivozall 1 mg/ml concentrate for solution for infusion. The RMP details important risks of Ivozall 1 mg/ml concentrate for solution for infusion, how these risks can be minimised, and how more information will be obtained about Ivozall 1 mg/ml concentrate for solution for infusion risks and uncertainties (missing information).

Ivozall 1 mg/ml concentrate for solution for infusion summary of product characteristics (SmPC) and patient leaflet give essential information to healthcare professionals and patients on how Ivozall 1 mg/ml concentrate for solution for infusion should be used.

Important new concerns or changes to the current ones will be included in updates of Ivozall 1 mg/ml concentrate for solution for infusion RMP.

I. The medicine and what it is used for

Ivozall 1 mg/ml concentrate for solution for infusion is authorised for Treatment of acute lymphoblastic leukaemia (ALL) in paediatric patients who have relapsed or are refractory after receiving at least two prior regimens and where there is no other treatment option anticipated to result in a durable response. It contains clofarabine as the active substance and it is given by intravenous route.

Further information about the evaluation of Ivozall 1 mg/ml concentrate for solution for infusion 's benefits can be found in Ivozall 1 mg/ml concentrate for solution for infusion 's EPAR, including in its plain-language summary, available on the EMA website, under the EMA webpage https://www.ema.europa.eu/en/medicines/human/EPAR/ivozall.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Ivozall 1 mg/ml concentrate for solution for infusion together with measures to minimise such risks and the proposed studies for learning more about Ivozall 1 mg/ml concentrate for solution for infusion risks, are outlined below.

Measures to minimise the risks identified for medicinal products include specific information, such as warnings, precautions, and advice on correct use, in the SmPC addressed to healthcare professionals.

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, 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 Ivozall 1 mg/ml concentrate for solution for infusion is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Ivozall 1 mg/ml concentrate for solution for infusion 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 Ivozall 1 mg/ml concentrate for solution for infusion. 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);

List of important risks and missing information	
Important identified risks	Bone marrow failure (myelosuppression) Infection (septic shock, sepsis, bacteremia, pneumonia, herpes zoster, herpes simplex, Clostridium difficile colitis, oral candidiasis) Hepatotoxicity Veno-occlusive liver disease Cardiotoxicity Tumor lysis syndrome Systemic inflammatory response syndrome and capillary leak syndrome Stevens Johnson syndrome and toxic epidermal necrolysis Pancreatitis Rash Enterocolitis, including neutropenic colitis, caecitis and C. difficile colitis Hemorrhage, including cerebral, gastrointestinal and pulmonary hemorrhage Hepatitis Hepatic failure
Important potential risks	Nephropathy toxic Teratogenicity Infertility Off-label use in pediatric AML, in ALL patients with less than two prior regimens, or in combination with other drugs
Missing information	Safety of use for more than 3 cycles Drug interaction with commonly used co-medications Tolerability and pharmacokinetics in renal impairment Tolerability and pharmacokinetics in hepatic impairment Tolerability and pharmacokinetics in cardiac impairment

List of important risks and missing information	
	Pregnancy

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

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 Ivozall 1 mg/ml concentrate for solution for infusion.

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

There are no studies required for Ivozall 1 mg/ml concentrate for solution for infusion.