# PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

**Summary of Risk Management Plan for Clinimix, solution for infusion**

This is a summary of the Risk Management Plan (RMP) for the following Clinimix, solution for infusion formulations: N9G15E, N9G20E, N12G20, N12G20E, N14G30, N14G30E, N17G35 and N17G35E (all hereafter referenced as Clinimix). The RMP provides details on the risks of Clinimix, how these risks can be minimized and how more information will be obtained about the important risks.

The Summary of Product Characteristics (SmPC) and Package Leaflet (PL) for Clinimix provide essential information to healthcare professionals and patients on how Clinimix 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**

Clinimix is authorized for parenteral nutrition when oral or enteral alimentation is impossible, insufficient, or contraindicated; refer to the SmPC for complete indication wording. Clinimix is given intravenously, and it contains the following active substances:

L-alanine, L-arginine, glycine, L-histidine, L-isoleucine, L-leucine, L-lysine as hydrochloride, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine, L-valine, glucose monohydrate

Clinimix formulations with electrolytes also contain sodium acetate trihydrate, dibasic potassium phosphate, sodium chloride, magnesium chloride hexahydrate, calcium chloride dihydrate.

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

The important risks of Clinimix, together with measures to minimize such risks are outlined below. Measures to minimize 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 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).

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

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including periodic safety update report assessment, 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 table below presents the list of important risks and missing information included in the RMP for Clinimix.

| **List of important risks and missing information** | |
|---|---|
| **Important identified risk** | None |
| **Important potential risk** | Adverse outcomes in neonates treated with solutions not protected from light |
| **Missing information** | None |

### *II.B Summary of important risks and missing information*

| **Important potential risk: Adverse outcomes in neonates treated with solutions not protected from light** | |
|---|---|
| **Evidence for linking the risk to the medicine** | Medical literature. |

| | |
|---|---|
| **Risk factors and risk groups** | Light exposure of solutions for intravenous parenteral nutrition, especially after admixture with trace elements and/or vitamins, may have adverse effects on clinical outcome in neonates due to the generation of peroxides and other degradation products. Several conditions related to prematurity with insufficient anti-oxidative capacity are thought to be risk factors for the underlying pathological mechanism related to generation of peroxides. Very premature neonates are considered at high risk of oxidative stress related to multiple risk factors including oxygen therapy, weak immune system and inflammatory response with reduced oxidant defense and exposure to high energy light (phototherapy). |
| **Risk minimization measures** | **Routine risk minimization measures:**<br>Discussed in the SmPC sections 4.2, 4.4, 6.3 and 6.6.<br>Discussed in the PL sections 2, 3 and 5.<br>Discussed in the PL, sections 2, 3 and 4, under the information intended for healthcare professionals only.<br>Legal status: subject to medical prescription.<br>**Additional risk minimization measures:**<br>DHPC (completed). |

## *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 Clinimix.

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

There are no studies required for Clinimix.