Summary of risk management plan for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe (filgrastim)

This is a summary of the risk management plan (RMP) for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe. The RMP details important risks for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe, how these risks can be minimised, and how more information will be obtained about for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe's risks and uncertainties (missing information).

Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe should be used.

This summary of the RMP for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/ infusion in pre-filled syringe 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 Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe's RMP.

I. The medicine and what it is used for

Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe is indicated for the reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes) (see SmPC for the full indication).
It contains filgrastim as the active substance and it is given by subcutaneous or intravenous route.

Further information about the evaluation of Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe's benefits can be found in Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe's EPAR, including in its plain-

language summary, available on the EMA website, under the medicine's webpage. https://www.ema.europa.eu/en/medicines/human/EPAR/grastofil

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

Important risks of Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe, together with measures to minimise such risks and the proposed studies for learning more about Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe'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 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 and signal management activity, 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 Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe 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 Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/ infusion in pre-filled syringe. 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 risks	• Acute febrile neutrophilic dermatosis (Sweet's syndrome) • Acute respiratory distress syndrome • Capillary leak syndrome • Cutaneous Vasculitis • Exacerbation of rheumatoid arthritis • Graft versus Host Disease (GvHD) • Haemoptysis • Hypersensitivity (including anaphylaxis) • Interstitial pneumonia • Lung infiltration • Osteoporosis in patient with SCN • Pulmonary haemorrhage • Sickle cell anaemia with crisis • Splenomegaly/Splenic rupture • Transformation to leukaemia or myelodisplastic syndrome (in patients with severe chronic neutropenia) • Thrombocytopenia
Important potential risks	• Cytokine release syndrome • Immunogenicity • Interaction with lithium • Malignant cell growth (haematological malignancy and myelodysplastic syndrome) in healthy stem cell donors • Risks in long term use • Risks in off-label use • Extramedullary hematopoiesis

Missing information	• Risks in pregnancy and lactation

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 conditions of the marketing authorization or specific obligation of Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe.

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

There are no studies required for Grastofil 30 MU/0.5 ml and 48 MU/0.5 ml solution for injection/infusion in pre-filled syringe as post-authorisation development plan.