Summary of the risk management plan for Sogroya (somapacitan)

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

Sogroya's Summary of Product Characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals (HCPs) and patients on how Sogroya should be used.

This summary of the RMP for Sogroya 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 EPAR.

Important new concerns or changes to the current ones will be included in the updates of Sogroya's RMP.

I. The medicine and what it is used for

Sogroya is authorised for the indication of adults with growth hormone deficiency (AGHD; see SmPC for the full indication). Sogroya contains somapacitan, a long-acting recombinant human growth hormone (rhGH) derivative and it is given once weekly by subcutaneous (s.c.) injection.

Further information about the evaluation of Sogroya's benefits can be found in Sogroya's EPAR, including in its plain-language summary, available on the EMA website under the medicine's webpage: EPAR link.

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

Important risks of Sogroya, together with measures to minimise such risks and the proposed studies for learning more about Sogroya's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be as follows:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and the SmPC addressed to patients and HCPs;
- 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 public (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 events 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 Sogroya is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Sogroya 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 Sogroya. 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). An overview of important risks and missing information for Sogroya is provided in the table below.

List of important risks and missing information	
Important identified risks	None
Important potential risks	• Neoplasms • Diabetes mellitus type 2 • Medication errors (Incorrect dose administration rate) • Off-label paediatric use
Missing information	• Patient with heart failure, NYHA class >2 • Patients with severe hepatic impairment • Long-term safety

Abbreviations: NYHA = New York Heart Association.

II.B Summary of important risks and missing information

There are no important identified risks for Sogroya.

Important potential risk – Neoplasms	
Evidence for linking the risk to the medicine	• Completed Sogroya phase 3 clinical trials • Post-marketing safety surveillance of marketed GH products • Literature of marketed GH products
Risk factors and risk groups	• Patients with a previous neoplasm have an increased risk of relapse of the same tumour type without treatment due to the biology of the disease. • Patients with prior neoplasms may have an increased risk of developing second neoplasms when treated with GH, especially if they had received prior treatment with radiotherapy. The risk of second neoplasms in patients with previous neoplasms treated with growth hormone treatment (GHT) was lower after an extended follow-up and became non-significant after adjusting for sex, age at primary diagnosis, dose/time, and treatment type. A recent metanalysis does not find increased risks of recurrence or second neoplasms in childhood cancer survivors treated with GH.
Risk minimisation measures	**Routine risk minimisation measures** <u>Routine risk communication</u>: • SmPC Section 4.3, where a contraindication concerning any evidence of activity of a tumour is included. <u>Risk minimisation activities recommending specific clinical measures to address the risk</u>: • SmPC Section 4.4, where a special warning is included on neoplasms. • PL Section 2, where information is included on tumours. <u>Other risk minimisation measures beyond the Product Information</u>: • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	PASS NN8640-4515

Abbreviations: GH = growth hormone; PASS = post-authorisation safety study; PL = package leaflet; SmPC = Summary of Product Characteristics.

Important potential risk − Diabetes mellitus type 2	
Evidence for linking the risk to the medicine	A large observational study of patients treated with GH in childhood concluded that the patients had an increased risk of developing type 2 diabetes mellitus compared with the general population. However, most patients had diabetes risk factors and certain patient populations receiving GH treatment are inherently at risk of developing type 2 diabetes mellitus. Due to the low number of subjects exposed to Sogroya in the completed clinical trials, the strength of evidence for the risk of development of type 2 diabetes mellitus in Sogroya-treated subjects is limited.
Risk factors and risk groups	• Family history of diabetes mellitus • Pre-existing diabetes mellitus, type 1 or type 2 • Impaired glucose tolerance • Obesity
Risk minimisation measures	**Routine risk minimisation measures** Routine risk communication: • SmPC Section 4.2, where information is included concerning individual dose requirements based on the clinical response and serum IGF-I concentration. Risk minimisation activities recommending specific clinical measures to address the risk: • SmPC Section 4.4, where a special warning is included on glucose metabolism impairment. • PL Section 2, where information is included on high blood sugar. Other risk minimisation measures beyond the Product Information: • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	PASS NN8640-4515

Abbreviations: GH = growth hormone; IGF-I = insulin-like growth factor-I; PASS = post-authorisation safety study; PL = package leaflet; SmPC = Summary of Product Characteristics.

Important potential risk – Medication errors (Incorrect dose administration rate)	
Evidence for linking the risk to the medicine	When patients are used to taking their injection daily, there is a risk that this will continue.
Risk factors and risk groups	Patients switching from daily to weekly dosing.
Risk minimisation measures	**Routine risk minimisation measures** Routine risk communication: • SmPC Section 4.2, where information is included concerning the appropriately qualified and experienced physicians to initiate and monitor Sogroya treatment. In addition, Section 4.2 gives clear instructions regarding once-weekly dose, how to change the dosing day and the steps to follow when a dose is missed. • SmPC Section 5.1, where information regarding maintenance dose is included. Risk minimisation activities recommending specific clinical measures to address the risk: • Labelling Section 5, where the term 'Once weekly' is printed on the carton (on the inner and outer package in multi-package) and preload pen label. • PL Section 3, where information is included concerning how and when to use Sogroya. Other risk minimisation measures beyond the Product Information: • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	PASS NN8640-4515

Abbreviations: PASS = post-authorisation safety study; PL = package leaflet; SmPC = Summary of Product Characteristics.

Important potential risk – Off-label paediatric use	
Evidence for linking the risk to the medicine	The safety experience of Sogroya in the paediatric population below 18 years of age is limited. Novo Nordisk is conducting 3 clinical trials in paediatric population: two phase 2 trials (for GHD and children with short stature born small for gestational age) and one phase 3 trial (for GHD). As no completed phase 2 or phase 3 clinical trial data from the paediatric population are available, Novo Nordisk has included 'Off-label paediatric use' as an important potential risk.
Risk factors and risk groups	The paediatric populations (see above) that are currently evaluated in the ongoing clinical trials: • Children with GHD • Children with short stature born small for gestational age
Risk minimisation measures	**Routine risk minimisation measures** <u>Routine risk communication:</u> • SmPC Section 4.1, where information is included concerning the therapeutic indication. • SmPC Section 4.2, under 'Special population', where information is included on paediatric population below 18 years of age. <u>Risk minimisation activities recommending specific clinical measures to address the risk:</u> • SmPC Section 4.4, where a special warning is included on paediatric population below 18 years of age. • PL Section 2, where information is included on paediatric population below 18 years of age. <u>Other risk minimisation measures beyond the Product Information:</u> • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	None

Abbreviations: GHD = growth hormone deficiency; PL = package leaflet; SmPC = Summary of Product Characteristics.

Missing information − Patients with heart failure (NYHA class >2)	
Risk minimisation measures	**Routine risk minimisation measures** Routine risk communication: • SmPC Section 4.2, where information is included concerning individual dose requirements based on the clinical response and serum IGF-I concentration. Risk minimisation activities recommending specific clinical measures to address the risk: • None proposed Other risk minimisation measures beyond the Product Information: • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	PASS NN8640-4515

Abbreviations: IGF-I = insulin-like growth factor-I; NYHA = New York Heart Association; PASS = post-authorisation safety study; SmPC = Summary of Product Characteristics.

Missing information − Patients with severe hepatic impairment	
Risk minimisation measures	**Routine risk minimisation measures** Routine risk communication: • SmPC Section 4.2, where information is included concerning individual dose requirements based on the clinical response and serum IGF-I concentration. • SmPC Section 4.2, under 'Special population', where information is included on patients with severe hepatic impairment. Risk minimisation activities recommending specific clinical measures to address the risk: • None proposed Other risk minimisation measures beyond the Product Information: • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	PASS NN8640-4515

Abbreviations: IGF-I = insulin-like growth factor-I; PASS = post-authorisation safety study; SmPC = Summary of Product Characteristics.

Missing information − Long-term safety	
Risk minimisation measures	**Routine risk minimisation measures** <u>Routine risk communication:</u> • None proposed <u>Risk minimisation activities recommending specific clinical measures to address the risk:</u> • None proposed <u>Other risk minimisation measures beyond the Product Information:</u> • Medicine's legal status: • Sogroya is a restricted prescription-only medicine, prescribed by specialists. **Additional risk minimisation measures** • None proposed
Additional pharmacovigilance activities	PASS NN8640-4515

Abbreviations: PASS = post-authorisation safety study.

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.

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

Novo Nordisk will conduct a long-term post-authorisation safety study (PASS) in patients with AGHD. This is a multinational, multicentre, prospective, open-label, single-arm, observational, non-interventional PASS to investigate long-term safety of Sogroya in AGHD under normal clinical practice conditions.

Purpose of the study

The aim of this study is firstly to characterise the safety profile of Sogroya with special focus on the important potential risks (Neoplasms, Diabetes mellitus type 2 and Medication errors [Incorrect dose administration rate]) and missing information (Patients with heart failure, New York Heart Association [NYHA] class >2, Patients with severe hepatic impairment and Long-term safety), and secondly to further describe effectiveness parameters possibly associated with Sogroya treatment.