RMP Summary

Sogroya®

(somapacitan)

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Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of Sogroya® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Sogroya® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic.

Novo Nordisk Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Sogroya®.

Summary of the risk management plan for Sogroya®

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 the 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 has been authorised for the indications of adults with growth hormone deficiency (AGHD) and paediatric GHD (see SmPC for the full indications). 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: https://www.ema.europa.eu/en/medicines/human/EPAR/sogroya

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 minimises 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.

In connection with the submission of application for the paediatric GHD indication and the 15 mg/1.5 mL strength, the important potential risk 'Off-label paediatric use' has been removed.

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)
Missing information	• Patients with heart failure, NYHA class >2 (for AGHD only) • Patients with severe hepatic impairment (for AGHD only) • Long-term safety

Abbreviations: AGHD = adults with growth hormone deficiency; NYHA = New York Heart Association.

II.B Summary of important risks and missing information

Important identified risks

There are no important identified risks for Sogroya.

Important potential risks

The tables below summarise important potential risks for Sogroya.

Important potential risks	
Neoplasms	
Evidence for linking the risk to the medicine	Overall, based on the medical evaluation from the below sources, no causal relationship has been identified supporting an association with somapacitan and neoplasms. • Completed Sogroya phase 3a clinical trials • Post-marketing safety surveillance of marketed GH products • Literature of marketed GH products • Consensus safety report
Risk factors and risk groups	• Patients with previous neoplasms have an increased risk of relapse of the same tumour type without treatment due to the nature 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	**<u>Routine risk minimisation measures</u>** ***Routine risk communication:*** • SmPC Section 4.3, where a contraindication concerning any evidence of activity of a tumour is included. ***Risk minimisation activities recommending specific clinical measures to address the risk:*** • SmPC Section 4.4, where a special warning is included on neoplasms. • PL Section 2, where information is included on tumours.

	Other risk minimisation measures beyond the Product Information: • Medicine's legal status: ○ Sogroya is a restricted prescription-only medicine, prescribed by specialists. ***<u>Additional risk minimisation measures:</u>*** None proposed.
Additional pharmacovigilance activities	• Paediatric GHD register-based study NN8640-4787 • Trial NN8640-4172 with safety extension part • Trial NN8640-4263 with safety extension part • AGHD PASS NN8640-4515
Diabetes mellitus type 2	
Evidence for linking the risk to the medicine	In the observational Genetics and Neuroendocrinology of Short Stature International Study (GeNeSIS), data from 11,686 GH-treated patients were analysed for incidence of diabetes mellitus. In the GHD subpopulation (age 0−19 years), the incidence rate was 30.4 per 100,000 patient-years of exposure for type 1 diabetes and 40.5 for type 2 diabetes. From the Pfizer International Metabolic Database (KIMS), the incidence of diabetes was investigated in a cohort of 5,143 AGHD. Mean follow-up time was 3.9 years with a total number of 20,106 patient-years. In total, 10% of the patients developed diabetes after a median period of 1.7 years. The overall incidence of diabetes was 26 per 1,000 patient-years. The incidence gradually decreased from the highest level of 41 per 1,000 patient-years during the first year of GH treatment to 10 per 1,000 patient-years after more than 8 years of GH treatment. The incidence was the same for both genders. When compared to both the Swedish as well as other (European and US) age-matched reference populations the diabetes incidence in KIMS was significantly higher. The authors note that the patients who developed diabetes differed at baseline with regards to the classical risk factors of diabetes (e.g., being older, having a higher BMI, waist circumference, triglyceride concentrations, and blood pressure) compared to the patients who did not develop

	diabetes, and further, that the presence of any of these risk factors considerably increases the risk of developing diabetes.
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 indications of paediatric GHD and AGHD, 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: o Sogroya is a restricted prescription-only medicine, prescribed by specialists. ***Additional risk minimisation measures*** • None proposed
Additional pharmacovigilance activities	• Paediatric GHD register-based study NN8640-4787 • Trial NN8640-4172 with safety extension part • Trial NN8640-4263 with safety extension part • AGHD PASS NN8640-4515

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	**<u>Routine risk minimisation measures</u>** ***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. ***<u>Additional risk minimisation measures:</u>*** None proposed.
Additional pharmacovigilance activities	• Paediatric GHD register-based study NN8640-4787 • Trial NN8640-4172 with safety extension part • Trial NN8640-4263 with safety extension part • AGHD PASS NN8640-4515

Abbreviations: AGHD = adults with growth hormone deficiency; GH = growth hormone; GHD = growth hormone deficiency; IGF-I = insulin-like growth factor-I; KIMS = Pfizer International Metabolic Database; PASS = post-authorisation safety study; PL = package leaflet; SmPC = Summary of Product Characteristics.

Missing information

The tables below summarise missing information for Sogroya.

Missing information	
Patients with heart failure (NYHA class >2) (for AGHD only)	
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	AGHD PASS NN8640-4515
Patients with severe hepatic impairment (for AGHD only)	
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: o Sogroya is a restricted prescription-only medicine, prescribed by specialists. ***Additional risk minimisation measures*** None proposed
Additional pharmacovigilance activities	AGHD PASS NN8640-4515
Long-term safety	
Risk minimisation measures	**Routine risk minimisation measures** ***Routine risk communication:*** • None proposed ***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: o Sogroya is a restricted prescription-only medicine, prescribed by specialists. ***Additional risk minimisation measures*** None proposed

Additional pharmacovigilance activities	• Paediatric GHD register-based study NN8640-4787 • Trial NN8640-4172 with safety extension part • Trial NN8640-4263 with safety extension part • AGHD PASS NN8640-4515

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

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

Paediatric GHD

Register-based study NN8640-4787

Novo Nordisk will conduct a long-term post-authorisation register-based study in paediatric patients with GHD. This is a non-interventional, observational, register-based study to investigate long-term safety and clinical parameters of once-weekly somapacitan treatment in paediatric patients with GHD in the setting of routine clinical practice.

Purpose of the study

The aim of this register-based study is to evaluate long-term safety and clinical parameters of once- weekly Sogroya treatment in paediatric GHD in the setting of routine clinical practice.

Clinical trial NN8640-4172 (phase 2)

This is a randomised, multinational, active-controlled (open-labelled), dose finding (double-blinded), parallel group trial investigating efficacy and safety of once-weekly somapacitan treatment compared to daily GH treatment (Norditropin) in GH treatment naïve pre-pubertal children with GHD.

The trial has completed the main trial period and is now in the long-term safety extension period.

Purpose of the trial

The overall purpose of the trial is to evaluate the long-term efficacy and safety of multiple dose regimens of once-weekly somapacitan treatment in GH treatment naïve pre-pubertal children with GHD, compared to daily Norditropin.

Clinical trial NN8640-4263 (phase 3a)

This is a randomised trial comparing the effect and safety of once-weekly dosing of somapacitan with daily Norditropin in children with GHD.

The trial has completed the main trial period and is now in the safety extension period.

Purpose of the trial

The overall purpose of the trial is to compare the effect and safety of once-weekly somapacitan vs daily Norditropin in children with GHD.

Adults with growth hormone deficiency

Post-authorisation safety study NN8640-4515

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

Purpose of the study

The primary aim of this PASS is to characterise the long-term safety profile of Sogroya with special focus on the important potential risks (diabetes mellitus type 2, neoplasms and medication errors). Therefore, this PASS may allow a further evaluation of these potential risks in relation to treatment with Sogroya. Medication errors are of specific interest since some patients will switch from daily GH injections to weekly injections with Sogroya. Therefore, the PASS may provide information on whether this might lead to medication errors in clinical practice.