RMP Summary

Awiqli®

(insulin icodec)

Based on: EU RMP Version 0.1
Document Version: 1.0
Document Date: 30-Apr-2024

Novo Nordisk Pharma AG The Circle 32 / 38 CH-8058 Zürich www.novonordisk.ch Tel. +41 44 914 11 11

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 Awiqli® 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 Awiqli® 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 Awiqli®.

Summary of the risk management plan for Awiqli®

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

Awiqli's summary of product characteristics (EU PI) and its package leaflet give essential information to healthcare professionals and patients on how Awiqli should be used.

This summary of the RMP for Awiqli 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 updates of Awiqli's RMP.

I. The medicine and what it is used for

Awiqli is proposed for the treatment of diabetes mellitus in adults. It contains insulin icodec as the active substance and it is given by subcutaneous injection.

Further information about the evaluation of Awiqli's benefits can be found in Awiqli'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 Awiqli, together with measures to minimise such risks and the proposed studies for learning more about Awiqli'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 EU PI 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 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, 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 Awiqli 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 Awiqli. 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	• Hypoglycaemia • Hypersensitivity
Important potential risks	• Immunological events − formation of neutralising insulin antibodies • Medication errors due to potential mix-up • Medication errors during switch from daily basal insulin
Missing information	• Pregnancy and lactation • Elderly patients ≥75 years of age

II.B Summary of important risks and missing information

An overview of important identified risks, important potential risks and missing information for Awiqli is provided in the tables below.

Important identified risks	
Hypoglycaemia	
Evidence for linking the risk to the medicine	Hypoglycaemia is a well-established risk and the most commonly observed adverse reaction in patients using insulin products. This can be attributed to the pharmacological mechanism of action of insulin. For insulin icodec, the risk has been confirmed in clinical trial settings.
Risk factors and risk groups	• All patients with diabetes treated with insulin. • Individual factors such as dietary habits, dosage, switching between regimens, exercise, and stress. • Intensity of glucose control. • Hypoglycaemic symptom unawareness and long-duration diabetes. • Hepatic and/or renal insufficiency. • Treatment with substances reducing insulin requirements (OADs, GLP- 1, monoamine oxidase inhibitors, angiotensin-converting enzyme inhibitors, salicylates, anabolic steroids, and sulphonamides). • Treatment with substances masking symptoms of hypoglycaemia (beta-blockers).
Risk minimisation measures	**<u>Routine risk minimisation measures</u>** ***Routine risk communication:*** • The identified risk of hypoglycaemic reactions is addressed in Sections 4.4 , 4.5 , 4.8, and 4.9 of the SmPC • Additional information can be found in Section 2, Section 3, and Section 4 in the PL ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • Warnings concerning effects of exercise, illness, and meal omission, among other considerations, on hypoglycaemia frequency (Section 4.4 SmPC)

	• Warning that hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement (see Sections 4.4, 4.5, 4.8 and 4.9 SmPC) • Warning concerning switching from daily basal insulins and the potential risk for hypoglycaemia with the continuation of the one-time additional dose with subsequent dosing (Section 4.4 SmPC) • Warnings concerning hypoglycaemia awareness symptoms and changes to this which may occur during the treatment regimen (4.4 of SmPC, Section 2 of the PL) • Warning concerning the risk for hypoglycaemia with sudden changes to new injection site following rotation from an injection site with lipodystrophy or cutaneous amyloidosis (Section 4.4 of SmPC) • Listing of concomitant medicines which can increase chance of hypoglycaemic event (section 4.5 SmPC) ***Other risk minimisation measures beyond the Product Information:*** • This medicine is only available by prescription. ***<u>Additional risk minimisation measures:</u>*** • None.
Hypersensitivity	
Evidence for linking the risk to the medicine	This is a class risk for all protein-based medicinal products. The prevalence of insulin allergy has decreased with the use of recombinant insulin. Hypersensitivity (manifested with swelling of face and lips, and urticaria) has been observed across the phase 3a programme in study subjects with diabetes receiving insulin icodec. Hypersensitivity has been included as an uncommon ADR in the product information.
Risk factors and risk groups	Patients with a history of allergic reactions or with known hypersensitivity to insulin icodec or any of the excipients are at higher risk.

	The risk of hypersensitivity reactions is expected to be higher with the initial administrations compared with subsequent administrations.
Risk minimisation measures	**Routine risk minimisation measures** ***Routine risk communication:*** • The identified risk of hypersensitivity reactions is addressed in Section 4.8 of the SmPC and in section 2 of the PL • Known hypersensitivity to the active substance or any of the excipients is listed as a contradiction in Section 4.3 of the SmPC • Information concerning allergic reactions is addressed in Section 4 of the PL. ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • Warning that known hypersensitivity to the active substance or any of the excipients is listed as a contradiction in Section 4.3 of the SmPC • Warning, in Section 2 of the PL, not to use Awiqli if you are allergic to insulin icodec or any other ingredients in the medicine • Instruction to discontinue use and see a doctor if there is a serious allergic reaction to the insulin or any of the ingredients in Awiqli in Section 4 of the PL. ***Other risk minimisation measures beyond the Product Information:*** • This medicine is only available by prescription. ***Additional risk minimisation measures*** • None

Abbreviations: EU PI = European Union product information ; GLP-1 = glucagon-like peptide-1; OAD = oral anti-diabetic drug; PL = product leaflet ; SmPC = Summary of Product Characteristics.

Important potential risks	
Immunological events − formation of neutralising insulin antibodies	
Evidence for linking the risk to the medicine	Formation of neutralising antibodies is a potential risk with all protein-based drugs and could lead to potential neutralisation of the effects of insulin. While anti-insulin antibodies were reported as part of the phase 3a programme for insulin icodec, no clinical consequence corresponding to these cases has been described.
Risk factors and risk groups	All patients treated with insulin analogues are potentially at risk for the generation of anti-insulin antibodies with clinical consequence.
Risk minimisation measures	**Routine risk minimisation measures** ***Routine risk communication:*** • The potential risk of anti-insulin antibodies is addressed in Section 4.4 of the SmPC. ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • In Section 4.4 of the SmPC, the text specifies that, in rare cases, dose adjustment may be required to establish correct glycaemic control. • Warning, in Section 2 of the PL, not to use Awiqli if you are allergic to insulin icodec or any other ingredients in the medicine ***Other risk minimisation measures beyond the Product Information:*** • This medicine is only available by prescription. ***Additional risk minimisation measures*** • None
Medication errors due to potential mix-up	
Evidence for linking the risk to the medicine	Medication errors are a known risk for many insulin products. Medication errors in clinical trials are systematically collected and the cases are well documented. However, clinical trials are unrepresentative of clinical practice and the appearance of the device (labelling and cartridge colour) are not the same as the marketed device.

Risk factors and risk groups	Diabetic patients treated with basal–bolus insulin therapy (or other injectable medicine), patients with diabetes living with another person with diabetes, and visually impaired or colour-blind patients may be at a higher risk.
Risk minimisation measures	**Routine risk minimisation measures** ***Routine risk communication:*** • The risk of mix-ups is presented in Section 4.4 of the SmPC and Section 2 of the PL. ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • Instructions for avoidance of medication errors are described in Section 4.4 of the SmPC and Section 2 of the PL • Recommendations in Section 4.4 of the SmPC and Section 3 of the PL indicates that patients with impaired vision require assistance from a person with good vision • Product appearance is described in Section 6 of the PL to prevent misidentification of medicine ***Other risk minimisation measures beyond the Product Information:*** • Product differentiation strategy to reduce misidentification; includes trade name, label text, colour branding of the carton, container label and cartridge holder. • This medicine is only available by prescription. ***Additional risk minimisation measures*** • None
Medication errors during switch from daily basal insulin	
Evidence for linking the risk to the medicine	A one-time additional dose of insulin icodec is recommended to be utilised, during the switch to insulin icodec from daily basal insulins (and not for insulin-naïve patients). Incorrect dosing of the one-time additional dose, or following doses, can potentially result in hypoglycaemic events due to overdosing or hyperglycaemic events in the case of underdosing. Completed phase 3a studies using a device in which insulin icodec was used as the investigational drug are the evidence sources of this risk.

Risk factors and risk groups	Diabetic patients switching from daily basal insulins to insulin icodec represent the most significant risk group. Additionally, as with all injectable insulins using pen delivery systems, patients who have vision impairments may be at a higher risk due to challenges with selecting the correct dose and may require assistance to safely use the pen-injector correctly.
Risk minimisation measures	**Routine risk minimisation measures** ***Routine risk communication:*** • The risk related to switching from daily basal insulin products is presented in Sections 4.2, 4.4, and 4.9 of the SmPC and Section 2 of the PL ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • Instructions for switching from other daily basal insulins to insulin icodec, including a dose calculation table presenting the recommended one-time additional dose and second dose based on the daily basal insulin dosing regimen, are presented in Section 4.2 of the SmPC • Patients must be instructed to check that they inject the correct dose, especially in the first and second injection (Section 4.4 of the SmPC). It is also indicated in Section 4.2 of the SmPC and Section 2 of the PL that the one-time additional dose is not to be continued with subsequent doses • Patients who are uncertain about the correct dose must be instructed to consult their physician for further guidance (Section 4.4 of the SmPC) • A recommendation to only begin a switch to insulin icodec from another insulin under medical supervision is included in Section 4.4. of the SmPC and Section 2 of the PL • In Section 3 of the PL, switching to insulin icodec is discussed with specific mention that a doctor should prescribe you the first and second dose, and that subsequent doses should be determined in consultation with a doctor • In Section 4.9 of the SmPC, specific warning is included concerning the risk for overdose if the one-time additional dose continues to be taken with subsequent dosing.

	• Recommendations in Section 4.4 of the SmPC and Section 3 of the PL indicates that patients with impaired vision require assistance from a person with good vision ***Other risk minimisation measures beyond the Product Information:*** • This medicine is only available by prescription ***Additional risk minimisation measures*** • None

Abbreviations: EU PI = European Union product information ; PL = product leaflet ; SmPC = Summary of Product Characteristics.

Missing information	
Pregnancy and lactation	
Risk minimisation measures	***Routine risk communication:*** • Lack of experience in this population is mentioned in Section 4.6 of the SmPC (Fertility, pregnancy and lactation). ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • In Section 2 of the PL, patients are encouraged to discuss with a doctor, nurse or pharmacist whether to begin therapy with insulin icodec while pregnant or breast feeding. ***Other risk minimisation measures beyond the Product Information:*** • This medicine is only available by prescription.
Elderly patients ≥75 years of age	
Risk minimisation measures	***Routine risk communication:*** • In Section 4.2 in the SmPC under special populations the following text is included: Awiqli can be used in elderly patients. • It is also stated that the therapeutic experience in patients ≥ 75 years of age is limited. • In Section 5.2 in the SmPC, it is included that the pharmacokinetic properties of insulin icodec were preserved

	and there was no clinically relevant difference in exposure between elderly and younger adult subjects ***Routine risk minimisation activities recommending specific clinical measures to address the risk:*** • In Section 4.2 and 4.6 of the EU PI and Section 2 of the PL, elderly patients are encouraged to monitor their blood glucose more frequently ***Other risk minimisation measures beyond the Product Information:*** • This medicine is only available by prescription.

Abbreviations: EU PI = European Union product information ; PL = product leaflet ; 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 or specific obligation of Awiqli.

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

There are no studies required for Awiqli.