Part VI: Summary of the Risk Management Plan

Summary of the Risk Management Plan for BELKYRA (deoxycholic acid)

This is a summary of the Risk Management Plan (RMP) for BELKYRA®. The RMP details important risks of BELKYRA®, how these risks can be minimised, and how more information will be obtained about the risks and uncertainties (missing information) of BELKYRA®.

BELKYRA®'s Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how BELKYRA® should be used.

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

I. The medicine and what it is used for

Belkyra is indicated for the treatment of moderate to severe convexity or fullness associated with submental fat (see the SmPC for the full indication). It contains deoxycholic acid as the active substance and it is given via subcutaneous administration only.

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

Important risks of BELKYRA®, together with measures to minimise such risks and the proposed studies for learning more about BELKYRA®, '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 PL 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 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 a prescription) can help to minimise its risks.

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

In the case of BELKYRA®, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and is regularly analysed, including Periodic Safety Update Report (PSUR) assessment that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of BELKYRA® is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of BELKYRA® 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 BELKYRA®. 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).

Summary of safety concerns	
Important identified risks	Injection site nerve injury Injection site skin ulceration Injection site necrosis
Important potential risks	Off-label use
Missing information	Use during pregnancy Use during lactation

II.B Summary of important risks

Important identified risk • Injection site nerve injury	
Evidence for linking the risk to the medicine	AE data from the clinical study program and nonclinical data.
Risk factors and risk groups	Patients can be assumed to be at increased risk for nerve injury when BELKYRA is not administered strictly as recommended (eg, at higher volumes, outside of the submental area, with longer needles), or when the product is administered to patients with undiagnosed local pathologies or anatomical variations.

Risk minimisation measures	Routine risk communication: Listed in SmPC section(s): Undesirable effects Listed in PL section(s): Possible side effects Routine risk minimisation activities recommending specific clinical measures to address the risk: Recommendations included in SmPC section(s): Posology and method of administration; Special warnings and precautions for use; Recommendations included in PL: Warnings and precautions; Posology and method of administration; Other routine RMMs beyond the Product Information: Pack size: BELKYRA is supplied in ready-to-use, single-use vials Legal status: BELKYRA should only be administered by physicians with appropriate qualifications, expertise in the treatment and knowledge of the submental anatomy. Where national guidance permits, Belkyra may be administered by appropriately qualified healthcare professionals, under the supervision of a physician. Additional RMMs: Injector's Guide for Safe use of Belkyra
Additional pharmacovigilance activities	CONTOUR Registry (Australia) PASS Physicians' Survey to Assess Effectiveness of BELKYRA Risk Minimisation Activities (EU)

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

Important identified risk • Injection site skin ulceration	
Evidence for linking the risk to the medicine	AE data from post-marketing.
Risk factors and risk groups	It may be hypothesised that patients are at increased risk for injection site skin ulceration when BELKYRA is not administered strictly as recommended, e.g., in case of too superficial (intradermal) injection, injection during withdrawal of the syringe from the skin, or injection into infected tissue.
Risk minimisation measures	Routine risk communication: Listed in SmPC section(s): Undesirable effects Listed in PL section(s): Possible side effects Routine risk minimisation activities recommending specific clinical measures to address the risk: Recommendations included in SmPC section(s): Special warnings and precautions for use; Recommendations included in PL: Warnings and precautions; Other routine RMMs beyond the Product Information: Pack size: BELKYRA is supplied in ready-to-use, single-use vials Legal status: BELKYRA should only be administered by physicians with appropriate qualifications, expertise in the treatment and knowledge of the submental anatomy. Where national guidance permits, Belkyra may be administered by appropriately qualified healthcare professionals, under the supervision of a physician. Additional RMMs: Injector's Guide for Safe use of Belkyra
Additional pharmacovigilance activities	CONTOUR Registry (Australia) PASS Physicians' Survey to Assess Effectiveness of BELKYRA Risk Minimisation Activities (EU)

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

Important identified risk • Injection site necrosis	
Evidence for linking the risk to the medicine	AE data from the clinical study program and nonclinical data.
Risk factors and risk groups	It may be hypothesized that patients are at increased risk for injection site necrosis when BELKYRA is not administered strictly as recommended (e.g., in case of too superficial [intradermal] injection, injection during withdrawal of the syringe from the skin, or injection into infected tissue). highlight some contraindications for injection lipolysis treatment. These include immunocompromised patients, patients on anti-coagulant treatment (e.g. warfarin), patients with local skin conditions (like eczema or psoriasis), diabetic patients and patients with microangiopathy and vascular insufficiency.
Risk minimisation measures	Routine risk communication: Listed in SmPC section(s):): Undesirable effects Listed in PL section(s): Possible side effects Routine risk minimisation activities recommending specific clinical measures to address the risk: Recommendations included in SmPC section(s): Posology and method of administration; Special warnings and precautions for use; Recommendations included in PL: Warnings and precautions; Posology and method of administration; Other routine RMMs beyond the Product Information: Pack size: BELKYRA is supplied in ready-to-use, single-use vials Legal status: BELKYRA should only be administered by physicians with appropriate qualifications, expertise in the treatment and knowledge of the submental anatomy. Where national guidance permits, Belkyra may be administered by appropriately qualified healthcare professionals, under the supervision of a physician. Additional RMMs: Injector’s Guide for Safe use of Belkyra DHPC

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

Important potential risk • Off-label use	
Evidence for linking the risk to the medicine	AE data from the clinical study program and nonclinical data.
Risk factors and risk groups	Patients receiving BELKYRA are at risk of off-label use when BELKYRA is not administered strictly as recommended.
Risk minimisation measures	Routine risk communication: Not applicable. Routine risk minimisation activities recommending specific clinical measures to address the risk: Not applicable. Other routine RMMs beyond the Product Information: Pack size: BELKYRA is supplied in ready-to-use, single-use vials Legal status: BELKYRA should only be administered by physicians with appropriate qualifications, expertise in the treatment and knowledge of the submental anatomy. Where national guidance permits, Belkyra may be administered by appropriately qualified healthcare professionals, under the supervision of a physician. Additional RMMs: Injector's Guide for Safe use of Belkyra

Missing information • Use during pregnancy	
Risk minimisation measures	Routine risk communication: Not applicable. Routine risk minimisation activities recommending specific clinical measures to address the risk: Recommendations included in SmPC section(s): Fertility, pregnancy and lactation Recommendations included in PL: Pregnancy and breast-feeding Other routine RMMs beyond the Product Information: Pack size: BELKYRA is supplied in ready-to-use, single-use vials Legal status: BELKYRA should only be administered by physicians with appropriate qualifications, expertise in the treatment and knowledge of the submental anatomy. Where national guidance permits, Belkyra may be administered by appropriately qualified healthcare professionals, under the supervision of a physician.

Missing information • Use during lactation	
Risk minimisation measures	Routine risk communication: Not applicable. Routine risk minimisation activities recommending specific clinical measures to address the risk: Recommendations included in SmPC section(s): Fertility, pregnancy and lactation Recommendations included in PL: Pregnancy and breast-feeding Other routine RMMs beyond the Product Information: Pack size: BELKYRA is supplied in ready-to-use, single-use vials Legal status: BELKYRA should only be administered by physicians with appropriate qualifications, expertise in the treatment and knowledge of the submental anatomy. Where national guidance permits, Belkyra may be administered by appropriately qualified healthcare professionals, under the supervision of a physician.

II.C Post-authorisation development plan

II.C.1 Studies that are conditions of the marketing authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of BELKYRA.

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

CONTOUR Registry (Australia): The objectives of this study are to evaluate the long-term safety and maintenance of effect of deoxycholic acid.

PASS Physicians' Survey to Assess Effectiveness of BELKYRA Risk Minimisation Activities (EU): To assess physician understanding of the key safety messages contained in the Injector's Guide for the Safe Use of BELKYRA regarding injection site nerve injury and injection site skin ulceration.