Summary of the Risk Management Plan (RMP) for LANTUS®

LANTUS® (INSULIN GLARGINE)
Marketing Autorisation Holder : sanofi-aventis (suisse) sa
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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 minimize them. The RMP summary of LANTUS® 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 medicament” 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 LANTUS® in Switzerland is the “Arzneimittelinformation/ Information sur le medicament” (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Sanofi-aventis (suisse) sa is fully responsible for the accuracy and correctness of the content of this published summary RMP of LANTUS®.

1. THE MEDICINE AND WHAT IT IS USED FOR

According to Swiss label

LANTUS is authorized for treatment of diabetes mellitus in adults, adolescents and children aged 2 years or above, requiring insulin treatment.

According to EU-SmPC

Insulin glargine 100 U/mL (LANTUS) is authorized for treatment of diabetes mellitus in adults, adolescents and children aged 2 years or above.

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

https://www.ema.europa.eu/en/documents/overview/lantus-epar-summary-public_en.pdf

2. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of LANTUS, together with measures to minimize such risks and the proposed studies for learning more about LANTUS risks, are outlined in the next sections.

Measures to minimize 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 authorized 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 (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In the case of LANTUS, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, outlined in the next sections.

In addition to these measures, information about adverse reactions will be collected continuously and regularly analyzed, 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 LANTUS is not yet available, it is listed under “missing information” outlined in the next section.

2.1. List of important risks and missing information

Important risks of LANTUS are risks that need special risk management activities to further investigate or minimize 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 LANTUS. 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 (eg, on the long-term use of the medicine).

Table 1 - List of important risks and missing information

Important identified risk	Medication error due to mix-up between long-acting (basal) and short-acting (bolus) insulins
Important potential risks	Malignancies
	Medication errors: • Mix-up between long-acting 100 U/mL and 300 U/mL strength insulin products • Unnecessary dose or unit recalculation • Switching patients between standard 100 U/mL and 300 U/mL strength insulin products without dose adjustment
Missing information	Use in pregnancy (U300 only)

2.2. Summary of important risks

Table 2 - Important identified risk with corresponding risk minimization activities and additional pharmacovigilance activities: Medication error due to mix-up between long-acting (basal) and short-acting (bolus) insulins

Medication error due to mix-up between long-acting (basal) and short-acting (bolus) insulins	
Evidence for linking the risk to the medicine	Postmarketing data; The Human factors Validation study showed that no mix- up between TOUJEO and other insulins occurred.
Risk factors and risk groups	Visually impaired or color blind patients without help of a person trained for the use of the device.

Medication error due to mix-up between long-acting (basal) and short-acting (bolus) insulins	
Risk minimization measures	**Routine risk minimization measures:** <u>U100</u> SmPC: Labeled in sections 4.4 and 6.6. PL: Labeled in section 3. IFU: Step 1 <u>U300</u> SmPC: Labeled in sections 4.4 and 6.6. PL: Labeled in sections 2 and 3. IFU: “Learn to inject” and Step 1-A. To enhance differentiation (not only in countries where U100 vial and syringe are marketed) a different trade name is a way to prevent patient medication error or dispensing errors. The trade name for U300 Insulin glargine is TOUJEO (TOUJEO SoloStar for the small size pen, and TOUJEO DoubleStar for the large size pen), while LANTUS is used for U100. Medicinal product subject to medical prescription. Packaging (outer carton + label). Each strength and presentation has specific pen design and color, pen label, and outer pack specific color. **Additional risk minimization measures:** None

e-CTD: Electronic Common Technical Document; IFU: Instructions For Use; PL: Package Leaflet; SmPC: Summary of Product Characteristics.

Table 3 - Important potential risk with corresponding risk minimization activities and additional pharmacovigilance activities: Malignancies

Malignancies	
Evidence for linking the risk to the medicine	Literature, clinical data.

Risk factors and risk groups	A recently published quartet of observational studies (see **REFERENCES**) assessing whether different types of insulin confer different cancer risk were considered inconsistent and inconclusive with regard to specific insulin types, but consistent with the hypothesis that insulin therapy confers increased risk. In an accompanying editorial in the same journal issue, the commissioners of these studies commented that the available evidence points to the possibility that insulin in general, or different types of insulin, may be mitogenic, that is, they enhance growth and proliferation of neoplastic cells already present, rather than being mutagenic, that is, rather than causing the de novo appearance of malignancy in healthy tissue. Hence the evidence for increased risk appears confined to older patients with T2DM with occult foci of malignancy. Epidemiology data on the risk of cancer in the children population are provided in Part II SI of the RMP.
Risk minimization measures	**Routine risk minimization measures:** SmPC: None PL: None IFU: None Medicinal product subject to medical prescription. **Additional risk minimization measures:** None

IFU: Instructions for Use; PL: Package Leaflet; RMP: Risk Management Plan; SmPC: Summary of Product Characteristics; T2DM: Type 2 Diabetes Mellitus.

Table 4 - Important potential risk with corresponding risk minimization activities and additional pharmacovigilance: Medication errors

Table 4a - Mix-up between long-acting 100 U/mL and 300 U/mL strength insulin products	
Mix-up between long-acting 100 U/mL and 300 U/mL strength insulin products	
Evidence for linking the risk to the medicine	The Human factors Validation study showed that no mix-up between TOUJEO and other insulins occurred.
Risk factors and risk groups	Visually impaired or color blind patients without help of a person trained for the use of the device.

Risk minimization measures	**Routine risk minimization measures:** U100 SmPC: Labeled in sections 4.4 and 6.6. PL: Labeled in section 3. IFU: Step 1-A. Trade names are different. Packaging mentions the strength. Pack, pen and labels have different color and design. Medicinal product subject to medical prescription except during switch period, patients should not own products with different concentrations. U300 SmPC: Labeled in sections 4.4 and 6.6. PL: Labeled in sections 2 and 3. IFU: "Learn to inject" and Step 1-A. Trade names are different. Packaging mentions the strength. Pack and pen have different color and design. Medicinal product subject to medical prescription. Except during switch period, patients should not own products with different concentrations. **Additional risk minimization measures:** None

e-CTD: Electronic-Common Technical Document; IFU: Instructions For Use; PL: Package Leaflet; SmPC: Summary of Product Characteristics.

Table 4b - Unnecessary dose or unit recalculation

Unnecessary dose or unit recalculation	
Evidence for linking the risk to the medicine	The postmarketing experience with LANTUS: A cumulative search of the pharmacovigilance database through 20-Jan-2023 was performed for all solicited (related and unrelated) and unsolicited cases (including both diagnoses and symptoms). The review of the postmarketing pharmacovigilance databases for medication errors due to "unnecessary re-calculation of the units needed" revealed 19 cases. Human Factors study conducted in US confirmed the possibility of mistakes.
Risk factors and risk groups	Could impact the prescribers or patients if not familiar with the instructions for use.
Risk minimization measures	**Routine risk minimization measures:** U100 SmPC: None PL: None IFU: None Medicinal product subject to medical prescription. U300 SmPC: Labeled in section 4.2.

	PL: Labeled in section 3. IFU: Step 4 Medicinal product subject to medical prescription. The dose window of the pen shows the dose in units. **Additional risk minimization measures:** HCP educational material: HCP brochure Patient educational material: Patient brochure to patients treated with TOUJEO SoloStar/DoubleStar

HCP: Healthcare Professional; IFU: Instructions For Use; PL: Package Leaflet; SmPC: Summary of Product Characteristics; US: United States.

Table 4c - Medication error associated with Switching patients between standard 100 U/mL and 300 U/mL strength insulin products without dose adjustment

Switching patients between standard 100 U/mL and 300 U/mL strength insulin products without dose adjustment	
Evidence for linking the risk to the medicine	The postmarketing experience with LANTUS: Not applicable.
Risk factors and risk groups	Not applicable
Risk minimization measures	**Routine risk minimization measures:** U100 SmPC: Labeled in section 4.2. PL: None IFU: None Medicinal product subject to medical prescription. U300 SmPC: Labeled in sections 4.2 and 4.4. PL: Labeled in sections 2 and 3. IFU: Step 1-A Medicinal product subject to medical prescription. **Additional risk minimization measures:** HCP educational material: HCP brochure. Patient educational material: Patient brochure to patients treated with TOUJEO SoloStar/DoubleStar.

IFU: Instructions For Use; PL: Package Leaflet; SmPC: Summary of Product Characteristics.

e-CTD: Electronic-Common Technical Document; HCP: Healthcare Professional; IFU: Instructions For Use; PL: Package Leaflet; SmPC: Summary of Product Characteristics; US: United States.

Table 5 – Missing information with corresponding risk minimization activities and additional pharmacovigilance activities: Use in pregnancy (U300 only)

Use in pregnancy (U300 only)	
Risk minimization measures	**Routine risk minimization measures:** SmPC: Labeled in section 4.6. PL: Labeled in section 2. IFU: None Medicinal product subject to medical prescription. **Additional risk minimization measures:** None

IFU: Instructions for Use; PL: Package Leaflet; SmPC: Summary of Product Characteristics.

2.3. Post-authorization development plan

2.3.1. Studies which are conditions of the marketing authorization

None

2.3.2. Other studies in post-authorization development plan

None

REFERENCES

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