# IN USE PRODUCT SAFETY ASSESSMENT REPORT FOR TOUJEO® AND ABASAGLAR®▼ (INSULIN GLARGINES)

## SUMMARY OF ASSESSMENT AND ITS FINDINGS

### BACKGROUND

Lantus® (insulin glargine, 100 units/mL) solution for injection has been available since 2000, and until recently was the only insulin glargine product in the UK.

In August 2015, Sanofi-Aventis launched Toujeo®, a concentrated insulin glargine product of strength 300 units/mL. In September 2015, Eli Lilly launched Abasaglar®▼, a biosimilar version of insulin glargine of strength 100 units/mL.

The addition of a further two insulin glargine products to the UK market creates the potential for confusion. This review summarises safety considerations associated with the introduction of these products.

A UKMi briefing sheet: "Answers to commonly asked questions about biosimilar versions of insulin glargine" is available here Link.

### DETAILS OF PRODUCT (S) ASSESSED

The two new products assessed using the validated UKMi product assessment tool (1) are:

1. Toujeo® (insulin glargine) 300 units/mL solution for injection in a pre-filled pen; Sanofi-Aventis

2. Abasaglar®▼(insulin glargine) 100 units/mL solution for injection in cartridge & pre-filled pen; Eli Lilly

The products were compared with the originator glargine product, Lantus® (insulin glargine, 100 units/mL) solution for injection; Sanofi-Aventis (a formal assessment of Lantus® was not undertaken).

Assessments were carried out with reference to: high resolution images supplied by the manufacturers; summaries of product characteristics (SmPC) and packaging inserts (2-7); formulary application support packs (8,9); and the European Medicines Agency Public Assessment Reports (EPARs) for the products (10-12). The assessment process is summarised at the end of the report.

### CONCLUSION FOLLOWING APPLICATION OF VALIDATED ASSESSMENT TOOL

Overall the presentation, physical characteristics, and accompanying information for both products are considered appropriate. However, some inherent risks will be associated with the introduction of both the biosimilar (Abasaglar®▼), and Toujeo® (insulin glargine) 300 units/mL. These risks should be broadly manageable, but safe introduction will require some implementation work. Potential risks are identified below; mitigating and other necessary actions are considered in the next section.

***Interchangeability, substitution, and switching between products***

Toujeo® (300 units/mL) has a different formulation to Lantus®: it has been designed as a longer-acting product. Bioequivalence and inter-changeability between the two products does not, therefore, exist and direct substitution between Lantus® and Toujeo® is not expected. When switching from intermediate or long-acting insulin treatment regimens (including Lantus®) to Toujeo®, blood glucose monitoring and dose adjustment will be required. Switching protocols are included in the Toujeo® product literature to support this, with blood glucose monitoring recommendations during the switch period and in the initial weeks thereafter (2).

Similarly, for the biosimilar Abasaglar®▼, substitution and automatic switching from Lantus® cannot be undertaken, and would be counter to the MHRA's recommendation that all biological medicines are prescribed by brand name (13). Any switching from Lantus® to Abasaglar®▼ would require a managed approach with blood glucose monitoring, since dosage adjustment could theoretically be required. At the time of writing, specific guidance on the service or workload implications associated with such switching were not available.

***Potential for confusion between products***

From the UKMi risk assessment, the packaging and presentation between the 3 products is well differentiated and should enable rather than hinder differentiation: the higher "300 units/mL" strength, for example, is highlighted in honey gold on the Toujeo® product packaging. Confusion between the three available insulin glargine products is still possible, however. All presentations require refrigerated storage, this may restrict opportunities for physical separation, and hence particular risks may be present in pharmacy and other clinical locations where all three products are kept together.

There is a small potential for sound and look alike name confusion between insulin glulisine and insulin glargine; tall man lettering (glARGine) is used on both Abasaglar®▼ and Toujeo® product packaging to aid differentiation.

Glargine products are used across a range of care settings, and there are particular risks associated with this; for example, correct product selection at the transition between primary and secondary care. However, providing recommendations for brand name prescribing for all insulin products are adhered to (14), the risk of confusion can be mitigated against.

***Device issues***

Abasaglar ®▼ KwikPen and cartridge are labelled with the abbreviated unit sign: "u"; this is not consistent with national recommendations to use the term “units” in all contexts for insulin preparations (15). The use of the abbreviated symbol on products could potentially increase the risk of prescribing transcription errors; the tenfold dose error that could result would be a “never event” (16).

The packaging and insert for the Abasaglar®▼ cartridge product does not state which pen device the cartridge should be inserted into. Confusion around this could potentially lead to use of incorrect selection of devices and improper delivery of the insulin dose.

Toujeo® is only available as a pre-filled pen formulation and must be administered in this form, or severe overdose could result.

***Pharmacovigilance: known risks and on-going monitoring***

All known current risks associated with Lantus® will apply equally to Abasaglar®▼ and Toujeo®. Abasaglar®▼ is subject to additional monitoring as indicated by the black triangle symbol for new medicines; the EMA Risk Management Plan (RMP) summarises safety concerns including: low blood sugar, immediate allergic reactions, reaction at injection site, malignancies, immunogenicity. The RMP also details other measures to ensure Abasaglar®▼ is used safely as possible (12).

Brand and batch specific safety surveillance for biosimilars is recommended (17). Given that insulins are predominantly prescribed and dispensed in primary care, there may be particular implications in ensuring traceability for pharmacovigilance purposes.

## POTENTIAL NEXT STEPS AND MITIGATION ACTIONS

Potential next steps and mitigation actions can be considered in two respects: those of particular relevance to the NHS, and those of particular relevance to manufacturers.

**Safe introduction of new insulin glargine products to the NHS** will need to consider a number of actions:

1. **Brand name prescribing**

   Insulin products should be prescribed by the brand name, followed by the concentration and recommended daily dose in units, and a statement of the formulation (i.e. cartridge or disposable pen); these actions are vital to identify products appropriately at the points of dispensing and/or administration. Particular care will be necessary at transition of care to ensure the correct product is selected. These safety checks can be further supported by the use of the NPSA or a locally approved insulin passport. As with all

insulins, the label must always be checked before each injection to avoid wrong product medication errors.

Electronic prescribing systems should be reviewed to minimise the risk of prescribing the wrong product, this may include removal of the option of generic insulin glargine.

Education and training for prescribers, pharmacists, pharmacy staff, nurses, and others will also be necessary to inform healthcare professionals on the availability of new insulin glargine products, and to ensure brand name prescribing and identification occurs. Patient education to increase awareness of the product brand they are receiving will also be useful to reduce the potential for error.

2. **Switching between glargine products**

   Switching between insulin products has service workload implications and should only be carried out as part of a carefully planned programme by specialists. Such programmes will include: identification of suitable patient groups; dose switching protocols; and appropriate monitoring. Suitable patients will require full assessment and review in line with the local protocols.

3. **Storage**

   Strategies to mitigate the risk of picking errors between the glargine products should be considered. These may include review of the stock's location in pharmacy departments.

4. **Device**

   For patients prescribed Toujeo®, but subsequently unable to self-administer using the pre-filled pen (due to, for example, hospital admission), use of retractable pen needles will be required to reduce the risk of needle injury to healthcare staff.

   Other actions will include ensuring the correct pen device is selected for the Abasaglar®▼ cartridge formulation. This may include rationalising the range of insulin cartridges kept within local organisations, with a view to minimising the number of pen devices held, and supporting correct pen selection.

5. **Reporting and monitoring of patients through pharmacovigilance**

   Compliance with post-marketing surveillance systems is essential for safe introduction and on-going use. Access to brand name and batch number are necessary for clear traceability and identification. Currently the Abasaglar®▼ biosimilar is subject to additional monitoring.

In addition to actions for the NHS, this review also highlighted **two issues for, Eli Lilly, the manufacturer of Abasaglar®▼**

1. **Replace "u"**

   To minimise the risk of prescribing transcription errors, the product packaging for the Abasaglar®▼ KwikPen and cartridge should adopt the term "units" to replace the abbreviated "u". We feel this should be given urgent consideration by Eli Lilly.

2. **Clarity on cartridge compatibility**

   In addition, information on the compatibility of the Abasaglar®▼ cartridge with pen devices could be improved. Such information is presented on the dedicate website: www.abasaglar.co.uk , but could also be presented on the packaging and insert for the Abasaglar®▼ cartridge product.

This report was produced in October 2015 using photographic images (not physical products) of products from manufacturers as describe above. Images were obtained primarily from pharmaceutical companies but also from various sources within the NHS.

This report summarises product assessments undertaken by: London Medicines Information Service (Northwick Park Hospital) and London &South East Medicines Information Service (Guy's Hospital). We are also grateful for the input of clinical specialists (endocrine and diabetes) in completing this piece of work. For comments email lnwh-tr.medinfo@nhs.net

The UKMI product safety assessment group would appreciate your views on the usefulness of this report. We have devised a short survey which we would appreciate you completing, it should take approximately 10 minutes to complete. Click the following link to complete the survey: https://www.surveymonkey.com/r/UKMiProductSafetyAssessments.

**References**


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# PRODUCT PHOTOS


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