NHS Herts Valleys Clinical Commissioning Group

NHS East and North Hertfordshire Clinical Commissioning Group

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

BIOSIMILAR INSULIN GLARGINE (ABASAGLAR®) FOR DIABETES MELLITUS
RECOMMENDED FOR RESTRICTED USE

Name: generic (trade)	What it is	Indication	Date Decision last revised	Decision Status	NICE / SMC Guidance
biosimilar insulin glargine (100units/ml) (Abasaglar®)	basal insulin analogue	diabetes mellitus - type 1 & 2 (T1 & T2DM)	June 2016	Final	NICE - none SMC – none

Biosimilar insulin glargine (100units/ml) (Abasaglar®) is RECOMMENDED FOR RESTRICTED USE as 1st line insulin glargine product in new patients requiring insulin glargine as long-acting basal insulin analogue.

- All T2DM patients who need insulin therapy should be started on human insulin (NPH (isophane) insulin is 1st line basal insulin), other than in the groups previously identified in whom insulin analogues could be considered (see LINK)
- Prescribe BY BRAND to ensure brand/product continuity and minimise risk of substitution
- Healthcare professionals and patients need to understand the differences between Abasaglar® & other insulins to minimise the risk of medication error. Refer to MHRA advice (see LINK)
- Systematic switching is not currently supported given the resource implications and potential risks.

EFFICACY	SAFETY
• Bioequivalence between Abasaglar® and Lantus® has been shown in 5 phase 1 pharmacodynamic & pharmacokinetic studies in healthy participants. • Efficacy of Abasaglar® has been examined in the randomised ELEMENT trials. These studies demonstrated Abasaglar® as non-inferior to Lantus® for reduction in HbA1c from baseline to 24 weeks in T1 and T2DM.	• All biosimilar medicines should be prescribed by brand name so that products cannot be automatically substituted at the point of dispensing. • ELEMENT studies indicate Abasaglar® has similar safety profile to Lantus®. • SPC states Abasaglar® has same contraindications, adverse effects & interactions as Lantus®.
COST	**PATIENT FACTORS**
• Abasaglar® is available at a cost of £35.28 for 5x3mL (for cartridges & prefilled pens). Equivalent pack of Lantus®: £41.50. • Difference between the 2 in annual cost for one patient at dose of 40 units daily (estimated average dose for T2DM) would be around £60. • Abasaglar® is higher cost than NPH isophane insulin	• Patients need to understand the differences between Abasaglar® and other insulin products to minimise the risk of medication error. • Patients must be able to use the available insulin pens i.e. KwikPen® and HumaPen Savvio® • Pen device different to Lantus®. Abasaglar® cartridges cannot be used in the Lantus® pen device

Background Information

- Abasaglar® is licensed for the management of type 1 and 2 diabetes (T1DM and T2DM) in adults, young people and children aged 2 years and above.
- Abasaglar® was submitted as a biosimilar by the manufacturer, with Lantus® (insulin glargine 100units/ml) as reference medicinal product. A biosimilar medicine is developed to be similar to an existing biological medicine in terms of quality, efficacy and safety.
- Abasaglar® is a basal insulin for once-daily administration at any time of the day, preferably at the same time every day. The dose regimen (dose and timing) should be adjusted according to individual response.
- Each ml contains 100 units insulin glargine. Each cartridge (for HumaPen Savvio®) and pre-filled pen (KwikPen®) contains 3ml of solution for injection, equivalent to 300 units.
- In T1DM, Abasaglar® must be combined with short-/rapid-acting insulin to cover mealtime insulin requirements. In T2DM, Abasaglar® can also be given together with other anti-hyperglycaemic products.
- The potency of this medicinal product is stated in units. These units are equivalent between Abasaglar® and Lantus®. These units are not the same as IU or units used to express potency of other insulin analogues.
- The shelf-life is 24 months at 2-8°C, including an in-use period of up to 28 days up to 30°C.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness

- Refer to efficacy box.
- Primary amino acid sequence of Abasaglar® is the same as the active ingredient in Lantus. Abasaglar® has the same pharmaceutical form & strength as Lantus®. Abasaglar® differs from Lantus® with respect to excipients in the formulation:
- Abasaglar® has been examined in phase 3, multicentre, randomised ELEMENT trials. Studies designed to show non-inferiority of Abasaglar® vs Lantus® - change in HbA1c from baseline to 24 weeks (non-inferiority margin 0.4% HbA1c):
  - Abasaglar® was non-inferior to Lantus® in T1DM patients (ELEMENT 1) - reduction in HbA1c of -0.35% (Abasaglar®) & -0.46% (Lantus®) (treatment difference 0.11% (1.18mmol/mol) p>0.05. Non inferiority also confirmed at 52 weeks.
  - Abasaglar® was non-inferior to Lantus® in T2DM patients (ELEMENT 2) - reduction in HbA1c of -1.29% (Abasaglar®) and -1.34% (Lantus®) at 24 weeks (treatment difference 0.05% (0.57 mmol/mol) p>0.05.
- Both ELEMENT studies demonstrated no difference in dose after titration to tighten glucose blood control was required for patients switching from Lantus® to Abasaglar® at the same dose regimen.
- No published studies in children & limited patient oriented outcome data on macro/microvascular outcomes and longterm efficacy and safety data with Abasaglar®. However, specific studies not required for biosimlars where bioequivalence demonstrated. Hence Abasaglar® licensed in children and SPC references long term studies with Lantus®.

Safety

- Refer to safety and patient factors box.
- Abasaglar® is a new 'black triangle' (▼) product. It is therefore subject to additional monitoring.
- MHRA has issued guidance on commencing biosimilar insulins that healthcare professionals and patients need to understand the insulin strength of these products and how to use them correctly to minimise the risk of medication errors.

Cost of treatment and Cost Effectiveness

- Refer to cost box
- Abasaglar® manufacturer does not support switching from Lantus® to Abasaglar® and only aiming at new initiations.
- Although further biosimilar insulin glargine products are in the pipeline, at present none have been submitted to the EMA. Once more are available this is likely to reduce costs.

The needs of the population

- Refer to safety and patient factors box.
- The needs of the population may be low as Abasaglar® offers no particular clinical benefits over Lantus.

The needs of the community

- There would be reduced costs from initiating new patients on Abasaglar® instead of Lantus® and potential switch savings.
- There are some concerns that with the availability of a lower cost long acting insulin analogue the message to use NPH (isophane) insulin as 1st line basal insulin in T2DM may be weakened which may result in increased costs.

Policy Drivers

- NICE guideline on T1DM and T2DM
- AWMSG: Recommended for restricted use in accordance with NICE/AWMSG guidance for insulin glargine (Lantus®)
- Scottish Medicines Consortium: Decided that biosimilar medicines are 'out of remit' & will not formally evaluate full submissions. State 'managed introduction of biosimilar medicines into clinical practice in NHS Scotland is desirable.'
- MTRAC considers may be appropriate to initiate Abasaglar® in new patients, or when medication change needed.
- North Central London Joint Formulary Committee: Approved for all patients where insulin glargine is indicated.
- PrescQIPP: recommend Abasaglar® for restricted use in T1 & T2DM in preference to Lantus.
- UKMi safety assessment:
  - overall the presentation, physical characteristics, and accompanying information are considered appropriate. Some inherent risks associated with Abasaglar® introduction but are broadly manageable & require some implementation work.
  - 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.

Equity

- No impact anticipated.

Implementability

- See above safety and patient factor concerns and issues concerning switching (with recommendations to mitigate risk)

Selected References (full reference list available in HMMC evaluation)

- NICE Evidence Summary New Medicines: Diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar®) (Dec 2015) http://www.nice.org.uk/guidance/esnm64
- MHRA drug safety update. Draft consultation. High strength, fixed combination and biosimilar insulin products: minimising the risk of medication error. April 2015. LINK
- London Medicines Evaluation Network (LMEN). Answers to commonly asked questions about biosimilar versions of insulin glargine. LINK
- UKMi in use product safety assessment report for Abasaglar® (Oct 2015)
- Midlands Therapeutics Review & Advisory Committee (MTRAC) commissioning considerations for Abasaglar® (July 2015)
- All Wales Medicines Strategy Group (AWMSG): Abasaglar® Evaluation & Recommendations - Dec 2015
- PrescQIPP Bulletin and Briefing 130 for biosimilar insulin glargine (December 2015)

This HMMC recommendation is based upon the evidence available at the time of publication. The recommendation will be reviewed upon request in the light of new evidence becoming available.