Kent and Medway Policy Recommendation and Guidance Committee.

PR 2015-21: Insulin degludec/ liraglutide (IDegLira; Xultophy) for type 2 diabetes mellitus

Recommendation

The EKPG approved the PRGC recommendation that Insulin degludec/Liraglutide (IDegLira; Xultopy) is not routinely funded for the treatment of type-2 diabetes mellitus (T2DM) on the local NHS.

Approved by: East Kent Prescribing Group *(Representing Ashford CCG, Canterbury and Coastal CCG, South Kent Coast CCG and Thanet CCG)*
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Kent and Medway Policy Recommendation and Guidance Committee

Policy Recommendation

Policy:	**PR 2015-21: Insulin degludec/ liraglutide (IDegLira; Xultophy) for type 2 diabetes mellitus**
Issue date:	**November 2015**
Review date:	**November 2016**

The Kent and Medway Policy Recommendation and Guidance Committee (PRGC) considered national guidance, the baseline position, other CCGs' policies, evidence of safety, clinical- and cost-effectiveness and the views and opinions of stakeholders. All decisions were made with reference to the Ethical Framework. Taking these into account, the PRGC recommends that:

- Insulin degludec/ liraglutide (IDegLira; Xultophy) is not routinely funded for the treatment of type-2 diabetes mellitus (T2DM) on the local NHS

This policy recommendation will be reviewed in light of new evidence or guidance from NICE.

Clinical Commissioning Groups in Kent and Medway will always consider appropriate individual funding requests (IFRs) through their IFR process.

Supporting documents

Health Care Intervention Appraisal and Guidance (HCiAG) team (2015) *Insulin degludec/ liraglutide (IDegLira) for type 2 diabetes mellitus – Scoping report*

Equality Analysis Screening Tool – Insulin degludec/ liraglutide (IDegLira) for type 2 diabetes mellitus (2015)

Key points and rationale

What is diabetes?
Diabetes mellitus (DM) is a group of metabolic disorders in which blood glucose is persistently raised; type 2 diabetes mellitus (T2DM) is the most common form of diabetes, accounting for ~90% of cases. In people with T2DM, there is a variable combination of increased insulin resistance and progressive loss of pancreatic beta-cell function. T2DM is associated with long-term microvascular and macrovascular complications, and reduced quality of life and life expectancy.

How is T2DM currently managed?
Managing T2DM is complex; it is initially managed with lifestyle changes and oral anti-diabetic drugs, but with time, many people will require insulin therapy. The current NICE clinical guideline (CG) on T2DM (CG87; May 2009) and draft update recommend that when insulin therapy is necessary, human NPH insulin is the preferred option; the long-acting insulin analogues (LAIAs) insulin glargine (IGlar) and insulin detemir (IDet) can be considered in some people, in certain circumstances. Insulin degludec (IDeg) – another LAIA – was not included in CG87; according to the draft update, IDeg is not recommended as a treatment option in any circumstances. Consistent with this, Kent and Medway CCGs do not currently routinely fund IDeg for T2DM. In NICE TA203 (Oct. 2010), liraglutide (a GLP-1 receptor agonist [RA]) 1.2mg daily is recommended as an option for T2DM; liraglutide 1.8mg daily is not recommended.

What is insulin degludec/ liraglutide (IDegLira; Xultophy)?
IDegLira is a solution for subcutaneous injection containing both IDeg and liraglutide in a fixed-ratio combination. Both components were already available in the UK as the individual preparations. IDegLira is indicated for the treatment of adults with T2DM to improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 RA or basal insulin do not provide adequate glycaemic control. The company suggests that a potential place in therapy for IDegLira is adults with T2DM who are uncontrolled on basal insulin analogues (i.e. a subset of the licensed population). The simplicity and convenience of a fixed-ratio product may potentially improve patient adherence in some cases, but it offers less flexibility to titrate the individual components. There is no specific NICE guidance on IDegLira; none is planned.

What is the evidence base for IDegLira?
None of the studies in the study program for IDegLira compare IDegLira with GLP-1 RAs and basal insulins given together but as separate injections. Evidence relevant to the company's positioning of IDegLira is from two randomised, double-blind (DUAL II) or open-label (DUAL V) phase 3 studies in adults with inadequately controlled T2DM. DUAL II (N = 413) compared IDegLira with IDeg alone in adults with T2DM also taking metformin who had been previously treated with basal insulin. DUAL V (N = 557) compared IDegLira with IGlar in adults with T2DM who had previously been treated with IGlar and were also taking metformin. The maximum dose of IDegLira was 50 units/1.8mg; of IDeg was 50 units (DUAL II); there was no maximum for IGlar (DUAL V).

In DUAL II, IDegLira was superior to IDeg alone for change in HbA1c from baseline after 26 weeks of treatment. There was no significant difference between groups for cases of confirmed hypoglycaemia or daily insulin dose (both 45 units at the end of the study). Body weight decreased in the IDegLira group, whereas it remained stable with IDeg. In DUAL V, the company report IDegLira was superior to IGlar for change in HbA1c at 26 weeks. Secondary end points were supportive of the primary end point. The European public assessment report (EPAR) for Xultophy concluded that the safety profile for IDegLira is in general similar to that of the two included components, with no indications of additive toxicity, and that no new safety issues had been identified for the combination. The cost-effectiveness of IDegLira compared to existing alternatives is unclear. There were notable limitations in the cost-effectiveness analyses included in the company's submissions to the SMC and AWMSG, and no published cost-effectiveness studies were identified.

What is the comparative cost of IDegLira?
The annual cost per patient for the maximum licensed daily dose of IDegLira (50 units IDeg and 1.8mg liraglutide) is £1,937. The annual cost for a combination of liraglutide 1.2mg and IGlar (50

units) daily is £1,460, and £1,938 for a combination of liraglutide 1.8mg and IGlar (50 units) daily (see above for NICE guidance on liraglutide).

What would be the cost impact of prescribing IDegLira across Kent and Medway?
According to a specifically tailored analysis by the company, the cost impact across Kent and Medway CCGs should IDegLira be recommended is estimated to be £37,844 in year 1 (5% uptake), £52,983 in year 2 (7% uptake) and £75,689 in year 3 (10% uptake).

Why is IDegLira not recommended for adults with T2DM on the local NHS?
The Kent and Medway Policy Recommendation and Guidance Committee (PRGC) determined that IDegLira should not be recommended on the local NHS for adults with T2DM due to the lack of comparative evidence; clinical benefit over using separate basal insulin and GLP-1 RAs concomitantly has not been demonstrated. Also, fixed dose combination products offer less flexibility to titrate the individual components; IDeg alone is not recommended by draft NICE guidance on T2DM or local guidance; and the cost-effectiveness of IDegLira compared to existing alternatives is unclear.