Kent and Medway Policy Recommendation and Guidance Committee
Policy Recommendation

Policy:	**PR 2019-06: Insulin degludec (IDeg) for adults with type 2 diabetes mellitus**
Issue date:	**March 2019**
This policy recommendation replaces PR2016-06	

The Kent and Medway Policy Recommendation and Guidance Committee (PRGC) considered national guidance, evidence on clinical- and cost-effectiveness, the baseline position, other CCG policies, the potential impact of implementing a new policy, and the views of local specialists. All decisions were made with reference to the Ethical Framework. Taking these into account the PRGC recommends:

Insulin degludec is not routinely funded on the local NHS for the treatment of type 2 diabetes mellitus in adults unless the following criteria are met:

- It is initiated by a consultant or a GP with an extended role (GPwER) in diabetes AND
- The patient has tried other basal insulin regimens (i.e. NPH insulin and insulin detemir or insulin glargine) and these have been unsuccessful AND
- The patient meets one of the following criteria:
  - Attempts to achieve target HbA1c levels result in recurrent symptomatic hypoglycaemia, **or**
  - There is significant hypoglycaemia on basal insulin irrespective of the level of HbA1c, **or**
  - There is a risk of hypoglycaemia because of reduced awareness, **or**
  - A wide window of timing of administration is essential, **or**
  - There is a diagnosed allergy to either detemir or glargine.

This policy recommendation will be reviewed when new information becomes available that is likely to have a material effect on the current recommendation.

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

Supporting documents

NEL Health Policy Support Unit (HPSU) (2019) *Insulin degludec (IDeg) for adults with type 2 diabetes mellitus – Scoping report*

Equality analysis screening tool – Insulin degludec (IDeg) for adults with type 2 diabetes mellitus (2019)

Key points and rationale

What is type 2 diabetes (T2DM)?
T2DM is caused by a combination of insulin resistance (where the body is unable to respond to normal levels of insulin) and insulin deficiency (where the pancreas is unable to secrete enough insulin to compensate for this resistance), resulting in high blood glucose levels (hyperglycaemia). Complications arising from sustained periods of hyperglycaemia include retinopathy, nephropathy, neuropathy and cardiovascular, cerebrovascular, and peripheral arterial disease. The risk of these is greatly reduced by treatment that keeps glucose levels to as near normal as possible. T2DM is the most common form of diabetes, accounting for ~90% of cases.

How is T2DM managed?
Lifestyle interventions (such as diet and physical activity) are initially used to manage T2DM. However, over time, many people will require antidiabetic drug treatments, including insulin. Two types of insulin – basal insulin and bolus insulin – can be used to help maintain an optimal blood glucose level, replicating the body's normal functioning as closely as possible. Basal insulin regulates glucose levels through periods of fasting and separate injections of shorter acting bolus insulin prevents rises in blood glucose levels from meals. Basal insulin supply for people with T2DM can be provided by NPH (isophane) insulin (e.g. Insulatard, Humulin I or Insuman Basal) or long-acting insulin analogues (LAIAs): insulin glargine (Lantus, the biosimilars Abasaglar and Semglee or high-strength Toujeo), insulin detemir (Levemir) or insulin degludec (Tresiba).

The main adverse effect of insulin treatment is hypoglycaemia (low blood glucose levels), which may present as severe (requiring third-party intervention) or non-severe (self-managed) episodes and may occur at any time of the day or night. Hypoglycaemia and the fear of hypoglycaemia are significant limiting factors in achieving glycaemic control with insulin because they challenge the willingness of clinicians and patients to titrate insulin to the doses required to achieve guideline-recommended levels of glycaemia. In addition, recurrent episodes of hypoglycaemia can lead to the development of impaired awareness of hypoglycaemia (IAH). The risk of severe hypoglycaemia increases several-fold if a person has IAH.

What is insulin degludec (IDeg)?
IDeg (Tresiba) is licensed for the treatment of diabetes in people from the age of one year. Degludec is given once daily as a subcutaneous injection. In T2DM, IDeg can be administered alone or in any combination with oral antidiabetic medicinal products, GLP-1 receptor agonists and bolus insulin. Degludec has a long duration of action (beyond 42 hours), with less variability in its glucose-lowering effect than glargine. On occasions when administration at the same time each day is not possible, degludec allows for flexibility in the timing of insulin administration. The list price of IDeg was lowered (by 35%) on 1 July 2016.

What does national guidance say?
NICE have not developed technology appraisal (TA) guidance on degludec and have no plans to. NICE guideline (NG) 28 (2015) on the management of T2DM recommends that when insulin therapy is necessary, it should be started from a choice of a number of insulin types and regimens. NPH insulin injected once or twice daily according to need is the preferred option. Detemir or glargine can be considered as an alternative in certain circumstances. NG28 does not recommend IDeg, but this guidance was published prior to the substantial price reduction of degludec. Both the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSG) have now accepted IDeg for use in NHS Scotland and NHS Wales respectively, following a reduction in price and re-submission.

What does local guidance say?
According to PR2016-06 (issued 2016), IDeg is not currently funded on the NHS in Kent and Medway for T2DM in adults. PR2016-06 was issued prior to the price reduction of degludec.

What does the evidence say?
An evidence review identified five treat-to-target[1] RCTs comparing degludec and glargine in adults with T2DM ('BEGIN' trials), two further RCTs (SWITCH-2 and DEVOTE) and one meta-analysis. There were no consistent significant differences between degludec and glargine in rates of overall

[1] In treat-to-target studies the insulin dose is adjusted for each individual patient with the aim of achieving identical HbA1c targets. In such studies, any treatment differences are therefore detected via other parameters, such as the rate of hypoglycaemia.

confirmed, nocturnal or severe hypoglycaemia across the individual BEGIN trials, although differences were generally significant when results were pooled in a meta-analysis.

The BEGIN trials excluded people most at risk of hypoglycaemia or adverse cardiovascular effects. This limitation was addressed by two additional treat-to-target RCTs: SWITCH-2 (involving participants at risk of hypoglycaemia) and DEVOTE (involving participants with cardiovascular and renal disease). The SWITCH-2 trial reported a significant reduction in nocturnal and severe hypoglycaemia with degludec compared to glargine. The DEVOTE trial concluded that degludec significantly reduced the rate of severe hypoglycaemia compared to glargine, without increasing the risk of cardiovascular events.

New published short-term cost-utility analyses based on the reduced list price of IDeg and insulin glargine, and results from SWITCH-2 and DEVOTE, report an incremental cost effectiveness ratio (ICER) of:

- ~£18,000 per quality adjusted life year (QALY) for IDeg versus glargine when used in a basal-oral regimen
- ~£24,000 per QALY for IDeg versus glargine when used in a basal-bolus regimen.

NICE's 'threshold,' over which treatments are less likely to be recommended for use in the NHS, is typically between £20,000 and £30,000 per QALY gained.

No clinical or cost-effectiveness evidence comparing IDeg to insulin detemir or NPH insulin were identified.

What is the cost impact of implementing PR2019-06?

Implementation of PR2019-06 is estimated to lead to a net cost pressure across Kent and Medway of: ~£13,000 to ~£18,000 in year 1, ~£28,000 to ~£38,000 in year 2, and ~£41,000 to ~£56,000 in year 3. This calculation includes savings from prevented episodes of hypoglycaemia. However, these ranges are likely to be underestimates because they do not take into consideration the patient population currently using detemir (52% of total LAIA-treated adult population in Kent and Medway), because there are no RCTs comparing detemir to degludec in people with T2DM.

What is the rationale for PR2019-06?

PR2019-06 is based on new clinical trial evidence that reports a statistically significant reduction in hypoglycaemia events in adults with T2DM prescribed degludec compared to glargine. Further, published and peer-reviewed studies estimate degludec to be cost-effective for both basal-oral and basal-bolus therapy in T2DM, and national guidelines (AWMSG and SMC) support its use.

The criteria presented in the policy recommendation are supported by local specialists. They are also broadly consistent with NG28. NICE NG28 recognises NPH insulin as the preferred option when starting insulin therapy in adults with T2DM, with detemir or glargine as alternatives if there are problems with hypoglycaemia. Further, IDeg has a long duration of action (beyond 42 hours) and a steady-state profile, thereby enabling a wide window of timing of administration.

Change sheet

Reason for review:
The current Kent and Medway policy on degludec for T2DM in adults was reviewed in light of new national guidance, new data from clinical and cost-effectiveness studies and a reduction in the prices of both degludec and glargine since the current policy was determined.

Changes made to current policy:
The current Kent and Medway policy, not to routinely fund degludec for T2DM in adults, is changed to enable access to degludec according to specific criteria.

Rationale for changes:
PR2019-06 is based on new clinical trial evidence that reports a statistically significant reduction in hypoglycaemia events in adults with T2DM prescribed degludec compared to glargine. Further, published and peer-reviewed studies estimate degludec to be cost-effective for both basal-oral and basal-bolus therapy in T2DM, and national guidelines (AWMSG and SMC) support its use.

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Estimated cost impact of implementing PR2018-06:
Implementation of PR2019-06 is estimated to lead to a net cost pressure across Kent and Medway of: ~£13,000 to ~£18,000 in year 1, ~£28,000 to ~£38,000 in year 2, and ~£41,000 to ~£56,000 in year 3. This calculation includes savings from prevented episodes of hypoglycaemia. However, these ranges are likely to be underestimates because they do not take into consideration the patient population currently using detemir (52% of total LAIA-treated adult population in Kent and Medway) because there are no RCTs comparing detemir to degludec in people with T2DM.