Kent and Medway Policy Recommendation and Guidance Committee

Policy Recommendation

Policy:	**PR 2017-04: Insulin degludec for type 1 diabetes in adults**
Issue Date:	**January 2017**
Review Date:	**January 2020**
This policy recommendation replaces PR2016-05	
See PR2016-06 for insulin degludec for type 2 diabetes in adults	

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

- IDeg is funded on the local NHS for the treatment of T1DM in adults provided:
  - the patient has tried other basal insulin regimens as recommended in NICE NG17 (i.e. twice daily IDet or if twice daily is unacceptable, once daily IDet or IGlar) AND meets criteria 1, 2 or 3:
    1) Attempts to achieve target HbA1c levels result in the person experiencing disabling hypoglycaemia[1], *or* HbA1c levels have remained ≥8.5% (69 mmol/mol) despite a high level of care *and* insulin pump therapy is being considered (or patient is unsuitable for insulin pump therapy)
    2) Risk of hypoglycaemia because of reduced awareness[2]
    3) More than 2 episodes of documented DKA related admission in the last 12 months
  - IDeg is initiated by consultant only

[1] Defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life.

[2] NICE NG17 recommends the Gold score or Clarke score to quantify awareness of hypoglycaemia in adults with T1DM. The Gold score is based on the response to a single question: 'Do you know when your hypos are commencing?' Results are expressed by a 7-point Likert scale where 1 = 'always aware' and 7 = 'never aware'. Impaired awareness of hypoglycaemia (IAH) is suggested by a value of 4 or more. The Clarke score is made up of 8 questions characterising an individual's exposure to episodes of moderate and severe hypoglycaemia to assess the glycaemic threshold for and symptomatic response to hypoglycaemia. The assessment gives a score where a value of 4 or more indicates IAH.

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

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

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Supporting documents

Health Care Intervention Appraisal and Guidance (HCiAG) team (2017) *Insulin degludec for adults with type-1 diabetes mellitus – Scoping report*

Equality Analysis Screening Tool – Insulin degludec for adults with type-1 diabetes mellitus (2017)

Key points and rationale

What is diabetes mellitus (DM)?
DM is a group of metabolic disorders in which blood glucose is persistently raised. Type 1 diabetes mellitus (T1DM) results from destruction of the cells that normally make insulin. Loss of insulin secretion results in high blood glucose and other metabolic and haematological abnormalities, which have both short-term and long-term adverse effects on health.

How is T1DM managed?
Patients with T1DM require insulin therapy. NICE guideline (NG) 17 on T1DM in adults (2015) recommends basal-bolus insulin regimens, which involve taking a longer acting form of insulin (basal insulin) to keep blood glucose levels stable through periods of fasting, and separate injections of rapid-acting insulin (bolus dose) to prevent rises in blood glucose levels resulting from meals. The main adverse effect of insulin treatment is hypoglycaemia.

What is insulin degludec (IDeg)?
IDeg (Tresiba®) is the third long-acting insulin analogue (LAIA) licensed for treating diabetes; the others are insulin glargine (IGlar; Lantus®, the biosimilar Abasaglar® or high-strength Toujeo®) and insulin detemir (IDet; Levemir®). IDeg is given once daily as a subcutaneous injection for basal insulin therapy. The licensed indication is treatment of DM in adults, adolescents and children from the age of 1 year. In T1DM, IDeg must be combined with short-/rapid-acting insulin to cover mealtime insulin requirements. IDeg has an ultra-long and stable action profile, with less variability in its glucose-lowering effect than IGlar.

The list price of IDeg reduced substantially on 1 July 2016, such that it is now associated with lower annual drug costs than IGlar (Lantus) in T1DM (based on the doses used in clinical trials).

What does national guidance say?
According to NICE NG17, twice-daily IDet is recommended as the preferred basal insulin therapy. An existing insulin regimen can be considered as an alternative if that is achieving agreed targets. Once-daily IGlar or IDet can also be considered if twice-daily basal insulin injections are not acceptable or IDet is not tolerated. Other basal insulin regimens should only be considered if the regimens detailed above do not deliver agreed targets. NG17 does not give any specific recommendation on IDeg and was developed before the reduction in IDeg list price. According to NG17 there is no evidence that IDeg is more clinically effective than IGlar or IDet in T1DM.

The Scottish Medicines Consortium (SMC; 2016) and All Wales Medicines Strategy Group (AWMSG; 2016) have published new advice recommending IDeg as a treatment option for DM in adults based on the new list price for IDeg; IDeg was previously not recommended for use by the SMC or AWMSG.

What does local guidance say?
According to PR2016-05 (issued Jan. 2016), IDeg is not routinely funded on the NHS in Kent and Medway for T1DM in adults.

What is the clinical evidence base for IDeg in T1DM?

The evidence base for IDeg in T1DM consists primarily of three phase III, treat-to-target[1] RCTs, comparing IDeg to IGlar (2 trials) or IDet (1 trial) considered by the PRGC when determining PR2016-05. Non-inferiority in terms of change in HbA1c from baseline to end of treatment was demonstrated for IDeg versus comparator in all phase III trials. There were no significant differences between IDeg and IGlar or IDet in rates of severe or confirmed hypoglycaemia in any of the individual trials or when results were pooled in meta-analyses. When nocturnal hypoglycaemia was defined as confirmed hypoglycaemia occurring between midnight and 6am, significantly lower rates were reported for IDeg versus comparator in all of the individual trials, but not consistently in meta-analyses when the definition of nocturnal hypoglycaemia was altered.

New evidence since PR2016-05 was issued comprises three observational studies in patients with T1DM who switched to IDeg due to treatment-limiting problems with other insulins; these patients generally reported reductions in baseline HbA1c, insulin dosing and patient-reported hypoglycaemia.

New cost utility analyses provided by the company based on the reduced list price of IDeg suggest IDeg is cost-saving (versus Lantus) in T1DM, largely driven by lower drug costs for IDeg due to a lower dosing requirement. However, treatment with IDeg may be more expensive than with the IGlar biosimilar, Abasaglar. The cost-effectiveness of IDeg versus IDet is unknown.

Why is IDeg recommended for adults with T1DM on the local NHS in some circumstances?
The PRGC recommendation is consistent with NG17 and NICE TA151 on insulin pump therapy (which would be an option in some patients if IDeg were not available). It is also broadly consistent with SMC and AWMSG advice, recently reconsidered in light of the reduced list price for IDeg and new supporting evidence from 'real world' studies. Local clinicians support the use of IDeg in adults who meet the eligibility criteria specified in this recommendation (see accompanying scoping report for more information, especially Section 7).

What is the estimated cost impact of implementing PR2017-04?
Funding of IDeg is estimated to cost Kent and Medway CCGs collectively, -£6,364 to £2,015 (year 1), -£12,727 to £4,029 (year 2), -£19,091 to £6,044 (year 3). These estimates are based on a number of assumptions and should be treated with caution.

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

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Change sheet

Reason for review: The current Kent and Medway policy (PR2016-05; issued January 2016), recommending that insulin degludec (IDeg) is not routinely funded for type 1 diabetes mellitus (T1DM) in adults is due for routine review. Since PR2016-05 was issued, the list price of IDeg has reduced substantially, and the Scottish Medicines Consortium (SMC) and All Wales Medicines Strategy Group (AWMSG) have published new advice, which now recommends IDeg as a treatment option for diabetes mellitus (DM) in adults. Consequently, elements of the rationale underpinning the local policy to not fund IDeg for T1DM are no longer valid.

Change from baseline position: Current local guidance on this topic (PR2016-05) recommends that IDeg is not routinely funded on the local NHS for DM in adults. PR2017-04 recommends funding IDeg for adults with T1DM in certain specific circumstances.

What is the rationale for this change? The PRGC recommendation is consistent with NICE guideline 17 on T1DM in adults and NICE TA151 on insulin pump therapy (which would be an option in some patients if IDeg were not available). It is also broadly consistent with SMC and AWMSG advice recently reconsidered in light of the reduced list price for IDeg and new supporting evidence from 'real world' studies. Local clinicians support the use of IDeg in adults who meet the eligibility criteria specified in PR2017-04 (see accompanying scoping report for more information, especially Section 7).

Estimated cost impact of implementation of policy: Funding of IDeg (according to specified criteria) is estimated to cost Kent and Medway CCGs collectively, -£6,364 to £2,015 (year 1), -£12,727 to £4,029 (year 2), -£19,091 to £6,044 (year 3). These estimates are based on a number of assumptions and should be treated with caution.

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