



**Shropshire, Telford
and Wrekin**
Clinical Commissioning Group

Insulin degludec (Tresiba®▼) for Type 1 and restricted use in Type 2 diabetes Policy

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Version:	V5
Approval Date:	September 2021
Review Date:	September 2023

Document Control Sheet

Title:	Insulin degludec (Tresiba®▼) for Type 1 and restricted use in Type 2 diabetes policy		
Electronic File Name:	\\10.201.56.151\Shared\New SCCG Medicines Management\Policies, Procedures & Guidelines\Policies		
Placement in Organisational Structure:	Medicines Management, Quality Directorate		
Consultation with stakeholders:	Diabetes specialists, clinical commissioning committee, area prescribing committee		
Approval Level:	Clinical commissioning committee		
Dissemination Date:	25/02/22 (New CCG rebadged version)	Implementation Date:	January 2019
Method of Dissemination:	Website, area prescribing committee members circulation		

Document Amendment History

Version No.	Date	Brief Description
5	30/09/2021	Rebadged to Shropshire, Telford and Wrekin CCG. Content reviewed and unchanged.

The formally approved version of this document is that held on the NHS Shropshire, Telford and Wrekin CCG website: www.shropshiretelfordandwrekinccg.nhs.uk

Printed copies or those saved electronically must be checked to ensure they match the current online version.

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1 Policy Statement

Type 1 diabetes

NHS Shropshire, Telford and Wrekin CCG support the use of insulin degludec **ONLY** to avoid the use of a continuous subcutaneous insulin infusion, in patients with type 1 diabetes who have nocturnal/severe hypoglycaemia as defined in NICE TA 151 **OR** recurrent diabetic ketoacidosis (DKA) despite good compliance with their current insulin regime.

Type 2 diabetes

NHS Shropshire, Telford and Wrekin CCG support the use of insulin degludec in small cohort (approximately 2%) of Type 2 diabetes.

2 Introduction

Background

Diabetes mellitus is a group of metabolic disorders, in which persistent hyperglycaemia is caused by deficient insulin secretion, or by resistance to the actions of insulin, often combined with relative insulin deficiency. Insulin deficiency and insulin resistance leads to the abnormalities of carbohydrate, fat, and protein metabolism, which are characteristic of diabetes mellitus.¹ Insulin degludec is an ultra-long acting basal analogue insulin, which forms soluble multi-hexamers upon subcutaneous injection, resulting in a depot from which insulin degludec is continuously and slowly absorbed into the circulation. This leads to a flat and stable glucose-lowering effect.¹ Insulin degludec has a cited duration of action between 36 and 42 hours with a half-life of approximately 25 hours independent of dose.¹

3 Rationale for the decision

Summary of the evidence in adults with type 1 diabetes¹

There have been two open-label, phase 3, non-inferiority trials comparing insulin degludec with insulin glargine once daily.¹ Both trials were for patients with Type 1 diabetes mellitus.

Trial 1: 6,629 patients who had been treated with basal bolus insulin for at least a year and had an HbA1c level of 61-86mmol/mol (7.7%-10%), received either insulin glargine or insulin degludec once daily. Insulin aspart was used at mealtimes.

Trial 2: 7,493 patients received either insulin degludec, administered at a variable interval of between 8 to 40 hours or insulin glargine 100 units/ml, which were given at a fixed time each day for 26 weeks.

The primary outcome measure was the mean decrease in HbA1c for which insulin degludec and insulin glargine were comparable. Nocturnal hypoglycaemia was assessed as a secondary endpoint in both trials and was reported as lower in

patients being treated with insulin degludec vs insulin glargine in trial 1 but not in trial 2.¹ The overall clinical significance of this is unclear.

Summary of the evidence in Children with type 1 diabetes¹

In a 26 week, randomised open label, parallel group, non-inferiority trial, 350 children aged between one and 17 years with type 1 diabetes, received either insulin degludec once daily (n=174) or insulin detemir (n=176) once or twice daily. Both groups received mealtime insulin aspart. The primary endpoint was change in baseline in Hb1Ac after 26 weeks' treatment.¹ Non-inferiority was confirmed with respect to change in baseline for Hb1Ac; estimated treatment difference 0.15% [0.03; 0.32]. At 52 weeks, HbA1c was 7.9% with insulin degludec vs 7.8% insulin detemir. Overall hypoglycaemia rates did not differ significantly between degludec and detemir. Nocturnal hypoglycaemic rates were lower in the degludec group but serious hypoglycaemic episodes occurred more frequently. Rates of hyperglycaemia with ketosis were lower in those treated with insulin degludec vs insulin detemir.¹

Summary of the evidence in adults with type 2 evidence

Insulin degludec compared with insulin glargine⁵

Two open-label RCTs compared insulin degludec with insulin glargine. One in people who had previously used basal insulin (Garber et al. 2012) and the other in people who were insulin naive (Zinman et al. 2012). Both RCTs found insulin degludec was non-inferior to insulin glargine in terms of glycaemic control. Both basal insulins reduced HbA1c levels from baseline to week 52 to a similar degree (as would be expected with a treat-to-target trial design). In addition, non-inferiority was confirmed in both the intention-to-treat analyses and the per-protocol analyses.

In BEGIN Basal-Bolus Type 2 (Garber et al. 2012), the reduction in fasting plasma glucose was similar between the insulins. However, in BEGIN Once Long (Zinman et al. 2012), the reduction in fasting plasma glucose levels was statistically significantly greater with insulin degludec compared with insulin glargine (estimated treatment difference -0.43 mmol/l; 95% confidence interval [CI] -0.74 to 0.13, p=0.005).

Insulin degludec compared with sitagliptin⁵

In BEGIN Early (Philis-Tsimikas et al. 2013), insulin degludec was superior to sitagliptin in terms of glycaemic control in people who were insulin naive. After 26 weeks of treatment, HbA1c levels were reduced by 1.52% with insulin degludec compared with a reduction of 1.09% with sitagliptin (estimated treatment difference -0.43% (95% CI -0.61 to -0.24; p<0.0001). The reduction in fasting plasma glucose levels from baseline was also statistically significantly greater with insulin degludec compared with sitagliptin (estimated treatment difference -2.17 mmol/l; 95% CI -2.59 to -1.74; p<0.0001). More participants achieved an HbA1c level of less than 7.0% points (53 mmol/mol) at the end of the trial with insulin degludec compared with sitagliptin (41% compared with 28%, odds ratio [OR] 1.60; 95% CI 1.04 to 2.47; p=0.034). However, the proportion of participants achieving this HbA1c target without

experiencing confirmed hypoglycaemic episodes was not statistically significantly different (25% with insulin degludec and 23% with sitagliptin, OR 0.92; 95% CI 0.55 to 1.53).

Evidence strengths and limitations¹

- Insulin degludec has been shown to be non-inferior to insulin glargine 100 units/ml. There are no superiority trials.
- There is limited comparative evidence with other insulins. There are no trials comparing it to Neutral Protamine Hagedorn (NPH) insulin.
- There is no evidence to confirm that insulin degludec use is associated with a reduction in hospital admissions for diabetes related complications.
- There are no patient-oriented outcome data for the effects of insulin degludec on macrovascular or microvascular outcomes.
- There is limited long-term safety data.
- There is no evidence which directly compares insulin degludec with insulin pumps.

4 Clinical Criteria

Exclusion criteria for type 1 and 2 diabetes

- Insulin degludec should not be prescribed to simply allow for flexible dosing
- Insulin degludec should not be prescribed first-line for type 1 or type 2 diabetes before other NPH/long-acting basal analogue insulins have been tried.

Funding criteria for insulin degludec in Type 1 diabetes

Initiation of insulin degludec by secondary care in Type 1 diabetes

Insulin degludec is recommended for restricted use in patients with **Type 1 diabetes who** (following initiation and stabilisation by a specialist team in **SECONDARY CARE**) fulfil the following criteria:

- **Nocturnal hypoglycaemia** (with or without hypoglycaemic unawareness) which has been confirmed by continuous blood glucose monitoring or on a home blood glucose meter, which otherwise would require the patient to start on insulin pump therapy.

OR

- **Severe hypoglycaemic episodes** (with or without hypoglycaemic unawareness) which have resulted in requiring **third party intervention (assistance from another person) to treat** which may cause employment issues (for example, leading to possible loss of driving licence), significant impact on daily activities or performance impairment.

For this policy, severe hypoglycaemia is defined as having low blood glucose levels (<4.0mmol/litre) which precipitates recognised signs of severe hypoglycaemia (confusion and disorientation, convulsions/fitting/seizures, intense nightmares, loss of consciousness, coma).

OR

- **To avoid patient commencing on insulin pump therapy or patient who wish to revert to basal-bolus insulin regimen.**

OR

- **Recurrent DKA episodes** (more than 2 admissions within 1 year) despite good compliance and who would otherwise progress to insulin pump therapy.

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Treatment should be initiated, stabilised and monitored by the diabetes specialist team.

Funding criteria for insulin degludec in Type 2 diabetes

Initiation of insulin degludec by diabetes specialist team in Type 2 diabetes

(restricted use)

Insulin degludec is recommended for restricted use in small cohort (approximately 2%) of patients with Type 2 diabetes who are likely to clinically benefit from its use. Treatment should only be initiated by or on the recommendation of a diabetes consultant.

Initiation should only take place after careful consideration has been given by the multidisciplinary team and the following clinical criteria are reviewed on an individual case by case basis;

- **Nocturnal hypoglycaemia** confirmed by a home blood glucose meter.

OR

- **Severe hypoglycaemic episodes** requiring third party intervention (assistance from another person) to treat which may cause employment issues (for example, leading to possible loss of driving licence), significant impact on daily activities or performance impairment.

For this policy, severe hypoglycaemia is defined as having low blood glucose levels (<4.0mmol/litre) which precipitates recognised signs of severe hypoglycaemia (confusion and disorientation, convulsions/fitting/seizures, intense nightmares, loss of consciousness, coma).

Treatment should be initiated, stabilised and monitored by the diabetes specialist team.

Continuation of insulin degludec in Type 1 and Type 2 diabetes

The prescribing responsibility of insulin degludec should remain with the specialist team until the patient is stabilised. Following this prescribing may be transferred to a **primary care clinician**.

The patient must be reviewed between 6-12 months by the specialist team as deemed clinically appropriate. Treatment can be continued provided the patient meets one or more of the following criteria:

- Reduction in frequency of nocturnal and/or severe hypoglycaemic episodes

OR

- A clinically significant reduction in HbA1c

OR

- Reduction in frequency of hospital admissions for DKA.

If a specialist is considering an insulin pump for a patient who is currently on insulin degludec, the specialist must switch the patient to a more cost-effective insulin to be administered via the insulin pump.

This policy is based on the best available information at the time of writing.

5 Dissemination

This policy will be disseminated by the following methods:

- Published to the Website
- Link included on Netformulary

6 Advice

For further advice on this document please contact:

Clare Stallard Senior Pharmaceutical Advisor, Primary Care and Place
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7 Reviewing and Compliance Monitoring

Prescribing of insulin degludec in Primary Care is monitored by the Medicines Management Team via epact2.

Audits of compliance of prescribing in line with the criteria outlined in this guidance may be requested by the CCG.

This document will be reviewed every two years unless superseded by National Guidance or new evidence becomes available.

8 References

- 1 The East of England Priorities Advisory Committee (2017) Insulin degludec (Tresiba®), Available at: <http://www.thurrockccg.nhs.uk/about-us/document-library/medicines-management/formulary-and-prescribing-guidelines/chapter-06-endocrine-system/4133-tresiba-pac-guidance/file> (Accessed: 21st September 2018).
- 2 Adopted from Herts Valleys, East and North Hertfordshire CCG and Birmingham, Sandwell, Solihull and environs Area Prescribing Committee (Accessed: 21st September 2018)
- 3 NICE Type 1 diabetes in adults; management (NG17). August 2015 (Accessed: 21st September 2018)
- 4 NICE. Diabetes (type 1 and type 2) in children and young people: diagnosis and management. (NG18). August 2015 (Accessed: 21st September 2018)
- 5 National Institute for Health and Care Excellence (NICE) (September 2013) Type 2 diabetes: insulin degludec, Available at: <https://www.nice.org.uk/advice/esnm25/chapter/Evidence-review> (Accessed: 30 January 2019).