NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Insulin icodec for treating type 1 and type 2 diabetes

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of insulin icodec within its marketing authorisation for treating type 1 and type 2 diabetes.

Background

Diabetes mellitus is a chronic metabolic disorder characterised by elevated blood glucose levels (hyperglycaemia) resulting from a lack of the hormone insulin or resistance to its action. Type 1 diabetes results from the body's own immune system destroying the cells that make insulin[1]. Type 2 diabetes results from reduced insulin secretion or reduced tissue sensitivity to insulin (known as insulin resistance)[1]. If not managed effectively, diabetes mellitus can lead to kidney failure, blindness, foot problems, and damage to the nervous system[2]. People with diabetes are also more at risk of cardiovascular disease[3].

There were around 3.6 million people in England with diagnosed diabetes mellitus in 2021[4,5]. Additionally, it is estimated that over 700,000 further people have undiagnosed diabetes in England[4,5]. Around 8% of people with diabetes have type 1 diabetes and around 90% have type 2 diabetes. Other rarer forms make up the remaining 2%. People from Black African, African Caribbean and South Asian family backgrounds are at a higher risk of developing type 2 diabetes from a younger age[6].

Type 1 diabetes

The management of type 1 diabetes in adults includes structured education, dietary control, physical activity, self-monitoring of blood glucose levels, insulin therapy, hypoglycaemia control, control of cardiovascular risk and treating complications. NICE's clinical guideline on the diagnosis and management of type 1 diabetes in adults (NG17) recommends flexible basal-bolus insulin regimens. This involves regular daily doses of longer-acting insulin to keep blood glucose levels stable during periods of fasting (basal insulin), and short-acting insulin to prevent increases in blood glucose levels after meals (bolus insulin). NG17 recommends the following long-acting basal insulin therapies:

- Twice-daily insulin detemir
- Once-daily insulin glargine, if insulin detemir is not tolerated or there is a strong preference for once-daily basal injections
- Once-daily insulin degludec, if there is a concern about nocturnal hypoglycaemia or for people who need help from a carer or healthcare professional to administer injections.

NG17 also recommends consideration of adding metformin, which does not currently have a marketing authorisation in the UK for treating type 1 diabetes, to insulin therapy in some circumstances.

NICE technology appraisal 622 recommends sotagliflozin with insulin in certain circumstances for treating type 1 diabetes in adults with a body mass index of at least 27 kg/m^2 when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy.

Type 2 diabetes

NICE's guideline on type 2 diabetes in adults: management (NG28) recommends reinforcing advice on diet, lifestyle and adherence to drug treatment for all people with type 2 diabetes.

If blood glucose levels are not controlled by diet and exercise alone, NG28 recommends the following first-line drug treatment:

- Standard-release metformin.
- For people with chronic heart failure, atherosclerotic cardiovascular disease or at high risk of cardiovascular disease: a dual therapy of a selective sodium glucose-cotransporter 2 (SGLT2) inhibitor with proven cardiovascular benefit and metformin.
- If metformin is contraindicated or not tolerated for people with chronic heart failure, atherosclerotic cardiovascular disease or at high risk of cardiovascular disease: an SGLT2 inhibitor with proven cardiovascular benefit.
- If metformin is contraindicated or not tolerated for people who are not at risk of or without cardiovascular disease: a dipeptidyl peptidase-4 (DPP-4) inhibitor, pioglitazone ,or a sulfonylurea.
- If a DPP-4 inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate: an SGLT2 inhibitor such as? canagliflozin, dapagliflozin, and empagliflozin (TA390) or ertugliflozin (TA572).

When there is inadequate glycaemic control following first-line monotherapy, NG28 recommends adding one of the following treatment options:

- A DPP-4 inhibitor, pioglitazone or a sulfonylurea.
- For people taking metformin and a sulfonylurea is contraindicated or not tolerated or the person is at significant risk of hypoglycaemia or its consequences: a SGLT2 inhibitor (canagliflozin [TA315], ertugliflozin [TA572], dapagliflozin [TA288] or empagliflozin [TA336]).

If there is inadequate glycaemic control with dual therapy, NG28 recommends either:

- Triple therapy by adding a DPP-4 inhibitor, pioglitazone or a sulfonylurea, or
- For people taking metformin and a sulfonylurea: triple therapy by adding a SGLT2 inhibitor (canagliflozin [TA315], dapagliflozin [TA418], empagliflozin [TA336]), or
- For people taking metformin and a thiazolidinedione: triple therapy by adding a SGLT2 inhibitor (canagliflozin [TA315], empagliflozin [TA336]), or

- For people taking metformin and a DPP-4 inhibitor which inadequately controls disease and for whom a sulfonylurea or pioglitazone is not appropriate: triple therapy by adding ertugliflozin (TA583), or

- Insulin-based treatment

If metformin is contraindicated or not tolerated and dual therapy with 2 oral drugs has provided inadequate control, NG28 recommends:

- Insulin-based treatment

If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, NG28 recommends triple therapy including a GLP-1 mimetic (such as tirzepatide [TA924]) for some people.

The technology

Insulin icodec (LAI287; Insulin 287, Novo Nordisk) is a long-acting basal insulin. It does not currently have a marketing authorisation in the UK for type 1 or type 2 diabetes mellitus. It has been compared with other long-acting insulin analogues:

- in people with type 1 diabetes in combination with fast-acting insulin,
- in people with type 2 diabetes with inadequate glycaemic control who are insulin treatment naïve in combination with background non-insulin anti-diabetic treatment.
- in people with type 2 diabetes previously treated with insulin in combination with or without background non-insulin anti-diabetic treatment.

Intervention(s)	Insulin icodec
Population(s)	Adults with type 1 or type 2 diabetes
Subgroup(s)	If the evidence allows, the following subgroup may be considered: • Previous use of insulin

Comparators	For people with type 1 diabetes: • twice-daily insulin detemir • once-daily insulin glargine • once-daily insulin degludec For people with type 2 diabetes, the following interventions as monotherapy or in combination regimens, in line with NICE guidance: • metformin • sulfonylureas • DPP-4 inhibitors • pioglitazone • GLP-1 mimetics • SGLT-2 inhibitors • other insulin treatments • tirzepatide
Outcomes	The outcome measures to be considered include: • HbA1c/glycaemic control/blood glucose variability • body mass index/change in body weight/waist circumference • frequency and severity of hypoglycaemia • changes in cardiovascular risk factors, including blood pressure and lipids • microvascular complications of diabetes, including damage to nerve, kidney and eye • macrovascular complications of diabetes including coronary artery disease, peripheral arterial disease, stroke and lower limb amputations • mortality • total daily insulin dose • adverse effects of treatment, including diabetic ketoacidosis, fractures, genital and urinary tract infections • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes (2023) NICE technology appraisal guidance 943 Tirzepatide for treating type 2 diabetes (2023) NICE technology appraisal guidance 924 Sotagliflozin with insulin for treating type 1 diabetes (2020) NICE technology appraisal guidance 622. Ertugliflozin with metformin and a dipeptidyl peptidase-4 inhibitor for treating type 2 diabetes (2019) NICE technology appraisal guidance 583 Ertugliflozin as monotherapy or with metformin for treating type 2 diabetes (2019) NICE technology appraisal guidance 572 Dapagliflozin in triple therapy for treating type 2 diabetes (2016) NICE technology appraisal guidance 418 Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016) NICE technology appraisal guidance 390 Empagliflozin in combination therapy for treating type 2 diabetes (2015) NICE technology appraisal guidance 336 Canagliflozin in combination therapy for treating type 2 diabetes (2014) NICE technology appraisal guidance 315

	Dapagliflozin in combination therapy for treating type 2 diabetes (2013, updated 2016) NICE technology appraisal guidance 288 Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (2008) NICE technology appraisal guidance 151 **Related NICE guidelines:** Type 2 diabetes in adults: management (2015, updated 2022) NICE guideline 28. Type 1 diabetes in adults: diagnosis and management (2015, updated 2022) NICE guideline 17. **Related NICE guidelines in development:** Type 2 diabetes in adults: management (medicines update). NICE guideline. Publication expected December 2024 **Related quality standards:** Type 2 diabetes in adults (2023) NICE quality standard 209 Type 1 diabetes in adults (2023) NICE quality standard 208
Related National Policy	NHS England (2024) NHS Type 2 Diabetes Path to Remission Programme service specification (2023) NHS England (2023) Prescribed specialised services manual (version 6) Chapter 9. Adult specialist endocrinology services The NHS Long Term Plan (2019) NHS Long Term Plan

Questions for consultation

Where do you consider insulin icodec will fit into the existing care pathway for type 1 diabetes?

Where do you consider insulin icodec will fit into the existing care pathway for type 2 diabetes? Would the positioning of insulin icodec in the treatment pathway for type 2 diabetes differ according to previous use of insulin? If so, how?

Would insulin icodec be a candidate for managed access?

Do you consider that the use of insulin icodec can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which insulin icodec will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. NHS Diabetes. Accessed March 2024
2. Diabetes UK Complications of diabetes. Accessed March 2024
3. Diabetes UK Diabetes and heart disease. Accessed March 2024
4. Diabetes UK Statistics: How many people in the UK have diabetes?. Accessed March 2024
5. ONS: Population estimates. Accessed March 2024
6. Diabetes UK Diabetes ethnicity: Ethnicity and type 2 diabetes. Accessed March 2024