National Institute for Health and Care Excellence

Health Technology Evaluation

Insulin icodec for treating type 2 diabetes [ID6175]

Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Diabetes UK (patient)	We think it is appropriate to evaluate Insulin Icodec.	Thank you for your comment.
	Novo Nordisk (Company)	Novo Nordisk agrees that insulin icodec should be evaluated as a single technology appraisal for patients with type 2 diabetes mellitus (T2DM). Novo Nordisk is not seeking a recommendation for use in treating type 1 diabetes mellitus (T1DM) as part of this appraisal.	Thank you for your comment. The scope has been updated following consultation and will now only focus on type 2 diabetes.
Wording	Novo Nordisk (Company)	The wording of the remit does not reflect the intended scope of this appraisal. Novo Nordisk suggests that the wording of the remit should be: "To appraise the clinical and cost effectiveness of insulin icodec on part of its marketing authorisation, focusing on treating type 2 diabetes."	Thank you for your comment. The scope has been updated following consultation and will now only focus on type 2 diabetes.

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Timing	Diabetes UK (patient)	We do not think this is particularly urgent. A once weekly insulin could potentially be useful for easing the burden on NHS resources e.g people type 2 diabetes needing a once daily administration from a district nurse. And potentially people with type 1 diabetes who struggle with insulin adherence especially if they have frequent DKA admissions. But we are unsure about the evidence for long term use of risk of hypos (especially in a type 1 population) and so may not be a need to need to rush this through.	Thank you for your comment. The remit has been updated following scoping consultation.
	Novo Nordisk (Company)	There is an important unmet need for a basal insulin therapy with a less burdensome dosing regimen which improves glycaemic control in people with T2DM. Insulin icodec is a novel treatment option for adults with T2DM who require a long-acting basal insulin analogue. With its once weekly-injection frequency, insulin icodec offers less burdensome dosing for patients, which may result in better adherence and persistence, consequently improving overall glycaemic control and diabetes management.	Thank you for your comment.
Additional comments on the draft remit	Diabetes UK (patient)	None	Noted
	Novo Nordisk (Company)	No additional comments	Noted

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Diabetes UK (patient)	We have updated our estimates of those diagnosed with diabetes to 4.4 million and the numbers of people living with diabetes in the UK (including undiagnosed): How many people in the UK have diabetes?	Thank you for your comment. The scope

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			has been updated to reflect this.
	Novo Nordisk (Company)	As Novo Nordisk is not seeking a recommendation for insulin icodec as a treatment option for people with T1DM as part of this appraisal, the company request that mention of this patient population be removed from the background information. In addition, Novo Nordisk does not consider it appropriate to specify tirzepatide (a GLP-1/GIP mimetic) without specifying GLP-1 mimetics which are available for use, such as semaglutide. Therefore, Novo Nordisk believes that the following bullet point included in the T2DM treatment pathway should be rewritten to better align with NG28 guidelines and provide more clarity regarding which people with T2DM are eligible for a triple therapy combination including a GLP-1 mimetic: "*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.*" Novo Nordisk suggests the text be amended to: "*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 (GLP-1 and GLP-1/GIP mimetics are recommended per NG28 and TA924).*	Thank you for your comment. The scope has been updated in light of the comment.
Population	Diabetes UK (patient)	Type 1 and type 2 have, but what about other types especially type 3 c and also LADA.	Thank you for your comment. The scope has been updated following consultation and will now only focus on type 2 diabetes.

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	Novo Nordisk (company)	As outlined previously, Novo Nordisk is seeking a recommendation for insulin icodec in people with T2DM who require a long-acting basal insulin analogue. As such, Novo Nordisk requests that mention of T1DM be removed from the scope of the appraisal. Therefore, Novo Nordisk recommends that the population should be defined as: "Adults with type 2 diabetes who require a long-acting basal insulin analogue"	Thank you for your comment. The scope has been updated following consultation and will now only focus on type 2 diabetes.
Subgroups	Diabetes UK (patient)	• People with dexterity issues and/or require help from a third party to administer insulin due to reduced burden on them and their carers or diabetes team. In terms of cost effectiveness, we think that people requiring third party insulin administration should be considered separately. • People with sight loss (due to diabetic retinopathy) have highlighted how important it is to have an insulin treatment that they can administer themselves and is easy to use and differentiate from their bolus treatment to avoid mistakes. • There could be additional benefits for newly diagnosed people on insulin who may find it easier to adjust to a weekly basal injection.	Thank you for your comment. Where appropriate, the committee may consider the differential clinical- or cost-effectiveness of the technology in relevant subgroups. This will be based on expectation of known, biological plausible mechanisms, or other clearly justified factors. If relevant, the committee may also consider particular benefits of the technology for specific groups. Where evidence allows, stakeholders are welcome to submit

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			evidence related to relevant subgroups.
	Novo Nordisk (company)	Novo Nordisk wishes to clarify that both people with prior use of basal insulin and those who are insulin naïve are considered relevant to this appraisal and will therefore be considered separately in the base-case analyses. Trial data in the basal insulin naïve population (ONWARDS 5), and for those who are insulin experienced, in the basal insulin switch population (ONWARDS 2), and in the basal-bolus population (ONWARDS 4) will be key data used to support this appraisal. At this stage, Novo Nordisk does not believe that there are any subgroups that should be examined separately.	Thank you for your comment. Subgroups in the scope have been updated in line with the populations included in the trials. The company is welcome to justify during the appraisal whether it considers them relevant.
Comparators	Diabetes UK (patient)	We think it would be useful to compare to pump use too - as we think that this should be a very limited treatment in type 1 diabetes until more evidence is available (especially on hypo risk) and we wouldn't want people being offered this as a new easier treatment over CSII – although we appreciate there is unlikely to be any trial data evidence comparing to pumps.	Thank you for your comment. The scope includes as a comparator other insulin treatment, in line with established clinical practice in the NHS. Stakeholders are welcome to describe how different options are used in within practice. As such, the scope remains unchanged.
	Novo Nordisk (company)	In the population of adults with T2DM who require a long-acting basal insulin analogue, the relevant comparators are the existing standard of care, once-	Thank you for your comment. Identification

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		daily long-acting basal insulin analogue therapies. In line with clinical guidelines, clinical expert opinion and the comparators observed in the ONWARDS 1 to 5 trials, these therapies are: • Insulin glargine U100 • Insulin glargine U300 • Insulin degludec Since basal insulin therapy is typically administered in combination with other anti-diabetic drugs, Novo Nordisk will include the following therapies in their analyses as concomitant therapies of the treatment arms, rather than as direct comparators: • metformin • sulfonylureas • DPP-4 inhibitors • pioglitazone • GLP-1 mimetics • SGLT-2 inhibitors Furthermore, as Novo Nordisk is not seeking recommendation in people with T1DM, comparators for T1DM are not relevant for this appraisal.	of potentially relevant comparators is inclusive at the scoping stage so there is no change to the insulin comparator in the scope. Guided by the established practice in the NHS, the committee will make decisions on the appropriate and relevant comparators at the appraisal stage. comparators related to T1MD have been removed from the scope
Outcomes	Diabetes UK (patient)	Will hypoglycaemia outcomes be considered separately for type 1 and type 2 (and any other) populations? Should also consider including effects on injection sites such as risk of lipodystrophy. • People with diabetes have highlighted need to look at quality of life benefits and importance of a treatment that is easy to use and also convenient to access through a pharmacy. • Also, how comfortable it is to use – does it sting or cause inflammation/pain at injection sites?	Thank you for your comment. The remit has been updated following scoping consultation and will now only focus on type 2 diabetes. The list of outcomes in the scope is not intended to be

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		• Someone mentioned some insulins can have a bad smell. • An effective treatment that improves blood glucose is the most important factor. • Avoiding hypoglycaemia was also a key concern and frequency and severity of these events is key concern. • Also, how it interacts with other medication and sustainability of pen equipment and packaging (can it be reused?)	exhaustive. The appraisal committee can consider other outcomes if appropriate. Information on outcomes not specified in the scope can be provided by the company in its submission.
	Novo Nordisk (company)	Novo Nordisk does not consider all the outcomes listed as appropriate and suggests that mention of diabetic ketoacidosis and fractures be removed from the scope, as published literature states that these events are more closely associated with people living with T1DM than people living with T2DM. Novo Nordisk also suggests that adverse events such as genital and urinary tract infections are more associated with treatment using SGLT-2 inhibitors, which are not considered relevant comparators for this appraisal.[20,22] In addition, Novo Nordisk suggests that the following outcomes be added to better capture the outcomes associated with insulin icodec as a treatment for T2DM: • time in range 3.9-10.0 mmol/L (70-180 mg/dL) • time from baseline to treatment discontinuation or intensification • change in Diabetes Treatment Satisfaction Questionnaire score (DTSQs) in total treatment satisfaction • change in Treatment Related Impact Measure for Diabetes (TRIM-D) compliance domain • injection site reactions	Thank you for your comment. The list of outcomes in the scope is inclusive at the scoping stage but not intended to be exhaustive. Time to treatment stopping or intensification has been added as an outcome in the scope. “Total daily insulin dose” has been

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		Further, Novo Nordisk suggests that 'total daily insulin dose' be amended to 'total weekly insulin dose' to reflect the once-weekly dosing regimen of insulin icodec.	amended to "total weekly insulin dose". Outcomes relating to HbA1c control, glycaemic control, adverse effects, and quality of life have been included in the scope. Where appropriate and relevant, the company is welcome to submit additional evidence relating to them for the committee's consideration during the appraisal.
Equality	Diabetes UK (patient)	We are concerned that that potentially people who don't fit pump criteria due to higher Hba1c levels may be put inappropriately on once weekly insulin because busy under-resourced clinics think it is an easier solution which potentially again widens the inequalities gap. This scope should also consider other types of diabetes treated with insulin such as type 3c. People tell us that their specific type of diabetes is sometimes a barrier to the treatments and tech they can access because they don't have type 1 or 2.	Thank you for your comment.

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	Novo Nordisk (company)	In the UK, T2DM disproportionately affects people from Black and South Asian communities. Furthermore, socioeconomic deprivation has a significant association with T2DM risk. These two factors have been shown to have significant interaction effects on T2DM risk. The COVID-19 pandemic highlighted the disparity in healthcare equality that existed before the pandemic, including higher rates of chronic disease and lower life expectancy affecting ethnic minority populations. Inequalities in diabetes care have been identified in a retrospective cohort study of over 84,000 people with T2DM in England. The study showed disparities in glycaemic control, with higher HbA_{1c} levels in the most deprived groups compared with the least deprived, and in individuals of Black ethnicity compared with those of White ethnicity. Furthermore, Black and Asian individuals were less likely to be prescribed newer therapies and have diabetes-related monitoring. No equality issues have been identified with the scope that could exclude or differentially impact any protected groups.	Thank you for your comment.
Other considerations	Diabetes UK (patient)	People with diabetes emphasize how vital it is to have support from healthcare professionals who are familiar with the treatment and can help people to switch to a new weekly basal treatment with guidance on how to adjust basal rates, what to do if a weekly dose is missed, what time of the day/week it is best to take the injection etc. • Another issue is the accessibility of the treatment – can it be sourced from a pharmacy and what about if people travel? Once weekly would help those with busy schedules but can it be found in other countries easily on holiday if an emergency? And how would people be	Thank you for your comment.

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		supported to switch back to another basal insulin treatment if this isn't available? • The question of how the treatment might be impacted by menstrual cycles was also raised.	
	Novo Nordisk (company)	No further comments.	Thank you for your comment.
Questions for consultation	Diabetes UK (patient)	• Where do you consider insulin icodec will fit into the existing care pathway for type 1 diabetes? There is a need to think about this in relation to tech - i.e easier for people with CGM. • 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? Need to consider - do the risks for hypoglycaemia outweigh the benefits in this population. • Specific consideration should be given for people requiring third party administration (by district nurses and carers) especially in relation to cost effectiveness. • Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts:	Thank you for your comment.
	Novo Nordisk (company)	Where do you consider insulin icodec will fit into the existing care pathway for type 1 diabetes?	Thank you for your comment.

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		As outlined above, Novo Nordisk is not seeking a recommendation for use of insulin icodec in people with T1DM as part of this appraisal. 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? Insulin icodec will be positioned as a treatment option for people with T2DM who require a long-acting basal insulin analogue, such as insulin glargine and insulin degludec. The positioning of insulin icodec is not impacted by whether an individual has received prior treatment with an insulin therapy. Insulin icodec will be an option for three groups of patients: 1) Insulin naïve 2) Previously treated with basal insulin only 3) Previously treated with basal-bolus insulin Would insulin icodec be a candidate for managed access? Novo Nordisk does not expect to enter any managed access agreement and anticipates approval for use through routine commissioning. 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. Insulin icodec is expected to provide health-related benefits that are unlikely to be included in the QALY calculation, including a reduced injection burden to patients, NHS and broader society, which may improve persistence and	

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		adherence to insulin therapy. In an analogous case, comparing once daily and once-weekly (OW) injectable GLP-1 receptor agonists, OW therapies have demonstrated improved outcomes in terms of adherence and clinical benefit in people with T2DM. In addition to health benefits, once-weekly insulin icodec is expected to have a favourable environmental impact, with a substantial reduction in the emissions released across every stage of the product life cycle and reduced plastic waste compared with once-daily basal insulin therapies. Considering the carbon dioxide (CO2) emissions per unit for needles and cartridges, once-weekly insulin icodec reduces CO2 emissions by 7.4kg per year compared with Tresiba FlexTouch U100 (2.6 vs 10.0 CO2 kg per year)	
	Novo Nordisk (company)	Insulin icodec as a once-weekly basal insulin Novo Nordisk requests that insulin icodec be described as a 'once-weekly basal insulin' to reflect its once-weekly dosing regimen and differentiate it from existing once-daily basal insulins.	Thank you for your comment. The scope has been updated in light of the comment.