Health Technology Briefing
October 2023

IcoSema for treating adults with type 2 diabetes

Company/Developer	Novo Nordisk Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 33795	NICE TSID: N/A	UKPS ID: N/A

Licensing and Market Availability Plans

Currently in phase 3 clinical trials.

Summary

IcoSema is currently in phase 3 clinical development for type 2 diabetes. Type 2 diabetes is a lifelong condition that develops when the body becomes resistant to or does not produce enough insulin – a hormone produced in the pancreas that enables sugar to enter body cells. Signs and symptoms of type 2 diabetes often develop slowly. When signs and symptoms are present, they may include increased thirst, frequent urination, increased hunger, unintended weight loss etc. Current treatment options vary from oral tablet medications to injectables including Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which help the body create insulin, and insulin itself.

IcoSema is an injectable combination of insulin icodec, and semaglutide. Insulin icodec is a new basal insulin analogue designed for once-weekly administration that is in development for the treatment of diabetes and semaglutide is a GLP-1 receptor analogue for once weekly administration. Semaglutide increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, and slows gastric emptying. It increases first- and second-phase insulin secretion, which drastically reduces the risk of hypoglycaemia. If licensed, IcoSema administered weekly by subcutaneous injection, will provide an additional treatment option for adult patients with type 2 diabetes.

Proposed Indication

Patients with type 2 diabetes inadequately controlled with daily basal insulin.[1]

Technology

Description

IcoSema is a combination of a new insulin, called insulin icodec, and a GLP-1 receptor analogue, called semaglutide.[2] Insulin icodec is a novel, long-acting insulin analogue designed to cover basal insulin requirements with once-weekly subcutaneous administration.[3] Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1. Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase. During hypoglycaemia, semaglutide diminishes insulin secretion and does not impair glucagon secretion.[4]

IcoSema is currently in phase 3 clinical development (NCT05013229, NCT05259033, NCT05352815) for the treatment of type 2 diabetes.[1,5,6] Patients will receive a subcutaneous injection of IcoSema once a week on the same day every week for 52 weeks.[1]

Key Innovation

IcoSema is a novel fixed-ratio combination drug of once-weekly basal insulin icodec and semaglutide. It is recommended for once-weekly administration, irrespective of meals, in order to improve patient adherence and outcomes.[7]

If licensed, a once-weekly option of IcoSema would be an improvement in the quality of life for people with type 2 diabetes, as the current treatment options involve daily treatment.

Regulatory & Development Status

IcoSema does not currently have marketing authorisation in the EU/UK for any indication.

IcoSema is currently in phase 3 clinical development for the treatment of type 2 diabetes.[8]

Patient Group

Disease Area and Clinical Need

Type 2 diabetes is a lifelong condition that develops when the body becomes resistant to, or does not produce enough insulin (a hormone produced in the pancreas).[9] In type 2 diabetes, the body builds up resistance to insulin and more insulin is needed to bring down blood glucose levels. As a result the pancreas needs to produce more insulin than it would normally need to. If the pancreas can no longer produce enough insulin to bring down sugar levels, the symptoms of diabetes will begin to appear. Type 2 diabetes comes on gradually and it can take up to years for symptoms to appear.[10] Signs and symptoms of type 2 diabetes often develop slowly. When signs and symptoms are present, they may include: increased thirst, frequent urination, increased hunger, unintended weight loss, fatigue, blurred vision, slow-healing sores, frequent infections, numbness or tingling in the hands or feet, areas of darkened skin, usually in the armpits and neck.[11] Type 2 diabetes is caused by several factors, including being overweight and having obesity, not being physically active, insulin resistance and genes.[12] Comorbidities that tend to coexist with type 2 diabetes include: obesity, hypertension, dyslipidaemia, depression and arthritis.[13] Type 2 diabetes is more

common in people of African, African-Caribbean and South Asian family background. It can occur in all age groups and is increasingly being diagnosed in adolescents and young adults.[14]

In the UK, more than 4.9 million people have diabetes with 13.6 million more at an increased risk of Type 2 diabetes. Of those with diabetes, around 90% have Type 2 diabetes.[14,15] In 2019, 3,319,266 individuals in England had diabetes.[16] Using the estimation that 90% of individuals have type 2 diabetes, almost 3 million people would be eligible for this treatment in England. In 2022-23, in England, there were 56,673 finished consultant episodes (FCE) for type 2 diabetes (ICD code E11), 32,095 admissions and 261,242 FCE bed days and 4,093 day cases.[17]

Recommended Treatment Options

National institute for Health and Care Excellence (NICE) recommended treatment options for type 2 diabetes are:[14]

- Metformin
- SGLT-2 inhibitors
- DPP-4 inhibitors
- Pioglitazone
- Sulfonylureas
- GLP-1 receptor agonists
- Insulin (glargine, detemir, degludec, neutral protamine hagedorn)

Clinical Trial Information

Trial	**COMBINE 3,** NCT05013229, EudraCT 2020-005309-18; A 52 Week Study Comparing the Efficacy and Safety of Once Weekly IcoSema and Daily Insulin Glargine 100 Units/mL Combined With Insulin Aspart, Both Treatment Arms With or Without Oral Anti Diabetic Drugs, in Participants With Type 2 Diabetes Inadequately Controlled With Daily Basal Insulin. **Phase 3:** Active, not recruiting. **Locations:** US and 7 EU countries **Primary Completion date:** November 2023
Trial Design	Randomised, Parallel assignment, Open label
Population	N=680 (estimated); male or female aged 18+; diagnosed with type 2 diabetes; treated with once daily or twice-daily basal insulin
Intervention(s)	IcoSema (subcutaneously administered)
Comparator(s)	Insulin glargine/insulin aspart (subcutaneously administered)
Outcome(s)	Primary outcome measures: • Change in HbA1c from baseline week 0 (V2) to week 52 (V54) See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	**COMBINE 2,** NCT05259033, EudraCT2020 005308 21; A 52 Week Study Comparing the Efficacy and Safety of Once Weekly IcoSema and Once Weekly Semaglutide, Both Treatment Arms With or Without Oral Anti Diabetic Drugs, in Participants With Type 2 Diabetes Inadequately Controlled With a GLP 1 Receptor Agonist. **Phase 3:** Active, not recruiting. **Locations:** US, Canada and 5 EU countries. **Primary completion date:** December 2023
Trial Design	Randomised, Parallel assignment, Open label
Population	N=680 (estimated); males or females aged 18+; diagnosed with type 2 diabetes; treated with stable doses of daily or weekly GLP-1 receptor agonist
Intervention(s)	IcoSema (Subcutaneously administered)
Comparator(s)	Semaglutide 1 mg (Subcutaneously administered)
Outcome(s)	Primary outcome measures: • Change in glycated haemoglobin (HbA1c) [Time frame: from baseline week 0 (V2) to week 52 (V54)] See trial record for Secondary outcome measures
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	**COMBINE 1,** NCT05352815, EudraCT2020 005281 34 ; A 52 Week Study Comparing the Efficacy and Safety of Once Weekly IcoSema and Once Weekly Insulin Icodec, Both Treatment Arms With or Without Oral Anti Diabetic Drugs, in Participants With Type 2 Diabetes Inadequately Controlled With Daily Basal Insulin. **Phase 3:** Active, not recruiting. **Locations:** Australia, US and 9 EU countries. **Primary completion date:** March 2024
Trial Design	Randomised, Parallel assignment, Open label
Population	N=1,290 (estimated); male or female aged 18+; diagnosed with type 2 diabetes; treated with once daily or twice daily basal insulin
Intervention(s)	IcoSema (Subcutaneously administered)
Comparator(s)	Insulin Icodec (Subcutaneously administered)
Outcome(s)	Primary outcome measures: • Change in glycated haemoglobin (HbA1c) [Time frame: from baseline week 0 (V2) to week 52 (V54)]

	See full trial record for secondary outcome measures.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of IcoSema is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Sotagliflozin for treating type 2 diabetes. [ID1657]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tirzepatide for treating type 2 diabetes. [ID3938]. Expected date of issue October 2023.
- NICE technology appraisal. Ertugliflozin with metformin and a dipeptidyl peptidase-4 inhibitor for treating type 2 diabetes. (TA583). June 2019.
- NICE technology appraisal. Ertugliflozin as monotherapy or with metformin for treating type 2 diabetes (TA572). March 2019.
- NICE technology appraisal. Dapagliflozin in combination therapy for treating type 2 diabetes (TA288). June 2013. Last updated: November 2016.
- NICE technology appraisal. Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes. (TA390). May 2016
- NICE technology appraisal. Dapagliflozin in triple therapy for treating type 2 diabetes (TA418). November 2016. NICE technology appraisal. Empagliflozin in combination therapy for treating type 2 diabetes (TA336). March 2015.
- NICE technology appraisal. Canagliflozin in combination therapy for treating type 2 diabetes (TA315). June 2014.
- NICE clinical guideline. Type 2 diabetes in adults: management (NG28). December 2015. Last updated: June 2022.

NHS England (Policy/Commissioning) Guidance

- NHS England. Action for Diabetes. January 2014.
- NHS England. 2013/14 NHS Standard Contract for specialised endocrinology services (Adult) A03/S/a.

Other Guidance

- Scottish Intercollegiate Guidelines Network (SIGN). Pharmacological management of glycaemic control in people with type 2 diabetes. 2017.[18]
- Scottish Intercollegiate Guidelines Network (SIGN). Management of diabetes. 2017.[19]

Additional Information

Novo Nordisk Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources.

UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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2 Global Clinical Practice Network. *A Research Study to Look at How Insulin Icodec and Semaglutide Work in the Body of People From China With Type 2 Diabetes When Given Alone or Together*. 2023. Available from: https://ichgcp.net/clinical-trials-registry/NCT05435677 [Accessed 01 October 2023].

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