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Health Technology Briefing
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Ziltivekimab for managing atherosclerotic cardiovascular disease, chronic kidney disease and systemic inflammation

Company/Developer	Novo Nordisk Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 27958	NICE ID: Not Available	UKPS ID: 674886

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Ziltivikemab is currently being developed as a treatment for atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), and inflammation. ASCVD occurs when fatty deposits build up in arteries (a type of blood vessel), making them narrower. CKD occurs when the kidney loses its ability to function properly. High blood pressure and high cholesterol level (a type of fat in the blood) increases the risk of both conditions. Interleukin-6 is a protein in the body that contributes the development and worsening of ASCVD. Many people continue to have inflammation despite treatment for ASCVD. Inflammation plays a key role in damaging blood vessels and kidney tissue, contributing to the progression of both ASCVD and CKD.

Ziltivekimab is injected into the fat under the skin (subcutaneously) on a monthly basis. Ziltivekimab is a type of medicine called a monoclonal antibody, a lab-made protein that works like the body's immune system to fight harmful substances. Ziltivekimab blocks the protein, interleukin-6, which drives inflammation; because ziltivekimab targets the interleukin-6 protein itself (not its receptor, a protein attached to its surface), it may cause fewer side effects on cholesterol, blood counts, and liver function than similar medicines. If approved, ziltivekimab may provide a new treatment option for ASCVD, CKD and inflammation.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Treatment of atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD) and systemic inflammation in adults.[1]

Technology

Description

Ziltivikemab is a narrow-spectrum fully human monoclonal antibody that targets the interleukin-6 (IL-6) ligand.[2] IL-6 is an inflammatory mediator and key contributor to cardiovascular disease (CVD) pathophysiology. IL-6 plays a prominent role in promoting several aspects of ASCVD.[3] Ziltivekimab works by targeting and blocking the effects of IL-6.[4]

Ziltivikemab is currently in development for the treatment of ASCVD, CKD and systemic inflammation in adults. In the phase III clinical trial (ZEUS; NCT05021835), participants received subcutaneous administration of ziltivekimab once monthly up to four years.[1]

Key Innovation

Despite optimal treatment, cardiovascular inflammatory risk often remains in patients with ASCVD.[5] Cardiovascular inflammation is a major determinant of atherosclerotic disease, and inhibition of the central signalling cytokine, IL-6, is a promising target. Patients with CKD commonly have plasma elevations of inflammatory biomarkers such as IL-6 and are at high risk for life-threatening atherosclerotic events as well as loss of kidney function and might therefore benefit from IL-6 inhibition.[6] IL-6 has emerged as a pivotal factor in atherothrombosis, yet, the safety and efficacy of IL-6 inhibition among individuals at high atherosclerotic risk but without a systemic inflammatory disorder is unknown.[2]

Ziltivekimab as a fully human monoclonal antibody is directed against the IL-6 ligand rather than the IL-6 receptor.[2] This targeted approach means it can be used at lower doses, and therefore could have fewer adverse effects on lipid levels, haematological indices, and hepatic function compared with other approved IL-6 agents.[2] By reducing inflammation, ziltivekimab may help improve various health outcomes for patients with chronic diseases such as: reducing the risk of cardiovascular events like heart attacks and strokes, improving symptoms and physical function in people with heart failure, slowing the progression of kidney disease and reducing inflammation in the arteries, which may help prevent heart problems.[4] If licensed, ziltivekimab may provide a new treatment for adult patients with ASCVD, CKD and cardiovascular inflammation.

Regulatory & Development Status

Ziltivekimab does not currently have Marketing Authorisation in the EU/UK for any indication.

Ziltivekimab is also in phase II/III clinical development for the following indications: [7]

- Acute Myocardial Infarction
- Heart Failure with Preserved or Mildly Reduced Ejection Fraction

Patient Group

Disease Area and Clinical Need

ASCVD (also called atherosclerosis), occurs when arteries become narrowed, making it difficult for blood to flow through them. Atherosclerosis happens when fatty deposits build up within the arteries, causing them to narrow.[8,9] The risk factors for atherosclerosis include smoking, being over 65, high cholesterol

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level, high blood pressure, and family history of CVD. The symptoms may include chest pain, shortness of breath, weakness, and pain in the legs and arms following exercise.[9]

CKD is a long-term condition in which the kidneys do not work as well as they should. Symptoms include blood in urine, swollen feet, hands and ankles, shortness of breath, and tiredness.[10] CKD can be caused by high blood pressure, diabetes, high cholesterol, kidney infections, kidney stone, enlarged prostate, glomerulonephritis, or the long-term use of non-steroidal anti-inflammatory drugs.[10]

Inflammation is the immune system's natural response to injury or infection.[11] Inflammation represents one of the main pathways in the genesis of the atherosclerotic process leading to the formation of atherosclerotic plaque and its consequent clinical events.[12] Inflammation is a common biological response to infection and chronic inflammatory conditions.[13]

The prevalence of ASCVD in the UK has been estimated to be 6.82% (2022).[14] There were just under 2,238,000 people (4.4%) aged 18 years and over with a GP diagnosis of CKD in England (2024). This was an increase from 2,093,000 from the previous year.[15] In England (2024-25), there were 25,749 finished consultant episodes (FCEs) and 19,262 finished admission episodes for atherosclerosis (ICD-10 code I70), which resulted in 4,563 day cases and 157,491 FCE bed days.[16] There were 79,545 finished consultant episodes (FCEs) and 66,463 finished admission episodes for chronic kidney disease (ICD-10 code N18), which resulted in 45,264 day cases and 114017 FCE bed days.[16]

Recommended Treatment Options

Rivaroxaban plus aspirin is recommended for preventing atherothrombotic events in adults with coronary artery disease or symptomatic peripheral artery disease who are at high risk of ischaemic events.[17] Icosapent ethyl is recommended for reducing the risk of cardiovascular events in adults.[18]

The National Institute for Health and Care Excellence (NICE) recommends both empagliflozin and dapagliflozin for CKD as an add on to standard care.[19,20]

Clinical Trial Information

Trial	**ZEUS**; NCT05021835; CTIS 2023-506926-35-00, EudraCT 2020-004853-59; Effects of Ziltivekimab Versus Placebo on Cardiovascular Outcomes in Participants with Established ASCVD, CKD and Systemic Inflammation **Phase III** – Active, not recruiting **Location(s):** Eighteen EU countries, UK, USA, Canada, Australia, and other countries **Primary completion date:** June 2026 (estimated)
Trial Design	Randomised, parallel assignment, quadruple-blind, placebo controlled
Population	N=6200 (planned); participants aged 18 years and older with CKD (defined as either eGFR≥15 to <60 mL/min/1.73 m2 or eGFR ≥60 mL/min/1.73 m2 with UACR ≥200 mg/g, serum high-sensitivity C-reactive protein (hs-CRP) greater than or equal to 2.0 mg/L, and evidence of ASCVD
Intervention(s)	Subcutaneous administration of ziltivekimab once monthly up to four years In addition to standard of care
Comparator(s)	Matched placebo

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Outcome(s)	Primary outcome measure: • Time to first occurrence of 3-point major adverse cardiovascular event, a composite endpoint consisting of: Cardiovascular death, non-fatal Myocardial Infarction and non-fatal stroke [Time frame: from randomisation (month 0) to end-of-study (up to 48 months)] See the trial record for a full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**RESCUE;** NCT03926117; A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate Reduction in Inflammation in Patients with Advanced Chronic Renal Disease Utilizing Antibody Mediated IL-6 Inhibition. **Phase II** – Completed **Location(s):** USA **Primary completion date:** June 2020
Trial Design	Randomised, parallel assignment, quadruple-blind, placebo controlled
Population	N=264 (actual); participants aged 18 years and older with stage 3-5 CKD, and hs-CRP greater than 2.0 mg/L.
Intervention(s)	Subcutaneous administration of ziltivekimab in 7.5 mg, 15 mg or 30 mg every four weeks for 24 weeks.[2]
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: • Percent change from baseline in hs-CRP levels [Time frame: baseline (average of the hs-CRP value prior to randomization and day 1), week 13] See the trial record for a full list of other outcomes.
Results (efficacy)	At 12 weeks after randomisation, median hs-CRP levels were reduced by 77% for the 7·5 mg group, 88% for the 15 mg group, and 92% for the 30 mg group compared with 4% for the placebo group. As such, the median pairwise differences in percentage change in hs-CRP between the ziltivekimab and placebo groups, after aligning for strata, were −66·2% for the 7·5 mg group, −77·7% for the 15 mg group, and −87·8% for the 30 mg group (all p<0·0001).[2]
Results (safety)	Ziltivekimab was well tolerated, did not affect the total cholesterol to HDL cholesterol ratio, and there were no serious injection-site reactions, sustained grade 3 or 4 neutropenia or thrombocytopenia.[2]

Estimated Cost

The cost of ziltivekimab is not yet known.

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Relevant Guidance

NICE Guidance

ASCVD

- NICE technology appraisal. Rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral artery disease (TA607). October 2019
- NICE guideline. Cardiovascular disease: risk assessment and reduction, including lipid modification (NG238). December 2023

CKD

- NICE technology appraisal. Dapagliflozin for treating chronic kidney disease (TA1075). July 2025
- NICE technology appraisal. Empagliflozin for treating chronic kidney disease (TA942). December 2023
- NICE guideline. Chronic kidney disease: assessment and management (NG203). November 2021
- NICE quality standard. Chronic kidney disease in adults (QS5). July 2017

NHS England (Policy/Commissioning) Guidance

CKD

- NHS South Yorkshire Integrated Care Board. Chronic Kidney Disease Management in Adults a Guideline for Primary Care, Version 1.3. 2025.[21]
- NHS Sussex Area Prescribing Committee. Chronic Kidney Disease Guideline for Adults. 2025.[22]
- NHS Nottinghamshire Area Prescribing Committee. Guidelines for the Management of Chronic Kidney Disease (CKD) for Adults. 2024.[23]

Other Guidance

ASCVD

- European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). 2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias: Developed by the task force for the management of dyslipidaemias of the ESC and the EAS. 2025.[24]
- CaReMe UK. Use a Combined Cardio–Renal–Metabolic Approach to Treat Cardiovascular Disease in Patients with Kidney Disease or Diabetes. 2023.[25]

CKD

- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2024.[26]

Additional Information

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