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Health Technology Briefing
April 2026

Orforglipron for treating obesity or overweight with weight-related comorbidities in adolescents

Company/Developer	Eli Lilly and Company Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 39801	NICE ID: Not Available	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical trial.

Summary

Orforglipron is in clinical development for the treatment of obesity or overweight with weight-related comorbidities in adolescents aged 12 to 17 years. Overweight and obesity in children over 2 years old are typically defined by a body mass index (BMI) over or equal to the 91st and 98th centile, respectively. This is commonly caused by excessive calorie intake, particularly from high-fat and high-sugar foods, along with genetic and environmental factors. In the UK, about 1 in 3 children are overweight or obese, leading to higher risk of overweight and obesity in adulthood, but also serious heart conditions and diabetes. Currently, treatment for obesity and overweight in adolescents mainly focuses on making changes to lifestyle and behaviour, such as diet and physical activity. However, in very severe cases, when these changes do not help, medication may be considered. Even then, medical treatment options for adolescents are very limited.

Orforglipron is a GLP-1 receptor agonist. It acts in the same way as GLP-1 (a hormone produced in the gut) by increasing the amount of hormone called insulin released in response to food. This helps with the control of blood glucose levels. If licensed, orforglipron would offer an additional treatment option for obesity in adolescents, or for overweight in adolescents who have weight-related comorbidities.

Proposed Indication

Treatment of obesity or overweight with weight-related comorbidities in adolescents.[1]

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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Technology

Description

Orforglipron (LY3502970)[2] is a non-peptide oral glucagon-like peptide-1 (GLP-1) receptor agonist being studied for chronic weight management in participants with obesity or overweight.[3] Orforglipron is a potent partial agonist of the GLP-1 receptor that has a greater effect on cyclic AMP signalling than on β-arrestin recruitment - a pharmacologic profile that may offer lower receptor desensitization than full GLP-1 receptor agonists.[4] Since β-arrestin proteins are associated with receptor internalisation, intracellular trafficking and desensitisation, this feature is reported to enhance the efficacy of GLP-1 receptor agonism.[2] It also slows down how fast food travels through the digestive tract. This increases the feeling of being full for longer, reducing food intake and leading to weight loss.[5]

Orforglipron is in clinical development for the treatment of obesity or overweight with weight-related comorbidities in adolescent patients. In the phase III clinical trial (ADVANCE-ATTAIN-ADOLESCENTS, NCT06672939), orforglipron is given to participants once daily orally, for a period of 72 weeks.[1]

Key Innovation

Currently, there is only one medicine recommended for overweight and obesity in adolescents, and some patients either do not respond to therapy or suffer from moderate side effects.[6] Therefore, medical treatment options are extremely limited, indicating a critical need for new and more effective pharmacological therapies. Orforglipron's mechanism of action differs fundamentally from existing recommended therapy by reducing appetite and food intake in comparison to standard therapy, which decreases intestinal fat absorption.[2,6] Additionally, the drug is designed for once-daily, oral administration without restrictions on food or liquid intake, improving convenience and supporting patient adherence.[7]

If licensed, orforglipron will offer an additional treatment option for obesity or overweight with comorbidities in adolescent patients.

Regulatory & Development Status

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

Orforglipron is in phase III/II clinical development for:[8]

- Peripheral arterial disease
- Atherosclerotic cardiovascular disease
- Hypertension
- Stress urinary incontinence
- Osteoarthritis
- Chronic kidney disease

Patient Group

Disease Area and Clinical Need

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health.[9] For children from the age of 2 years, a child with BMI ≥91st or ≥98th centile is classified as overweight and obese, respectively.[10] Obesity and overweight are caused when extra calories, particularly those from foods high in fat and sugar, are stored in the body as fat. In most cases, obesity is a multifactorial disease due to obesogenic environments, psycho-social factors and genetic variants.[11] Overweight and

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obesity in childhood are associated with an increased risk of overweight and obesity in adulthood, and earlier onset of non-communicable diseases such as type 2 diabetes and cardiovascular diseases.[12] Living with obesity can cause a number of further problems, including difficulties with daily activities and health conditions including tiredness, joint and back pain and low confidence as well as more serious health conditions such as type 2 diabetes, osteoarthritis, sleep apnoea, hypertension, and heart disease.[13,14]

In 2022, among children aged 2 to 15, the prevalence of obesity was 15% and the prevalence of overweight (including obesity) was 27%.[12] In England (2024-25), there were 13,126 finished consultant episodes (FCE) and 11,835 admissions for obesity (ICD-10 code E66) which resulted in 23,093 FCE bed days and 2,878 day cases. For ages 10-17 years old, there were 625 FCE for this indication.[15]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends prevention and lifestyle weight management services for adolescents who are becoming overweight or obese. In children aged 12 years and older, treatment with orlistat is recommended only if physical comorbidities (such as orthopaedic problems or sleep apnoea) or severe psychological comorbidities are present.[13]

Clinical Trial Information

Trial	**ADVANCE-ATTAIN-ADOLESCENTS; NCT06672939;** Efficacy, Safety, and Pharmacokinetics of Orforglipron Once Daily Oral Versus Placebo in Adolescent Participants Who Have Obesity, or Overweight With Weight-Related Comorbidities: A Randomized, Double-Blind Trial **Phase III:** Recruiting **Locations:** two EU countries, UK, USA and other countries **Primary Completion Date:** February 2027
Trial Design	Randomised, parallel assignment, double blind
Population	N=125 (estimated); patients with obesity or with overweight and at least one weight-related comorbidity; aged 12 to 17
Intervention(s)	Oral orforglipron
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: percent change from baseline in BMI [time frame: baseline, week 72]. See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of orforglipron is not yet known.

Relevant Guidance

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NICE Guidance

- NICE clinical guideline. Overweight and obesity management (NG246). January 2025.
- NICE quality standard. Overweight and obesity management (QS212). August 2025.

NHS England (Policy/Commissioning) Guidance

- NHS England. Obesity surgery for young people (up to their 18th birthday) with severe complex obesity. [16053/P]. 2026.
- NHS England. Service specification. Specialised and complex obesity surgery for children. 170014/S. April 2017.
- NHS England. NHS Standard Contract for Severe and Complex Obesity – All Ages (A05/S/a). October 2013.

Other Guidance

- BDA The Association of UK Dietitians. Dietetic Obesity Management Interventions in Children and Young People: Review & Clinical Application. 2019.[16]

Additional Information

Eli Lilly and Company 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.

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

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