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HTA7

Hurdles to Reimbursement for Glucagon-Like Peptide-1 Receptor Agonist Therapies in Weight Management

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Background

- Obesity prevalence is increasing worldwide, and the incidence is expected to increase to 3.3 billion by 2035[1]
- Obesity significantly raises the risk of numerous chronic diseases, including type 2 diabetes, cardiovascular disease, certain cancers, and more[1]
- The interplay between obesity and these conditions creates a cycle of health complications that can lead to higher all-cause mortality[2]
- This complex overlap of comorbidities requires a multifaceted approach to medical management to delay or avoid further complications[3]
- Liraglutide and semaglutide are glucagon-like peptide-1 receptor agonists (GLP-1 RAs) that have received regulatory approval for use in patients with obesity

Objective

To identify the hurdles and uncertainty highlighted by health technology assessments (HTAs) that impacted access to GLP-1 RA therapies in weight management

Methods

- 8 HTA reports from 2020 to 2024 from England, France, Canada, Australia, and the Netherlands for semaglutide and liraglutide in weight management were examined
- The final reimbursement decision, any restrictions to reimbursement, and key uncertainties within these appraisals that influenced the final decision were captured

Results

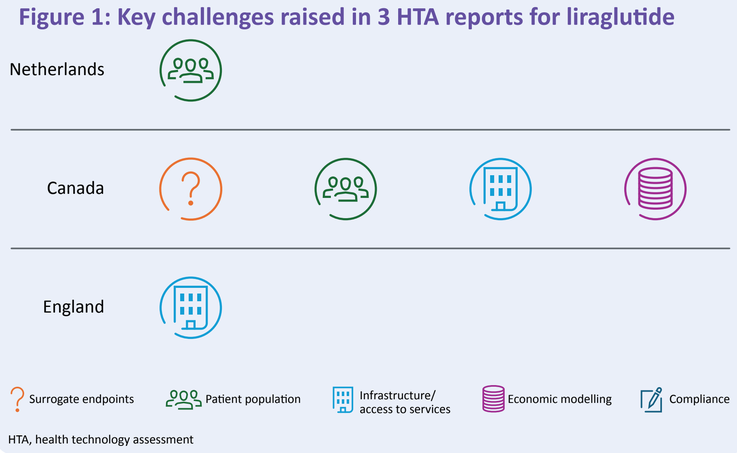
- Liraglutide and semaglutide were recommended for reimbursement in England with restrictions
- Liraglutide was also recommended for reimbursement in the Netherlands with restrictions. Semaglutide was not recommended
- Semaglutide was previously reimbursed in France based on a conditional decision, through an early access scheme until September 2023, when reimbursement was ceased. Liraglutide was not assessed
- Australia evaluated semaglutide but did not recommend it for reimbursement. Liraglutide was not assessed
- Canada evaluated both liraglutide and semaglutide and did not recommend either for reimbursement (**Table 1**)
- Where reimbursed, access to both GLP-1 RAs was restricted based on a defined body mass index criterion and the presence of weight-related comorbidities (England, Netherlands) or being ineligible for bariatric surgery (Netherlands); access to GLP-1 RA use required a reduced-calorie diet and increased physical activity (**Table 2**)
- It was noted in Canada that a limited tier 3/4 weight management infrastructure was a barrier to reimbursement. This was raised as a concern also in reports from England and Australia
- 6 of 8 HTAs assessed noted issues relating to the trial population (eg, representation of the local population), with 2 HTAs (Australia, England) highlighting the exclusion of patients with type 2 diabetes as a limitation in some trials submitted

Table 1: Reimbursement of semaglutide and liraglutide across 5 countries

	England NICE	Canada CDA-AMC	France HAS	Australia PBAC	Netherlands ZIN
Semaglutide	✓	✗	✗	✗	✗
Liraglutide	✓	✗	Not assessed	Not assessed	✓

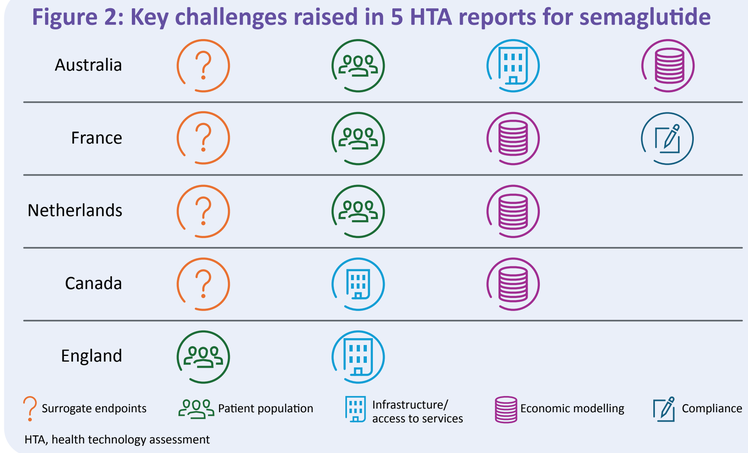
✓, reimbursed; ✗, not reimbursed
NICE, National Institute for Health and Care Excellence; CDA-AMC, Canada's Drug Agency, L'Agence des médicaments du Canada; HAS, Haute Autorité de Santé; PBAC, Pharmaceutical Benefits Advisory Committee; ZIN, Zorginstituut Nederland

Figure 1: Key challenges raised in 3 HTA reports for liraglutide



HTA, health technology assessment

Figure 2: Key challenges raised in 5 HTA reports for semaglutide



HTA, health technology assessment

Table 2: Reimbursement restrictions

Characteristic	Semaglutide	Liraglutide	
	England NICE	England NICE	Netherlands ZIN
Stopping rules	✓ Consider stopping semaglutide if less than 5% of the initial weight has been lost after 6 months of treatment	✗	✓ Discontinue if less than 5% of the initial weight has not decreased after 3 months of use at the maintenance dose
BMI criteria	✓ BMI of at least 35.0 kg/m² **or** A BMI of 30.0 to 34.9 kg/m² and meet the criteria for referral to specialist weight management services	✓ At least 35.0 kg/m²	✓ At least 35.0 kg/m²
Comorbidities	✓ At least 1 weight-related comorbidity	✓ Nondiabetic hyperglycaemia/fasting plasma glucose 5.5 to 6.9 mmol/L **and** High-risk CVD (based on risk factors, such as hypertension and dyslipidaemia)	✓ CVD, sleep apnoea, and/or osteoarthritis
Adjunct to a reduced-calorie diet and increased physical activity	✓	✓	✓
Requires specialist weight service	✓ Used within a specialist weight management service (including but not limited to tiers 3 and 4)	✓ Prescribed in secondary care by a specialist tier 3 weight management service	✗
Ineligible for bariatric surgery	✗	✗	✓
Exclude patients with diabetes	✗	✓	✓
1-Year previous lifestyle intervention not successful	✗	✗	✓

✓, restriction to reimbursement; ✗, no restriction specified; BMI, body mass index; CVD, cardiovascular disease; NICE, National Institute for Health and Care Excellence; ZIN, Zorginstituut Nederland

- Most HTAs challenged the use of surrogate/intermediate endpoints in place of long-term clinical outcome measures, which influenced the final reimbursement outcome
  - There was no evidence to show that weight loss (surrogate) translates to improvements in weight-related comorbidities (Australia, Canada, France)
  - However, England (semaglutide and liraglutide) and the Netherlands (liraglutide) accepted that the weight loss demonstrated in the trials was likely to result in cardiovascular benefits
  - All countries raised questions around the indefinite treatment periods due to the chronic nature of obesity and the absence of long-term data adding uncertainty in decision-making
  - In addition, the use of surrogate measures to predict impact on cardiovascular risk was considered a significant source of uncertainty in the economic modelling approach, particularly in Canada and Australia
- Concerns were raised about the impact of GLP-1 RA–associated gastrointestinal adverse events on discontinuation in the trial results (Canada, Australia) and on patient compliance in clinical practice (France) (**Figures 1 & 2**)

Conclusions

- Despite the significant rising public health and economic consequences of obesity, this analysis found that only 2 of 5 countries reimbursed GLP-1 RAs in obesity
- Where reimbursed, restrictions varied between countries and the 2 therapies
- Demonstration of long-term evidence of the impact of GLP-1 RAs in reducing cardiovascular events, providing a tolerable safety profile, and sustaining weight loss is of high value to HTAs, despite being limited in the submissions for liraglutide and semaglutide assessed
- To manage future hurdles for GLP-1 RAs in obesity, manufacturers should take lessons learnt from previous HTAs and shape their strategy to meet the reimbursement agencies' requirements

References

1. World Obesity Federation. Obesity Atlas 2024. Accessed 21 October 2024. https://data.worldobesity.org/publications/?cat=22
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3. Yumak V, et al. *Obes Facts*. 2015;8(6):402-424.

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