HAUTE AUTORITÉ DE SANTÉ

ASSESSING HEALTH TECHNOLOGIES

OPINION ON MEDICINAL PRODUCTS

semaglutide

WEGOVY 0.25 - 0.5 - 1.0 - 1.7 and 2.4 mg

solution for injection

First assessment

Adopted by the Transparency Committee on 14 December 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of the proprietary medicinal product WEGOVY (semaglutide) indicated alongside a low-calorie diet and increased exercise for weight management, including weight loss and weight maintenance, **only for adults with an initial body mass index (BMI) ≥ 35 kg/m² and aged ≤ 65 in cases of failure of well-conducted nutritional management (< 5% weight loss at six months).**

The retention of this opinion is **conditional** on the reassessment of WEGOVY (semaglutide) within not more than 2 years on the basis of the findings of the SELECT phase III study assessing the risk of cardiovascular events in overweight or obese patients who have previously presented with cardiovascular events (findings available in the first quarter of 2024).

Disapproval of reimbursement of the proprietary medicinal product WEGOVY (semaglutide) indicated alongside a low-calorie diet and increased exercise for weight management, including weight loss and weight maintenance for adult patients with an initial BMI < 35 kg/m².

Therapeutic improvement?

No therapeutic improvement, based on the data available.

Role in therapeutic strategy?

The first-line medical treatment of overweight and obesity in adults is based on active multidisciplinary management with at least two years of long-term regular follow-up, therapeutic education of the patient, dietary support, exercise, and psychological support. It involves lifestyle changes (diet and exercise). Medicinal treatment in obesity comes after introducing lifestyle changes and tailored nutritional management, when the patient's weight has still not reduced. In cases of failure of well-conducted nutritional management **(< 5% weight loss at six months**), particularly on dietary behaviour and subject to the patient's involvement in care, **a medicinal treatment may be proposed using a GLP1 analogue which has been granted a marketing authorisation in the indication of obesity of patients of obese status falling under levels 2 and 3 (patients with BMI ≥ 35 kg/m²).** It may be prescribed from the outset for patients whose obesity compromises their autonomy and is causing severe impairment of an organ function, and for whom lifestyle changes are limited.

Surgical treatment of obesity is only proposed as a second-line approach, after failure of well-managed medical treatment, for adult subjects with a body mass index (BMI) > 40 kg/m² or with a BMI > 35 kg/m² associated with comorbidities. Therefore, the surgical treatment of obesity is proposed as a last resort and is designed in line with the coordinated care pathway, with patient follow-up pre- and post-surgery. Regardless of the procedure used, this treatment is effective, with a weight loss of between 20 and 40% maintained in the long term, but burdensome and invasive. Indeed, these procedures may be associated with surgical and functional complications and with nutritional deficiencies. In fact, bariatric surgery is not indicated for all patients on account of its risk (based on risk, physical or mental health) and outcomes vary significantly from one patient to another, with long-term failure observed in approximately one-third of patients.

Role of the medicinal product

In view of the current therapeutic strategy recommended by HAS and the medical need for obesity treatment in adults, WEGOVY (semaglutide) is a **second-line treatment in association with a low-calorie diet and exercise, to be reserved only for adult patients with an initial body mass index (BMI) ≥ 35 kg/m² and aged ≤ 65 years in cases of failure of well-conducted nutritional management (< 5% weight loss at six months),** the cohort at the highest risk of obesity-related complications for whom HAS has recommended medicinal treatment with a GLP1 analogue which has been granted a marketing authorisation in the obesity indication.

The Committee recommends that semaglutide (WEGOVY) only be prescribed after review by an obesity management specialist.

Beyond 2 years of treatment, the efficacy and safety data are limited, entailing a systematic reassessment of continued treatment beyond this period.

Special recommendations

In view of the specific characteristics of the product and in order to ensure correct use of WEGOVY (semaglutide) (subcutaneous injection, position in the therapeutic strategy as a second-line approach in association with lifestyle and dietary measures, uncertainties in respect to a rebound effect when treatment is discontinued), the Committee requests that initial prescription be reserved for **practitioners and establishments involved in level 2 and 3 obesity management,** namely:

- Medical obesity specialist (nutritionist doctor) practising in partnership with other practitioners involved in obesity, follow-up and convalescence care specialised in “gastroenterology, endocrinology, diabetes care, nutrition”,
- Obesity specialist centres or university hospital centres.

Committee’s conclusions

Clinical Benefit

- Obesity is a chronic condition with potentially serious complications with particularly an increase in cardiovascular risk, arterial hypertension, hyperlipidaemia, and type 2 diabetes.
- The proprietary medicinal product WEGOVY (semaglutide) is a curative and symptomatic medicinal product.
- Its efficacy/adverse effect ratio is moderate considering that the efficacy data relating to WEGOVY (semaglutide) are only based on intermediate outcome measures.
- An alternative medication is available, but it is not approved for reimbursement.
- WEGOVY (semaglutide) represents a second-line treatment only for adult patients with an initial body mass index (BMI) ≥ 35 kg/m² and aged ≤ 65 years in cases of failure of well-conducted nutritional management (< 5% weight loss at six months) and in association with a low-calorie diet and exercise, the cohort at the highest risk of obesity-related complications for whom HAS has recommended medicinal treatment with a GLP1 analogue which has been granted a marketing authorisation in the obesity indication.

➔ Public health benefit

Considering:

- the severity of the disease: the burden of obesity, through its morbid complications, its social impact and impairment of quality of life caused, represents a significant public health burden.
- the insufficiently met medical need,
- the lack of longer-term data (lack of guarantee of transposability of data on account in particular of the lack of data on continued efficacy and on long-term safety and the lack of clinical data on the reduction of obesity-related comorbidities),
- the lack of additional response to the identified need in the absence of evidence of an additional impact on morbidity-mortality,
- the lack of data making it possible to assess the additional impact on delivery of care in terms of referral for surgery for example,

WEGOVY (semaglutide) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of WEGOVY (semaglutide) is significant only for adult patients with an initial body mass index (BMI) ≥ 35 kg/m² and aged ≤ 65 years in cases of failure of well-conducted nutritional management (< 5% weight loss at six months) and in association with a low-calorie diet and exercise.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the indication at the dosages of the marketing authorisation, only for adult patients with an initial body mass index (BMI) ≥ 35 kg/m² and aged ≤ 65 years in cases of failure of well-conducted nutritional management (< 5% weight loss at six months) and in association with a low-calorie diet and exercise.

The Committee disapproves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the indication at the dosages of the marketing authorisation of the proprietary medicinal product WEGOVY (semaglutide) indicated alongside a low-calorie diet and increased exercise for weight management, including weight loss and weight maintenance for adult patients with an initial BMI < 35 kg/m².

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the evidence of superiority of semaglutide versus placebo and versus an active comparator (liraglutide) on weight loss outcome measures in six phase III clinical studies:
  - the relative variation of body weight at week 68 with respect to inclusion (first ranked co-primary outcome measure), with an estimated mean difference between the semaglutide and placebo group of the order of -6% to -15% confirmed at week 104 (benefit on semaglutide on long-term administration with a relative mean weight loss of -12.55%, suggesting a lack of significant failure over this period) ($p < 0.0001$),
  - the proportion of patients with a decrease in body weight ≥ 5% at 68 weeks (second ranked co-primary outcome measure),
- the evidence of superiority of semaglutide versus placebo and versus an active comparator (liraglutide) on ranked secondary outcome measures,
- the acceptable safety profile characterised by transient mild to moderate gastrointestinal adverse effects (such as nausea, diarrhoea, constipation and vomiting), which are well-known and expected for a GLP-1 class treatment.

and despite:

- the lack of robust data making it possible to demonstrate the impact of WEGOVY on obesity-related cardiovascular morbidity-mortality apart from 2 cardiometabolic factors (systolic blood pressure and waist circumference),
- the lack of data making it possible to assess the effects of treatment discontinuation on metabolic parameter and comorbidity outcomes,

- the fact that the efficacy data are only based on intermediate outcome measure and not clinical outcome measures,
- the unknowns around long-term safety in the case of long-term treatment,
- the uncertainties around long-term semaglutide compliance in the context of indefinite long-term treatment, numerous gastrointestinal adverse effects and the difficult for patients to observe a medicinal treatment and a low-calorie diet at the same time,

the Transparency Committee deems that, based on the data currently available, WEGOVY (semaglutide) provides no clinical added value (**CAV V**) in the therapeutic strategy of adult patients with an initial body mass index (BMI) ≥ 35 kg/m² and aged ≤ 65 years in cases of failure of well-conducted nutritional management (< 5% weight loss at six months) and in association with a low-calorie diet and exercise.