Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	5th September 2017
Appraisal & Details	**Liraglutide (Saxenda®) for the treatment of obesity.** The Northern (NHS) Treatment Advisory Group considered an appraisal of the use of Liraglutide (Saxenda®) as an adjunct to a reduced calorie diet and increased physical activity for weight management in obese or overweight adults with at least one co-morbidity. *NB Liraglutide (Saxenda®) is a different licensed product to liraglutide (Victoza®) and the doses of liraglutide (Saxenda®) used for weight management are different to that used in managing type 2 diabetes (Victoza®).*
Recommendation	**The Northern (NHS) Treatment Advisory Group does <u>not recommend</u> the use of liraglutide (Saxenda®) for the treatment of obesity.** The group was concerned about the following: • EMA guidance states that a placebo corrected weight loss of at least 5% is a valid end point. This degree of weight loss was not achieved in one of the clinical trials with Saxenda® (SCALE-Diabetes clinical trial) • The phase III trials were limited to 56 weeks whereas obesity is a long term condition. • Participants in the clinical trials were likely to be very motivated, given the requirement to lose 5% of their body weight during the run in phase. • One clinical trial found that participants regained approximately 2kg within 12 weeks of discontinuation. • The primary outcomes in each trial were assessed using the last observation carried forward (LOCF) method, which assumes that people who dropped out did not regain any weight lost during the trial period. An FDA analysis found that the LOCF approach consistently over-estimated weight loss with liraglutide and under-estimated the response in the placebo group. • There is no direct comparative data with orlistat or other drugs for weight loss and there is limited data comparing weight loss over a sustained period of time to bariatric surgery. • There are no available data assessing the effect of Saxenda on clinical outcomes such as cardiovascular morbidity. • There were high drop-out rates in both the liraglutide and placebo groups in all of the studies so continuation with treatment may be a problem in practice. • Saxenda is considerably more costly than the other pharmacological options for treatment of obesity.

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Clinical evidence summary	Liraglutide (Saxenda) has been compared to placebo in randomised controlled trials (RCTs) but there are currently no published double-blind RCTs comparing it with other medicines for weight management. Studies have shown statistically significant weight losses with liraglutide compared with placebo in people with and without type 2 diabetes. In obese or overweight patients without diabetes there was a mean change in body weight from baseline of -8.0% for liraglutide compared with -2.6% with placebo. (Treatment difference of -5.4%, statistically significant). In obese and overweight patients with diabetes there was a mean change in body weight from baseline of -6.0% for liraglutide compared with -2.0% with placebo (treatment difference of -4.0%, statistically significant but doesn't meet EMA criteria). However it is unlikely that any potential weight loss would be sustained after treatment with liraglutide is stopped.
Safety	No new safety concerns were raised in the liraglutide trial programme, although known adverse events (AEs) such as nausea and vomiting occurred more frequently at higher doses. The total number of recorded AEs was similar in the liraglutide and placebo arms of the published trial (91.5% vs. 88.6%).Gastrointestinal AEs were substantially more common with liraglutide 3 mg (73.6% vs. 45.2%), with higher rates of nausea, constipation, diarrhoea, vomiting, dyspepsia and abdominal pain. GI events were most common in the first four weeks, occurring in 25% of liraglutide patients. Frequency decreased to around 10% by week 10, and 3% thereafter.
Patient Perspective	Liraglutide is given by subcutaneous injection. Orlistat is an oral treatment, which may be preferable to some patients. Orlistat and liraglutide have different adverse effect profiles, which also need to be considered. More participants in the liraglutide groups withdrew from the studies due to adverse events compared with the placebo groups. Gastrointestinal disorders were the most common adverse events reported in the studies.
Cost analysis summary	Overweight and obesity are estimated to cost the NHS approximately £6 billion per year. Saxenda® is marketed at an equivalent price to Victoza®, and costs approximately £2,381 per patient per year for the 3mg dose. It is difficult to estimate how many patients may have been eligible for treatment if approved and there is no indication of mean duration of treatment. Additional costs may be incurred in training patients to self-inject.
Financial impact PbR: In-tariff	As Saxenda® is not recommended, no financial impact is expected.