LIRAGLUTIDE (Saxenda®▼) for weight management

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of LIRAGLUTIDE (Saxenda®▼) 6mg/ml solution for subcutaneous injection for weight management

Saxenda® is not interchangeable with the other licensed brand of liraglutide, Victoza®, which is only licensed for the management of diabetes. Victoza® is not licensed as a pharmacological treatment option for weight management and should not be used for this indication.

Liraglutide (Saxenda®) is licensed for use as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients with an initial Body Mass Index (BMI) of ≥ 30 kg/m² (obese), or ≥ 27 kg/m² to < 30 kg/m² (overweight) in the presence of at least one weight-related comorbidity.¹

The doses of liraglutide (Saxenda®) used for weight management are higher than those used in managing type 2 diabetes. Saxenda® maintenance dose is 3mg daily, whereas Victoza® is 1.8mg daily. No length of course or exit strategy for Saxenda® is provided by the manufacturer except that treatment should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight.

The Pan Mersey APC does not recommend liraglutide (Saxenda®) for weight management because:

> The trials in NICE ES14³ showed only modest difference in effect between liraglutide with lifestyle changes vs lifestyle changes alone. Only one of these trials showed a treatment difference of weight loss greater than 5% after 56 weeks. Obesity is a condition that could require long term or repeat treatment, but there is no evidence of effectiveness or safety data beyond 56 weeks.

> Although at this time a NICE Technology Appraisal (TA) was not considered appropriate due to the intention of the manufacturers to only promote the use of liraglutide (Saxenda®) on private prescription in the UK, the licence does not debar NHS use. From latest statistics (2014) 58% of women and 65% of men were overweight or obese¹. Large numbers of people could be eligible for treatment which could potentially be long-term, leading to high overall costs for liraglutide (Saxenda®). Therefore, in these circumstances more certainty is needed that liraglutide (Saxenda®) will provide value for the NHS before use could be recommended.

This BLACK recommendation will be revised should a NICE TA become available.

Treatment of obesity and overweight patients should follow the guidance from NICE CG189.

Obesity: identification, assessment and management

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.
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**EFFECTIVENESS**
NICE identified four RCTs to produce ES14. Three were randomised controlled trials (RCTs) in adults who were obese or overweight (BMI 27 kg/m² or above) plus weight-related comorphobies. All three trials compared liraglutide 3mg daily vs placebo with both groups also undergoing lifestyle changes.

Pi-Sunyer et al 2015 (56 weeks) the mean change in body weight from baseline was −8.0% in the liraglutide group and −2.6% in the placebo group with an estimated treatment difference of −5.4% (95% CI −5.8 to −5.0%, p<0.001).

Davies et al 2015 (56 weeks) the estimated mean change in body weight from baseline was −6.0% in the liraglutide group and −2.0% in the placebo group with an estimated treatment difference of −4.0% (95% CI −5.1 to −2.9%, p<0.001).

Blackman et al 2016 (32 weeks) the mean change in body weight from baseline was −5.7% in the liraglutide group and −1.6% in the placebo group with an estimated treatment difference of −4.2% (95% CI −5.2 to −3.1%, p<0.0001). The fourth RCT (leRoux et al 2017) had an outcome of development of type 2 diabetes, not weight reduction.

Only one trial achieved the Public Health success criteria for loss of a minimum of 5% initial body weight. There were high drop-out rates in both arms of all trials.

**COST**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maintenance regimen</th>
<th>Cost per patient per year (ex V.A.T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat oral</td>
<td>120mg tds</td>
<td>£178</td>
</tr>
<tr>
<td>Liraglutide s/c injection</td>
<td>3mg daily</td>
<td>£2,387</td>
</tr>
</tbody>
</table>

Costs based on Electronic Dictionary of Medicines and devices / Drug Tariff prices Accessed 09 Nov 2017. This table does not imply therapeutic equivalence of drugs or doses.

**SAFETY**

Special warnings and precautions for use of Saxenda® include:
- Must not be used as a substitute for insulin in patients with diabetes mellitus.
- Should not be used in combination with another GLP-1 receptor agonist due to increased risk of pancreatitis.
- For subcutaneous use only. It must not be administered intravenously or intramuscularly.
- Should not be used in patients with congestive heart failure New York Heart Association (NYHA) class IV.

**Very Common side effects (≥1/10)**
Nausea, vomiting, diarrhoea, constipation.

**Common side effects (≥1/100 to <1/10)**
Hypoglycaemia, insomnia, dizziness, dysgeusia, dry mouth, dyspepsia, gastritis, gastro-oesophageal reflux disease, upper abdominal pain, flatulence, eructation, abdominal distension, cholelithiasis, injection site reactions, asthenia, fatigue, increased lipase, increased amylase.

Consult the Summary of Product Characteristics SPC for further details.

**PATIENT FACTORS**

Patient groups for whom the use of Saxenda® is not recommended include: aged 75 years and older; children and adolescents below 18 years of age; severe renal impairment (CrCl <30ml/min); severe hepatic impairment; congestive heart failure class III to IV; inflammatory bowel disease; pregnancy; breastfeeding; obesity secondary to endocrine or eating disorders or obesity caused by another medicinal treatment. Liraglutide is given by daily subcutaneous injection. Orlistat is an oral treatment, which may be preferable to some patients.

**PRESCRIBING INFORMATION**
The Pan Mersey APC does not recommend liraglutide (Saxenda®) for NHS prescribing because:
- Evidence demonstrating sustained clinically meaningful weight loss is lacking and no evidence for longer-term effectiveness is available.
- There are safety considerations and no longer-term safety data is available beyond 56 weeks. The SPC includes warnings on pancreatitis, cholelithiasis and cholecystitis, thyroid disease, heart rate, dehydration and hypoglycaemia in people with type 2 diabetes.
- If used within the licensed indication, a very large cohort of patients would be eligible for Saxenda®, with a potential for significant resource impact. More certainty is needed that it will provide value for the NHS.

**REFERENCES**