Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2455

liraglutide 6mg/mL solution for injection in pre-filled pen (Saxenda®)

Novo Nordisk Limited

8 April 2022

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a resubmission

liraglutide (Saxenda®) is accepted for restricted use within NHSScotland.

Indication under review: 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:

• ≥30kg/m² (obese), or

• ≥27kg/m² to <30kg/m² (overweight) in the presence of at least one weight-related comorbidity such as dysglycaemia (prediabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea.

SMC restriction: BMI ≥35kg/m²* (obesity class II and above) with:

- Non-diabetic hyperglycaemia (prediabetes) at high risk of type 2 diabetes which is defined as having either:
  - Fasting plasma glucose level of 5.5 to 6.9mmol/L or
  - HbA_{1c} of 6.0 to 6.4% (42 to 47mmol/mol), and
- High risk of cardiovascular disease (CVD):
  - Total cholesterol >5mmol/L, or
  - High-density lipoprotein (HDL) <1.0mmol/L for men and <1.3mmol/L for women, or
  - Systolic blood pressure (SBP) >140mmHg.

Patients should be treated in a specialist weight management service.

In a phase III study, liraglutide, as an adjunct to diet and exercise, was associated with significant reduction in body weight compared with placebo in patients with BMI ≥30kg/m² or ≥27kg/m² if they had dyslipidaemia or hypertension.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

*a lower BMI cut-off may be more appropriate for members of minority ethnic groups known to be at equivalent risk of the consequences of obesity at a lower BMI than the white population.

Chairman
Scottish Medicines Consortium

Indication

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:

• ≥30kg/m² (obese),

or

• ≥27kg/m² to <30kg/m² (overweight) in the presence of at least one weight-related comorbidity such as dysglycaemia (prediabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea.

Treatment with liraglutide should be discontinued after 12 weeks on the 3.0mg/day dose if patients have not lost at least 5% of their initial body weight.[1]

Dosing Information

The starting dose is 0.6mg subcutaneously once daily. The dose should be increased to 3.0mg once daily in increments of 0.6mg with at least one week intervals to improve gastro-intestinal tolerability (see table 1). If escalation to the next dose step is not tolerated for two consecutive weeks, consider discontinuing treatment. Daily doses higher than 3.0mg are not recommended. See Summary of product characteristics (SPC) for more details.[1]

Table 1. Liraglutide dosing.[1]

	Dose	Weeks
Dose escalation 4 weeks	0.6mg	1
	1.2mg	1
	1.8mg	1
	2.4mg	1
Maintenance dose	3.0mg	

Product availability date

1 January 2017

Summary of evidence on comparative efficacy

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist. GLP-1 is a physiological regulator of appetite and food intake, but the exact mechanism of action remains unclear. Liraglutide is the first in its class to be approved for use in weight management.[1, 2]The submitting company has requested that SMC considers liraglutide when positioned for use in the following group:

BMI ≥35kg/m² (obesity class II and above) with:

- Non-diabetic hyperglycaemia (prediabetes) at high risk of type 2 diabetes which is defined as having either:
    - Fasting plasma glucose level of 5.5 to 6.9mmol/L or
    - HbA_{1c} of 6.0 to 6.4% (42 to 47mmol/mol), and

- High risk of cardiovascular disease (CVD):
    - Total cholesterol >5mmol/L, or
    - High-density lipoprotein (HDL) <1.0mmol/L for men and <1.3mmol/L for women, or
    - Systolic blood pressure (SBP) >140mmHg.

In addition, patients should be treated in a specialist weight management service.

Evidence to support the efficacy and safety of liraglutide comes from Trial 1839, a multicentre, randomised, double-blind, phase III study in patients who did not have type 2 diabetes (T2DM) and who had a BMI ≥30kg/m^2 or a BMI ≥27kg/m^2 if they had treated or untreated dyslipidaemia or hypertension. Patients were randomised 2:1 to receive liraglutide subcutaneously once daily, starting at 0.6mg with weekly increases in dose of 0.6mg until 3mg maintenance (n=2,487) or placebo (n=1,244). Both groups received counselling on energy-restricted diet and exercise. Treatment was to continue for 56 weeks or 160 weeks for patients with prediabetes, defined according to American Diabetes Association 2010 criteria: 5.7 to 6.4% glycated haemoglobin, or fasting plasma glucose concentration between 5.6mmol/L and 6.9mmol/L, or 2 hour post challenge plasma glucose concentration between 7.8mmol/L and 11.0mmol/L. At week 56, patients in the liraglutide group without prediabetes at screening were re-randomised equally to receive continued liraglutide treatment or placebo for a further 12 weeks. Randomisation was stratified in the full study population according to prediabetes status at screening and according to BMI (≥30 versus <30).[3, 4]

There were four co-primary outcomes for Trial 1839: weight change from baseline (week 56), proportion of patients who lost at least 5% of their baseline body weight (week 56), proportion of patients who lost more than 10% of their baseline body weight (week 56), and time to onset of T2DM (week 160, patients with prediabetes only). Efficacy analyses were performed in the full-analysis set, which included all patients who underwent randomisation and received at least one dose of a study medicine and had at least one assessment after baseline. Co-primary outcomes were analysed in hierarchical order and last observation carried forward (LOCF) was used to impute missing data.[3, 4]

For all four co-primary outcomes, liraglutide was superior to placebo (see Table 2).[3, 4] Results for the post-hoc subgroup of patients (n=800) that supports the company's proposed positioning were consistent with the broader study population.

Table 2. Co-primary and secondary outcomes of Trial 1839 (FAS population).[3, 4]

	Liraglutide	Placebo	Difference (95% CI)
Co-primary outcomes at week 56			
n	2,437	1,225	
Change in body weight (%)	-8.0%	-2.6%	-5.4% (-6.0 to -5.1) p<0.001
Proportion of patients with ≥5% loss of body weight	63%	27%	OR= 4.8 (4.1 to 5.6) p<0.001

Proportion of patients with ≥10% loss of body weight	33%	11%	OR= 4.3 (3.5 to 5.3) p<0.001
Co-primary outcome at week 160 – time to onset of T2DM – patients with pre-diabetes			
n	1,472	738	
Events	26	46	
Mean time to T2DM diagnosis	99 weeks	87 weeks	HR= 0.21 (0.13 to 0.34) p<0.001
Secondary outcomes (week 160, patients with prediabetes)			
Change in waist circumference (cm)	-6.9	-3.4	-3.5
Change in SBP (mmHg)	-3.2	-0.5	-2.8
Change in fasting glucose (mmol/L)	-0.37	0.05	-0.41

BMI = body mass index; CI = confidence interval; FAS = full analysis set; HR = hazard ratio; OR = odds ratio; SBP = systolic blood pressure; T2DM = type 2 diabetes mellitus

Health Related Quality of Life (HRQoL) was assessed using the SF-36, Impact of Weight on Quality of Life–Lite (IWQoL-Lite), and TRIM-Weight questionnaires. At week 160, mean changes from baseline scores for all domains of SF-36 were greater in the liraglutide group than the placebo group, however these differences were numerically small. IWQoL-Lite results similarly favoured liraglutide. HRQoL was not assessed in the submitting company's proposed indication subgroup.

Summary of evidence on comparative safety

In the prediabetes subpopulation of Trial 1839, the total number of adverse events (AEs) reported by week 162 was 95% in the liraglutide group (n=1,501) and 89% in the placebo group (n=747). The number of serious AEs in each group was 15% versus 13% respectively.[4]

The most frequently reported AEs of any grade with an incidence ≥10% in the liraglutide group versus the placebo group were: nausea (41% versus 17%), diarrhoea (25% versus 14%), constipation (22% versus 11%), vomiting (20% versus 5.4%), dyspepsia (10% versus 4.7%), fatigue (10% versus 7.6%), nasopharyngitis (26% versus 28%), upper respiratory tract infection (16% versus 16%), influenza (12% versus 11%), lipase increased (10% versus 3.1%), decreased appetite (11% versus 3.5%), back pain (13% versus 16%), arthralgia (12% versus 13%), headache (18% versus 16%), dizziness (10% versus 7.2%).[4]

The safety profile of liraglutide 3mg once daily is similar to what has previously been reported for liraglutide 1.8mg in type 2 diabetes. The most commonly reported AEs with liraglutide 3mg were gastrointestinal disorders like nausea, diarrhoea, constipation, and vomiting. More data are required to assess if uncommon AEs such as pancreatitis and neoplasms are dose dependent.[2]

Summary of clinical effectiveness issues

Obesity is one of the most significant public health challenges globally, and Scotland has one of the highest levels of obesity worldwide. In 2019, 29% of adults in Scotland were obese and 66% were overweight/obese. Obesity has many serious health consequences, including hypertension, hyperglycaemia, dyslipidaemia, certain types of cancer, obstructive sleep apnoea and atherosclerosis. Obesity and overweight are also risk factors for cardiovascular disease including serious acute events like myocardial infarction, stroke and T2DM. Obesity adversely affects physical and mental health and reduces quality of life. Treatment can be challenging as the causes of obesity and overweight are multifactorial. Options include dietary modifications, behavioural and exercise counselling (often first-line), pharmacotherapy (typically used as an adjunct to lifestyle interventions) and surgical interventions for selected patients. Two medicines have previously been licensed for use in this setting: orlistat and naltrexone/bupropion. Orlistat predates the establishment of SMC and naltrexone/bupropion is not recommended by SMC due to non-submission (SMC2086). Orlistat is associated with several side effects that limit tolerability and NHSScotland prescribing data indicates that its use has declined in recent years. Clinical experts consulted by SMC considered that liraglutide fills an unmet need in this therapeutic area due to the lack of effective, tolerable treatments.[2, 5]

Reductions in body weight associated with liraglutide were both statistically significant and clinically meaningful compared with placebo in Trial 1839. Results for the subgroup of patients with prediabetes, randomised to 160 weeks of treatment, were consistent with the overall study population; loss of ≥10% body weight:25% in liraglutide group versus 9.9% in placebo group. The fourth co-primary outcome, time to onset of T2DM in patients with prediabetes at week 160, also achieved statistical significance, favouring liraglutide over placebo. However, these data may be immature as only 1.8% and 6.2% of the respective groups were diagnosed with T2DM during the study.[2-4]

There were some limitations to the evidence presented. The evidence to support the submitting company's proposed positioning comes from a post-hoc analysis of a subgroup: this type of analysis has inherent limitations.

Secondary outcomes such as systolic blood pressure, diastolic blood pressure and lipid parameters favoured treatment with liraglutide, however absolute differences were modest. There is uncertainty if these benefits are directly attributable to liraglutide independent of weight loss. The incidence of adjudication-confirmed major adverse cardiovascular events was similarly low in both treatment groups (0.19 events per 100 person-years of observation for liraglutide versus 0.20 for placebo). The cardiovascular benefits of treatment with liraglutide, as evaluated in Trial 1839, are uncertain. However, it is generally accepted in the wider literature that weight loss reduces long-term risk of cardiovascular disease.[2, 4]

There was a high rate of withdrawal in Trial 1839; and even higher in the subgroup of prediabetic patients randomised to 160 weeks of treatment. These rates are expected for placebo controlled

studies in this setting. However, this places more importance in the methods for addressing missing data. Last observation carried forward was used in the primary analysis which can favour active treatment. Sensitivity analyses were performed using baseline observation carried forward (BOCF) and multiple-imputation for measurement error (MI-ME), which are more conservative methods for imputing missing data. Based on these sensitivity analyses, results at week 160 still favoured liraglutide but were less pronounced.[2-4]

Patients with prediabetes who received treatment up to week 160 were not followed up after discontinuation. There is some evidence to suggest that weight could return to baseline. In Trial 1839, patients without prediabetes treated with liraglutide who had completed 1 year of treatment were re-randomised to 3-months treatment with liraglutide or placebo. Patients who switched from liraglutide to placebo gained a mean 2.91% (2.63kg) of body weight compared to 0.69% (0.61kg) in those who continued on liraglutide.[2]

Patients with obesity that is secondary to endocrinologic disorders (for example Cushing's Syndrome), treatment with medicines that may cause weight gain (such as insulin or psychotropic medicines), or eating disorders were not included in the study. Efficacy in these populations has not been established. Moreover, data in patients aged ≥75 years old are limited and liraglutide is not recommended for use in this setting for this group.[1, 2]

Clinical experts consulted by SMC considered that liraglutide is a therapeutic advancement in the treatment of obesity. Daily subcutaneous injections may impact patients who at present may receive no pharmacotherapy for their weight management. Liraglutide would be delivered as part of specialist weight management services and access to such services may vary throughout Scotland.

Patients from south Asian, Chinese, Black African and African-Caribbean ethnic groups are at an increased risk of chronic health conditions at a lower BMI than the White population.[6, 7] Clinical experts consulted by SMC agreed that this should be considered when prescribing liraglutide for weight management.

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis evaluating liraglutide 3.0mg, as an adjunct to reduced-calorie diet and increased physical activity (subsequently 'diet and exercise'), within its licensed indication with an additional restriction to patients who have a BMI ≥35 kg/m^2, prediabetes and a high risk of cardiovascular disease as described above. Comparison was made against diet and exercise alone, with no comparisons made to pharmacotherapy. Clinical expert responses suggest this was generally appropriate, although a small number of the experts consulted by SMC suggested that orlistat represents a relevant comparator.

A cohort-level Markov model was used to represent the disease pathway, focusing on the occurrence of specific complications of obesity and T2DM. This was essentially comprised of three

diabetes-related states ('prediabetes', 'normal glucose tolerance', 'type II diabetes mellitus' [T2DM]), with additional states representing the occurrence of first and further complications. Patients entered the model in the prediabetes health state with no complications, and could revert to normal glucose tolerance (after the first cycle only) or progress to T2DM, as well as experiencing a first complication of acute coronary syndrome (ACS), stroke, or cancer (in scenario analyses only). All patients experiencing ACS or stroke were assumed to develop T2DM. The 'further complications' level represented a combination of two of the complications described above (ACS/stroke/cancer), again with the occurrence of T2DM assumed following a cardiovascular event. Patients could also experience a number of health-state independent events at any time, representing the onset of sleep apnoea, or receipt of knee replacement or bariatric surgery. A cycle length of three months was applied for the first year of the model, followed by an annual cycle length for the remainder of the forty year time horizon.

A post hoc analysis of Trial 1839 was used to inform the proportion of patients achieving a treatment response (≥ 5% weight loss at 12 weeks on the maintenance dose), the proportion of patients achieving reversion to normal glucose tolerance or progressing to T2DM.[4] The post hoc analysis also provided key characteristics (baseline characteristics, as well as change in BMI, systolic blood pressure, total cholesterol and HDL cholesterol to week 104), which informed the numerous published BMI-dependent risk models for clinical complications. The risk models were applied for each of the complications, including the risk of T2DM, cardiovascular events (separately modelled for each diabetes-related state) and the health state-independent events.[8-11] Non-responders to liraglutide were assumed to revert to equivalent effectiveness of the full diet and exercise cohort, while an assumption of linear treatment effect waning (33.3% reduction per year) was assumed for the three years following treatment discontinuation for responders. Background mortality was modelled according to Scottish life tables, and adjusted based on risk of death due to specific cardiovascular events (myocardial infarction, angina, stroke) per health state[12-16], as well as death due to bariatric surgery or knee replacement.

Baseline utilities were estimated using a study published by Søltoft *et al.*, 2009[17], which evaluated the relationship between EQ-5D derived utility and BMI. However, this relationship was only reported up to a BMI of 35kg/m^2, and a separate logarithmic function was applied to extrapolate utilities to levels above this threshold. Age-related adjustment was applied, and disutilities applied for T2DM (-0.037), post-ACS events (-0.037), post-stroke (-0.035) and cancer (-0.078). Larger temporary decrements were applied for bariatric surgery, knee replacement, obstructive sleep apnoea and various cardiovascular events for the year in which the event occurred. A scenario analysis was presented utilising EQ-5D data from the SCALE 1839 study, which used a multiple linear regression model to estimate coefficients of a baseline, BMI, age and gender-dependent utility function.

Medicines costs included the acquisition of liraglutide, as well as medications for blood pressure and T2DM. Liraglutide was assumed to be administered to all patients for a total of 16 weeks (four week titration and 12 weeks maintenance), at which point non-responders discontinued treatment. A subgroup analysis of data from responders in the SCALE 1839 study provided a time-to-event discontinuation curve to the two year time point, at which point all patients were

assumed to discontinue treatment. The assumption of this two year stopping rule was based on clinical input received by the company, which suggested patients will receive liraglutide for an average of 1-2 years; in the resubmission, the submitting company provided a number of real-world data analyses to support this assumption. A variety of published sources were utilised for the application of health-state specific resource use, and the costs of severe gastrointestinal adverse events were included for liraglutide.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a simple discount was offered on the list price.

The base case results are shown in table 3. Liraglutide was associated with a slight increase in QALYs driven by an increased proportion of patients reverting to normal glucose tolerance and reduced progression to T2DM, with a corresponding slight increase in costs driven by liraglutide acquisition and balanced against reduced costs of obesity complications.

Table 3: Base-case results based on PAS price

Technologies	Costs (£)	LYG	QALYs	ICER (£/QALY)
Liraglutide 3.0mg + diet & exercise	21,655	18.236	15.029	10,549
Diet & exercise	20,994	18.204	14.966	
Incremental	661	0.033	0.063	

LYG= life years gained; QALY= Quality-adjusted life year; ICER= Incremental cost-effectiveness ratio

Key scenario analyses are shown in table 4. The model was upwardly sensitive to the modification of the treatment waning effect, use of a reduced twenty year time horizon, removal of the assumption of automatic onset of T2DM following a cardiovascular event, alternative approach to modelling effectiveness for non-responders, and the use of alternative risk models. Removal of the two year treatment stopping rule also resulted in a significant increase in the ICER.

Table 4: Key scenario analyses

	Model settings	Scenario analysis setting	Incremental Cost	Incremental QALY	ICER (£/QALY)
	Base-case output	-	661	0.06	10,549
1.	Waning of treatment effect	Treatment effect is immediately lost one-year post treatment period	731	0.06	13,221
2.		Treatment effect is immediately lost three years post treatment period	441	0.09	4,794

3.	Model time horizon	20 years	694	0.05	15,003
4.	T2DM post CV event	Prediabetic patients do not automatically develop T2DM with a CV event	675	0.06	11,474
5.	Liraglutide non-responder effectiveness	Liraglutide non-responders have diet & exercise non-responder effectiveness	736	0.06	13,295
6.	Adverse events	Include disutility and costs of adverse events (liraglutide arm)	667	0.06	10,778
7.	Utility	SCALE 1839 trial utility co-efficients	661	0.06	10,826
	Additional requested scenarios				
8.	Baseline characteristics: history of cardiovascular disease	Framingham Heart Study Risk equation applied to estimate risk of subsequent CVD events for proportion of patients with history of CVD from SCALE 1839	605	0.061	9,852
9.	Two-year stopping rule	Removal of stopping rule, time-to-discontinuation extrapolated using best—fitting function (generalised gamma)	1,649	0.093	17,809
10.	NGT health state cost	NGT health state cost equivalent to prediabetes	713	0.063	11,380
11.	Combined scenario	Combination of plausible alternative scenarios: 1, 4, 5, 6, 7, 8, 9, 10 *plus* the use of MI-ME for missing trial data	1,922	0.071	27,192

QALY= Quality-adjusted life year; ICER= Incremental cost-effectiveness ratio; T2DM= type 2 diabetes mellitus; CV(D)= cardiovascular (disease); NGT = normal glucose tolerance; MI-ME = multiple-imputation for measurement error

The model was relatively stable to changes in individual parameters. In the resubmission, there were two main uncertainties discussed at NDC:

- Expert input suggested that orlistat may be considered a comparator for some patients, although the submitting company suggested that its uptake and ongoing use is limited by tolerability issues. Data was provided in the resubmission which indicated that orlistat prescriptions have declined significantly over the last five years; these data were verified by

more recent analysis received by SMC. On review of these data, NDC agreed that orlistat may not be a key comparator.

- A two-year stopping rule was applied in the model for all patients who respond to liraglutide. The submitting company initially stated that this was based upon an estimate from clinicians who suggest an average treatment duration of 1 – 2 years is expected. From SMC clinical expert responses, there may be concerns about arbitrarily stopping treatment for those patients who are willing to continue with the daily subcutaneous injections. Removal of the stopping rule, while instead extrapolating the Kaplan-Meier discontinuation data, results in an increased ICER (Scenario 9). However, in the resubmission, the submitting company provided a number of 'real world' studies which suggest that the duration of liraglutide treatment is likely to be less than two years for the majority of patients.

There were also a number of limitations and uncertainties that remained from the initial submission, however were considered to be adequately explored in scenario analyses:

- Although a treatment waning effect was applied following treatment discontinuation for responding patients, the duration that the treatment effect was sustained may overestimate the benefits of liraglutide post-treatment. A more conservative approach, such as assuming BMI reverts to baseline within one year, was felt more appropriate (Scenario 1).
- An additional limitation related to the treatment stopping rule was the assumption that patients who experience weight gain following discontinuation of liraglutide will not receive re-treatment. Clinical expert input received by SMC suggested that, for patients who had previously achieved a response, it is likely that liraglutide retreatment would be considered in practice. This limitation adds uncertainty to the analysis. However, it is acknowledged that a lack of evidence and methodological challenges preclude the modelling of both the costs and benefits of repeated liraglutide treatment.
- An assumption was made that patients who do not respond to liraglutide will revert to the clinical effects of the full diet and exercise cohort (responders and non-responders). However, as liraglutide is administered as an adjunct to diet and exercise, by definition patients also did not respond to the diet and exercise regimen. The use of data specifically for non-responders to the diet and exercise regimen was considered more appropriate, and led to an increased ICER (Scenario 5).
- In the base case, patients who experience a cardiovascular event were assumed to automatically develop T2DM. This assumption would seem to lack clinical validity. Removal of this assumption caused a slight increase in the ICER (Scenario 4).
- Patients who enter the normal glucose tolerance health state were assumed to require no ongoing monitoring costs relating to diabetes management. It was considered appropriate to assume equivalent costs to those patients in the prediabetes state, in which case the ICER increases slightly (Scenario 10).
- Patients entering the model were assumed to have no prior history of cardiovascular disease, despite this being the case for 12.9% of patients in the SCALE 1839 study. Use of alternative risk models (the Framingham Heart Study) allow for this risk factor to be considered and may be more appropriate in a combined scenario analysis. The effect of this modification is a slight reduction in the ICER (Scenario 8).

Overall, a number of assumptions have been made where plausible alternatives may be preferred. A combined scenario analysis was obtained which represents a plausible estimate (Table 4, Scenario 11).

Despite these uncertainties, the economic case was demonstrated.

Summary of patient and carer involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from Diabetes Scotland and Obesity UK. Diabetes Scotland is a Scottish Charitable Incorporated Organisation and Obesity UK is a registered charity.

- Diabetes Scotland has not received any pharmaceutical company funding in the past two years. Obesity UK has received 30% pharmaceutical company funding in the past two years, with none from the submitting company.

- Obesity is a complex issue with many different causes. Two-thirds of adults in Scotland have a BMI in the overweight or obese category, increasing their risk of developing T2DM and other serious health conditions. Obesity rates are highest (and increasing) among those from the most deprived communities. In addition, members of minority ethnic groups are known to be at equivalent risk of the consequences of obesity at a lower BMI than the white population. Obesity can diminish a person's overall quality of life as people living with obesity may experience depression, difficulty in hygiene practices, disability, sexual problems, shame and guilt, social isolation and, because of this, lower work achievements. People also often experience stigma and may encounter discrimination.

- For some people, combined lifestyle interventions - including diet, physical activity and sustained weight loss - can be effective in reducing the risk of T2DM. However, many people find it challenging to achieve a healthy weight. This medicine is part of a range of interventions that can help. There is currently only one option for pharmaceutical intervention for the treatment of obesity in Scotland. Having more choice in treatments may benefit the patient in a more holistic approach toward treatment, as what works for one person may not be suitable for another. Achieving weight loss with this medication may enable the patient to increase their levels of physical activity and mobility which could reduce their need for care and support from family members. The increased independence could also lead to improved outcomes for individuals.

Treatments need to be tailored to the patients' needs, with more choices and options becoming available to best suit the person's lifestyle, weight, personal circumstances, and potential health benefits. The patient group welcomes a treatment option that has shown, with lifestyle measures,

to achieve greater weight loss in people at high risk of T2DM compared to lifestyle measures alone, and to slow down the progression of its development.

Additional information: guidelines and protocols

The National Institute of Health and Clinical Excellence (NICE) Clinical guideline number 189 (CG189): Obesity: identification, assessment and management, was published in November 2014. This guideline recommends that, pharmacological treatment be considered only after dietary, exercise and behavioural approaches have been started and evaluated. In addition, drug treatment should only be considered in people who have not reached their target weight loss or have reached a plateau on dietary, activity and behavioural changes. Bariatric surgery is a treatment option for people with obesity if specified criteria are fulfilled and all appropriate non-surgical measures have been tried but the person has not achieved or maintained adequate, clinically beneficial weight loss.[18]

The Scottish Intercollegiate Guidelines Network (SIGN) Management of Obesity (SIGN 115) guideline was published in February 2010 but has been withdrawn. [7]

Additional information: comparators

Diet and exercise alone; orlistat

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
liraglutide (Saxenda®)	**Starting dose: 0.6mg subcutaneously once daily, increased to 3.0mg once daily in increments of 0.6mg with at least one week intervals. Maintenance dose: 3mg once daily**	**Year 1 cost: £2,289 Maintenance year cost: £2,381**

Cost from eMC Dictionary of Medicines and Devices Browser on 19 January 2022. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 562 patients eligible for treatment with liraglutide in year 1 rising to 960 in year 5. The estimated uptake rate was 25% in year 1 and 90% in year 5. This resulted in 140 patients estimated to receive treatment in year 1 rising to 864 patients in year 5.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

Note that the budget impact estimates are subject to a number of assumptions, particularly that only a small proportion of patients fitting the clinical eligibility criteria will utilise specialist weight management services and therefore be eligible to receive liraglutide.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 14 March 2022.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.