Medicines Management Programme

Managed Access Protocol- Liraglutide (Saxenda®) 6 mg/ml solution for injection, as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients, with an initial BMI of ≥ 35 kg/m^2 with prediabetes and high-risk for cardiovascular disease

Approved by:	Prof. Michael Barry, Clinical Lead, MMP.
Date approved:	11th May 2023
Version:	Version 1.2

Table of Contents

List of tables

List of Abbreviations

BMI	Body mass index
BP	Blood pressure
CDS	Community Drug Schemes
cm	Centimetres
CrCl	Creatinine clearance
CVD	Cardiovascular disease
DP	Drugs Payment
GLP-1	Glucagon-like peptide-1
GMS	General Medical Services
HbA1c	Haemoglobin A1c
HSE	Health Service Executive
Kg	Kilograms
MMP	Medicines Management Programme
NYHA	New York Heart Association
PCRS	Primary Care Reimbursement Service
PFP	Pre-filled pen
SmPC	Summary of Product Characteristics

1. Liraglutide

Liraglutide is an acylated human glucagon-like peptide-1 (GLP-1) analogue produced by recombinant DNA technology in *Saccharomyces cerevisiae*.

1.1 Licensed indication

Liraglutide (Saxenda®) is indicated 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 (obesity), or
- ≥ 27 kg/m² to < 30 kg/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 (Saxenda®) 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.[i]

Liraglutide (Saxenda®) can be used as an adjunct to healthy nutrition and increased physical activity for weight management in **adolescent patients (≥ 12 years)** with:

- obesity (BMI corresponding to ≥ 30 kg/m^2 for adults by international cut-off points) and
- body weight above 60 kg.

Treatment with liraglutide (Saxenda®) should be discontinued and re-evaluated if patients have not lost at least 4 % of their BMI or BMI z score after 12 weeks on the 3.0 mg/day or maximum tolerated dose.[i]

1.1.1 Dose escalation schedule for the initiation of liraglutide (Saxenda®)

The starting dose for liraglutide (Saxenda®) is 0.6 mg once daily by subcutaneous injection. The dose should be increased in increments of 0.6 mg with at least one-week intervals to a maintenance dose of 3.0 mg/day as outlined in table 1.

[i] Please refer to the Summary of Product Characteristics for full prescribing information.

Table 1: Dose escalation schedule for liraglutide (Saxenda®)

Week	Dose injected
Week 1	0.6 mg once a day
Week 2	1.2 mg once a day
Week 3	1.8 mg once a day
Week 4	2.4 mg once a day
Week 5 and onwards	3.0 mg once a day

1.2 Reimbursement

Conditional reimbursement of liraglutide (Saxenda®) 6 mg/ml solution for injection in pre-filled pen (PFP) is available under the Community Drug Schemes (CDS), specifically the Drugs Payment (DP) and General Medical Services (GMS) schemes, for weight management in a subgroup of the licensed population, that is:

- **As an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients, with an initial BMI of ≥ 35 kg/m^2 with prediabetes and high-risk for cardiovascular disease (CVD).**

  Treatment should be discontinued for patients who have not lost ≥ 5% of their initial body weight after 12 weeks of treatment on the 3.0 mg/day dose.

Prescribers are required to apply for reimbursement approval on an individual patient basis through the Health Service Executive (HSE) - Primary Care Reimbursement Service (PCRS) online application system. The process involves two phases of reimbursement approval.

1.2.1 Phase 1- Initiation

Phase 1 is to ascertain if a patient meets the criteria for initial reimbursement support. If a patient is recommended for reimbursement in this phase, authorisation is granted for an initial period of six months (24 weeks). The time frame takes into account the 4 - week dose titration interval (table 1), followed by 12 weeks at the therapeutic dose of 3.0 mg/day. An additional 8 weeks is permitted to facilitate the submission of updated data to assess the eligibility for continued reimbursement support in phase 2.

1.2.2 Phase 2- Continuation

Phase 2 is to demonstrate a patient's response to phase 1 and the requirement for continued reimbursement support. Prescribers are required to submit a phase 2 application once the patient has completed 12 weeks of treatment with liraglutide (Saxenda®) at a dose of 3.0 mg/day. A patient who meets the criteria for phase 2 is approved for continued reimbursement support for a total duration of two years (24 months) from the date of the initial phase 1 application. Each year up to 13 packs can be dispensed, with each pack containing five 3 ml PFPs of liraglutide (Saxenda®) 6 mg/ml solution for injection. If the prescriber does not submit a phase 2 application or the patient does not meet the designated phase 2 criteria, the patient will no longer be deemed eligible for continued reimbursement support after phase 1 (24 weeks).

1.2.3 Reimbursement details

The reimbursement details for liraglutide (Saxenda®) 6 mg/ml solution for injection in PFP, available under the CDS from 1st January 2023, are outlined in table 2.

Table 2: Reimbursement details for liraglutide (Saxenda®) 6 mg/ml solution for injection

Medicinal product (Pack size)	Reimbursement code	Reimbursement price*
Saxenda® 6 mg/ml solution for injection in pre-filled pen (5 x 3 ml)	37709	€ 186.98

*As of 01/01/2023

A commercial in confidence arrangement is in place with the marketing authorisation holder to reduce the net acquisition cost of this biological medicine to the HSE.

2. Prescribers

Prescribers should ensure liraglutide (Saxenda®) is prescribed in accordance with its license, as an adjunct to a reduced-calorie diet and increased physical activity for the treatment of weight management. Behaviour supports for non-pharmacological interventions should be available and referral to these services considered to meet the patient's needs as appropriate.

Due to the information that is required to be submitted, the prescriber responsible for the initiation of treatment should complete the online application. Approval for reimbursement support should be in place prior to issuing a prescription for reimbursement under the CDS.

3. Reimbursement criteria – Phase 1: Initiation Application

This section outlines the criteria that must be satisfied in phase 1 in order for a patient to be recommended for reimbursement of liraglutide (Saxenda®) for an initial period of six months (24 weeks).

3.1 Patient age

Applications for reimbursement approval will only be considered for adults aged 18 - 74 years at the time of application.

3.2 Body Mass Index (BMI) score

The calculation of the BMI score must be completed on the online application system by inputting the patient's weight in kilograms (kg) and height in centimetres (cm). These measurements should be taken at the time of submitting the application. Reimbursement of liraglutide (Saxenda®) will only be supported for a patient with a BMI score ≥ 35 kg/m^2.

3.3 Non-pharmacological interventions

The reimbursement of liraglutide (Saxenda®) will only be approved as an adjunct to a reduced-calorie diet and increased physical activity. Therefore, to be considered for reimbursement support, prescribers must confirm the patient is actively participating in non-pharmacological interventions.

3.4 Patient clinical history

In line with the exclusion criteria for the SCALE Obesity & Pre-diabetes trial (NCT01272219) and information contained within the Summary of Product Characteristics (SmPC), reimbursement of liraglutide (Saxenda®) will not be considered in the following circumstances:[1,2]

- patients with obesity secondary to endocrinological or eating disorders
- patients with uncontrolled hypothyroidism/hyperthyroidism
- patients who are pregnant or currently breastfeeding
- patients with New York Heart Association (NYHA) class IV heart failure
- patients with severe renal impairment- Creatinine Clearance (CrCl) < 30 ml/min
- patients with severe hepatic impairment- Child Pugh score > 9.

3.5 Non-diabetic hyperglycaemia (Prediabetes)

For reimbursement approval, the patient should have an established diagnosis of non-diabetic hyperglycaemia (prediabetes).

In this context, non-diabetic hyperglycaemia (prediabetes) is defined as having:

- fasting plasma glucose level of 5.5 - 6.9 mmol/L,
- haemoglobin A1c (HbA1c) level of 42 - 47 mmol/mol.

Prior to reimbursement approval, prescribers are required to confirm this diagnosis and submit information pertaining to both of the above parameters. The readings must have been taken within 30 days of the date of application.

3.6 Cardiovascular risk factors

Prior to reimbursement approval, prescribers are required to confirm a patient is at high-risk for CVD and submit information in relation to either of the parameters below. The readings must be taken within 30 days of the date of application.

In this context, high-risk for CVD is defined as having either:

- fasting total cholesterol level > 5 mmol/L, or
- mean systolic blood pressure (BP) > 140 mmHg confirmed on a 24-hour BP monitor.

Details of the patient's current pharmacological treatment(s) pertaining to the cardiovascular risk factor are also required. For applications where the parameters are outside of those specified above, pharmacological management of same will be taken into consideration.

4. Reimbursement criteria- Phase 2: Continuation Application

To be considered for continued reimbursement support after phase 1, it is compulsory for the prescriber to submit a phase 2 continuation application via the online application system once the patient has received 12 weeks of treatment with liraglutide (Saxenda®) at a dose of 3 mg/day. An additional 8 weeks of reimbursement support will be facilitated to allow the submission of this data. The total duration of phase 1 and phase 2 reimbursement support is two years (24 months) from the date of the phase 1 application. If a patient requires continued treatment after this time, the prescriber will be required to submit a new application via the online application system.

This section outlines the criteria that must be satisfied in phase 2 for a patient to be recommended for continued reimbursement support after the initial phase 1 approval.

4.1 Continuation of non-pharmacological interventions

To be considered for continued reimbursement support, prescribers are required to confirm the patient continues to participate in non-pharmacological interventions which includes a reduced-calorie diet and increased physical activity.

4.2 Responder to Treatment

To be considered for continued reimbursement support, a patient must be deemed a responder to phase 1 of treatment. A responder is defined as having a reduction of at least 5 % in their initial body weight after 12 weeks of treatment with liraglutide (Saxenda®) 3.0 mg/day. Prescribers are required to submit details of the patient's updated weight in kg. This measurement should be taken at the time of submitting the phase 2 application. The system will determine the percentage weight change based on the information submitted in the phase 1 application.

If a patient is deemed a responder and meets the criteria for phase 2, reimbursement support will be continued. A patient deemed a non-responder to treatment or who does not continue to participate in non-pharmacological interventions will no longer be eligible for continued reimbursement support after phase 1.

5. Prescribing of liraglutide (Saxenda®)

Prior to prescribing liraglutide (Saxenda®) for reimbursement under the CDS, prescribers must ensure that the patient has been approved for phase 1 or phase 2 reimbursement support via the online application system. As part of the online application process, prescribers must confirm the patient is aware that the application is being made on their behalf and that audits may occur during which their personal data will be reviewed. In addition, prescribers must ensure the patient is aware phase 1 reimbursement support is for a maximum duration of six months (24 weeks) and that updated criteria must be submitted in phase 2 to be considered for continued reimbursement support for a total duration of two years.

Prescribers should refer to the SmPC for liraglutide (Saxenda®) 6 mg/ml solution for injection in PFP for full prescribing information including monitoring and patient counselling requirements.

References

1. Pi-Sunyer X., Astrup A., Fujioka K., et al. A Randomised, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. *New England Journal of Medicine* 2015;373(1):11-22.
2. Saxenda® 6 mg/ml solution for injection in pre-filled pen. SmPC. Last revised 29/06/2022. Accessed at www.ema.europa.eu on 08/07/2022.