Liraglutide (Saxenda®) for the treatment of obesity: a commentary on NICE Technology Appraisal 664

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Abstract

Saxenda, Liraglutide 3.0 mg, is a glucagon-like peptide-1 (GLP-1) analogue that is licensed for the treatment of adults with overweight and obesity. In this commentary we review the NICE technology appraisal (TA664) on the use of Saxenda in the National Health Service (NHS) and its implication in clinical practice.

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The National Institute for Health and Care Excellence (NICE) published its single technology appraisal (TA) document on the use of liraglutide 3.0 mg (Saxenda®, Novo Nordisk) for obesity management on 9 December 2020.[1] The document signals a new era in the medical management of obesity in the National Health Service (NHS). Prior to this publication the only medicine available on the NHS for weight loss was orlistat, but now a glucagon-like peptide-1 (GLP-1) analogue is available for use by healthcare professionals within the boundaries set up by NICE, discussed below.

Obesity is a chronic relapsing disease affecting one in four of the adult population in the UK.[2] Obesity management in England is provided through a tiered system,[3] with Tier 1 including universal interventions and Tier 2 including short-term lifestyle interventions (eg, commercial weight management programmes, exercise on prescription) and pharmacotherapy (eg, orlistat). Tiers 1 and 2 are commissioned by local authorities. Tier 3 is provided by a multidisciplinary weight management team which, as a minimum, usually includes a clinician, dietitian and psychologist. Tier 4 is bariatric surgery. Tiers 3 and 4 services are commissioned by clinical commissioning groups (CCGs).[4] An enquiry by the All-Party Parliamentary Group on Obesity in 2018 suggested that 52% and 82% of local authorities commissioned Tier 1 and Tier 2 services, respectively. It also found that 57% of CCGs commissioned Tier 3 services and 73% commissioned Tier 4 services.[4]

Saxenda® is a licensed treatment for weight management in adults with obesity (body mass index (BMI) ≥30 kg/m^2) or those with BMI ≥27 kg/m^2 (but <30 kg/m^2) in the presence of at least one weight-related comorbidity (ie, pre-diabetes, type 2 diabetes, hypertension, dyslipidaemia or obstructive sleep apnoea).[5] In clinical studies, people with obesity taking Saxenda® achieved around 8% weight loss (5.4% compared with placebo) at 56 weeks.[5,6] There was also a higher remission of pre-diabetes in the treatment group compared with placebo (69.2% vs 32.7%).[5,6] The main side effects of GLP-1 analogues are gastrointestinal side effects, leading to 6.4% of patients discontinuing treatment with Saxenda®.[6]

The NICE single TA document recommends the use of Saxenda® alongside a reduced-calorie diet and increased physical activity in adults with obesity if all the following criteria are met:

(1) class II obesity, BMI ≥35 kg/m^2 (or at least 32.5 kg/m^2 for members of minority ethnic groups);
(2) pre-diabetes, defined as fasting plasma glucose (FPG) level of 5.5–6.9 mmol/L, or an HbA_{1c} of 42–47 mmol/mol;
(3) high risk of cardiovascular disease, defined as total cholesterol >5 mmol/L, or high-density lipoprotein <1.0 mmol/L for men and <1.3 mmol/L for women, or systolic blood pressure >140 mmHg;
(4) it is prescribed in secondary care by a specialist multidisciplinary Tier 3 weight management service; and
(5) the company provides it according to the commercial arrangement agreed with NICE. If the person achieves at least 5% weight loss at 3 months on Saxenda®, the treatment is continued for up to 2 years.[1,7]

While this approval represents a step forward in medical obesity management on the NHS, the above criteria might raise some challenges in practice.

1. The FPG cut-off used to define pre-diabetes in the TA appraisal (5.5 mmol/L) is lower than the current cut-off used in the UK

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(6.1 mmol/L)[8] and the cut-off used by the American Diabetic Association (5.6 mmol/L).[9] In the SCALE obesity and pre-diabetes study,[6] 60% of participants met the diagnosis of pre-diabetes (FPG 5.6–6.9 mmol/L, 2-hour plasma glucose 7.8–11 mmol/L on an oral glucose tolerance test, or HbA_{1c} 39–47 mmol/mol). As a result of using a lower cut-off of FPG to define pre-diabetes and the fact that many people attending Tier 3 services have severe obesity, it is likely that more people in Tier 3 services will be diagnosed with pre-diabetes and that Tier 3 services will receive more referrals from primary care for consideration of Saxenda®. However, Tier 3 services were not designed as a diabetes prevention programme and, without extra funding and investment to increase capacity, people may have to wait for a long time to access these services.

2. Patients will require education on how to use this injectable therapy. This will require nursing time that is not routinely available in most current Tier 3 services. Doctors and/or dietitians would be able to provide this education, but this will mean longer consultations and more responsibility and extra training for dietitians. This extra workload would probably be absorbed within current Tier 3 services structure, and some services may opt for group education to reduce cost.
3. The 5% weight loss target at 3 months is necessary to ensure that only those who would benefit most from this expensive treatment continue using it; in the SCALE Obesity and Prediabetes study one-third of participants taking Saxenda® did not achieve 5% weight loss at 12 weeks.[5,6] However, with many clinics being performed virtually, would a person's self-reported weight be acceptable? Should this assessment be performed in a Tier 3 service or primary care? Would this re-assessment fit in existing Tier 3 services care models or are extra visits needed? In reality, these extra weigh-in visits could probably be accommodated within existing Tier 3 services and performed by a healthcare assistant. It may also make sense to accept patients' self-reported weight until the COVID-19 pandemic is more under control.
4. If the treatment with Saxenda® is successful, it is continued for up to 2 years. This decision is likely driven by cost effectiveness. However, stopping treatment may lead to a regain of the weight lost. It is hard to take away a treatment from someone when it is working; we would not do that for people with other chronic health conditions such as hypertension. People embarking on treatment with Saxenda® must be fully informed about treatment duration and reasons for withdrawal. It is also important that prescribing be consistent (ie, all people receive similar duration of treatment). Furthermore, is this treatment a one-off intervention or would Tier 3 services accept a re-referral for another course of Saxenda®? We feel that, in terms of equality of access, a person should only be accepted once on a programme unless there is a strong reason to the contrary.
5. The decision to limit access to Saxenda® to those attending Tier 3 services is probably driven by the criteria set by the drug company in their application to NICE; as a way to limit the number of users thereby conserving NHS resources and ensuring cost effectiveness; to increase the chances of successful weight loss by combining treatment with dietary and psychology interventions; and the desire to offer an effective medical treatment for obesity to existing Tier 3 services. However, is this criterion just an extra hoop to be jumped through to get access to an effective medical treatment for obesity? Will this result in inappropriate referrals to Tier 3 services, where the person is not really interested in a multidisciplinary lifestyle intervention but rather a medical therapy to reduce weight and risk of type 2 diabetes? There are limited number of Tier 3 services and a large number of people with pre-diabetes. We believe that, to achieve fair access to treatment, there is a real need for more resources and expansion of existing Tier 3 services, with commissioning of such services where they do not exist.
6. A person's journey in a Tier 3 service is varied across the country and is usually commissioned for between 1 and 2 years. Saxenda® can be prescribed for up to 2 years. For Tier 3 services that offer a 1-year programme, keeping people under surveillance for another year is currently not possible. Thus, due to a post code lottery of commissioning policy, some people will receive one year of Saxenda®, some two, and others – in the absence of any commissioned Tier 3 service – may be denied treatment. Such a position is morally and ethically indefensible.
7. Lastly, the prescription of Saxenda® is likely to be a secondary care prescription only, 'red drug' on the formulary, in order to benefit from the NICE agreed NHS price discount. This means that clinicians in Tier 3 services will be responsible for time-consuming prescriptions. In areas where Tier 3 services are provided through primary care or private providers, it seems unlikely that NHS Trusts will accept paying for a drug that is not prescribed by their clinical teams. In addition, if provision of medications is restricted to a pharmacy located in secondary care, an effective method for medication home delivery service will be required or people with obesity will be subject to the expenses and time cost of visits to hospital, with unnecessarily increased exposure to COVID-19. Government policy appears to favour an enhanced role for Integrated Care Systems (formerly Sustainability and transformation Partnerships) which include NHS Trusts as well as the CCGs within a local health economy.

While Saxenda® is the first GLP-1 analogue that is licensed primarily for weight loss, recent trials suggest that medical therapy has an important role to play in obesity management in the future, bridging the gap between diet and lifestyle interventions on the one hand and weight loss surgery on the other. Semaglutide is another GLP-1 analogue that is currently being investigated as an obesity treatment. In the STEP 1 and STEP 2 trials, 50.5% of people with overweight or obesity (without type 2 diabetes; STEP 1) and 25.8% of adults with overweight or obesity and type 2 diabetes (STEP 2) taking semaglutide, 2.4 mg once a week, achieved 15% or more weight loss at 68 weeks.[10,11] Clinical trials are also ongoing to examine the practicality and cost effectiveness of using expensive medical weight loss therapies in real-life settings.[12]

Key messages

- Saxenda, Liraglutide 3.0 mg, is an effective medical treatment for obesity that is now available to adults in the Tier-3 weight management services in the NHS
- Better funding and expansion of Tier-3 services is urgently needed to improve access and reduce inequality of obesity care
- More investment and true collaboration between all stakeholders are essential if the NHS is to provide an effective system to manage obesity at a population level

In summary, the approval of Saxenda® by NICE opens a new and exciting chapter in obesity management in the NHS. However, restricting its use to Tier 3 services without investment and expansion of these services will be a block that will limit patients' access to a potentially effective treatment, and will add further pressure on already stretched Tier 3 services. Expansion and more investment in Tier 3 services are therefore needed. One way of increasing access to Saxenda®, in a climate of limited NHS resources, is allowing the prescription of Saxenda® to continue by primary care physicians for the duration recommended by NICE after its initiation in a Tier 3 service, rather than restricting all prescriptions to a secondary care setting.

It is also time to consider obesity as a chronic disease that requires lifelong treatment rather than an acute illness that could be managed by a short course of therapy; let it be lifestyle intervention, medical or weight loss surgery. In reality the tiered system of weight management services in England could be seen more as a way of rationing access to bariatric surgery rather than of effectively supporting at scale the large number of people facing serious and often lifelong problems with overweight and obesity. As the NHS emerges from the COVID-19 pandemic, a national review of these services is urgently required. However, while the tiered system needs to evolve if it is to remain relevant, replacing it with another system may not be the solution. Without more investment, genuine interest and better collaboration between the different stakeholders in the provision of treatment and prevention of obesity at a population level, any system is doomed to failure. Any review should recognise not just pharmaceutical developments but the emergence of new programmes such as low calorie diets. Ultimately, the goal should be to strengthen Weight Management Specialist Services and achieve integration with the emerging Primary Care Networks so that they become an essential element of all Integrated Care Systems and help to ensure that support for people with obesity is lifelong, not just for two years.

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