National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Liraglutide for managing overweight and obesity

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Association for the Study of Obesity	Yes, obesity is a public health challenge in the UK with only one available drug therapy. Hence, the topic of this appraisal is related to unmet need in the management of patients with obesity. As a result, we would strongly support referring this topic to NICE as liraglutide has the potential to address the treatment gap in patients with obesity.	Thank you for your comment.
	Obesity Group of the British Dietetic Association	Yes, in our view it would be so.	Thank you for your comment.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	It is highly appropriate that NICE appraise this topic	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
	Dorset CCG	Yes	Thank you for your comment.
	Novo Nordisk	Yes	Thank you for your comment.
	Royal College of Physicians	Yes, we would strongly support referring this topic to NICE for appraisal as there is significant unmet need for effective obesity treatment and liraglutide has the potential to help meet that need.	Thank you for your comment.
	Royal College of Pathologists	yes	Thank you for your comment.
	GlaxoSmithKline	Yes	Thank you for your comment.
Wording	Association for the Study of Obesity	The outcomes need to be expanded to include other obesity-related complications that have been show to benefit significantly from weight loss such as: glycaemic control in patients with Type 2 diabetes, idiopathic intracranial hypertension, Non-alcoholic fatty liver disease, obstructive sleep apnoea	Thank you for your comment. In order to allow flexibility, the remit for the scope has been kept broad. However, idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added to the outcomes.
	Obesity Group of the British	Yes.	Thank you for your comment.

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	Dietetic Association		
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	Yes	Thank you for your comment.
	Dorset CCG	For consistency should it be specified that the overweight with risk factors comment be clarified as > 27 kg/m2 as overweight is defined as >25 kg/m2	Thank you for your comment. This reflects the marketing authorisation for liraglutide (Saxenda).
	Novo Nordisk	For clarity, please amend: “in addition to diet and physical activity” To read “in addition to a reduced calorie diet and increased physical activity”	Thank you for your comment. The wording of the remit has been changed from ‘in addition to diet and physical activity’ to ‘in addition to a reduced calorie diet and increased physical activity’ to align with wording in the marking authorisation). Additional details about the adjuvant diet and exercises indicated are included in the

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			description of the technology in the scope.
	Royal College of Physicians	The remit should clearly highlight some of the other conditions that are caused by obesity such as non-alcoholic fatty liver disease (NAFLD) and benign intracranial hypertension in addition to cardiovascular disease, diabetes and sleep apnoea.	Thank you for your comment. In order to allow flexibility, the remit for the scope has been kept broad. However, these conditions have been added to the background information in the scope.
	Royal College of Pathologists	yes	Thank you for your comment.
	GlaxoSmithKline	Yes	Thank you for your comment.
Timeliness	Association for the Study of Obesity	The proposed appraisal needs to be considered urgently as it is relevant to an unmet need in the management of patients with obesity. In addition, liraglutide has been available for 18 months in the UK as a weight loss drug outside the NHS	Thank you for your comment.
	Obesity Group of the British Dietetic Association	Given the high prevalence of obesity within the UK population, the health impact associated with it, and the limited medication treatment options available in our view this is urgent.	Thank you for your comment.

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	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	Urgent. This appraisal will allow clinicians to offer this treatment to adults who are overweight and obese and have an increased risk of developing Type 2 diabetes.	Thank you for your comment.
	Dorset CCG	As obesity is a growing public health concern then it is important that there is clear guidance for the NHS about the clinical and cost-effectiveness of this treatment and its suitability for prescribing. Primary care, especially, needs clear guidance in order for them to offer clear explanations to patients as NICE has the statement that the company will not actively promote it on the NHS.	Thank you for your comment.
	Novo Nordisk	Given the high unmet need for the clinically effective medical management of obesity in the NHS, the urgency of the proposed appraisal is high.	Thank you for your comment.
	Royal College of Pathologists	moderate	Thank you for your comment.
	Royal College of Physicians	Liraglutide has been approved for nearly 3 years and available for over 18 months so there is urgency to reach a decision on its appropriate use in the NHS for the management of obesity.	Thank you for your comment.
Additional comments on the draft remit	Obesity Group of the British Dietetic Association	N/a.	Thank you for your comment.

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	Dorset CCG	No	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Association for the Study of Obesity	The conditions that are caused by obesity need to expand to include obstructive sleep apnoea, non-alcoholic fatty liver disease, cardiovascular disease, idiopathic intracranial hypertension, subfertility in men and women.	Thank you for your comment. These conditions have been added to the background information in the scope.
	Obesity Group of the British Dietetic Association	We have no comments related to this.	Thank you for your comment.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	Yes	Thank you for your comment.
	Dorset CCG	Accurate according to the reference. Should some consideration be given to the obesity trends over time as detailed in the report.	Thank you for your comment. Information about trends in overweight and obesity in England have been

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			added to the background section of the scope.
	Novo Nordisk	Novo Nordisk would also like the following information to be included in the background information: Current wording: People who are overweight or obese are at an increased risk of developing cardiovascular disease, type 2 diabetes, atherosclerosis (the presence of fatty deposits in the arteries), hypertension and dyslipidaemia (abnormal levels of fats in the blood). Suggested new wording: Obesity is also associated with an increased risk of comorbidities such as non-diabetic hyperglycaemia (prediabetes) and type 2 diabetes, cardiovascular disease (CVD), osteoarthritis, dyslipidaemia, obstructive sleep apnoea and certain cancer types (1,2). Prediabetes has been shown to increase the short-term absolute risk of type 2 diabetes five- to six fold. The development of type 2 diabetes can be delayed or sometimes prevented in individuals with obesity that are able to lose weight (3). Obesity is also associated with an increase in all-cause mortality and reduced life expectancy when compared with normal-weight individuals (4,5). Patients with obesity have reduced health-related quality of life and impaired physical functioning (6). There is evidence to suggest that for patients with obesity, ≥5 percent weight loss has significant health benefits (7).	Thank you for your comment. The background section of the scope is designed to give a brief overview, and is not able to comprehensively detail all aspects of a disease area. However, the background section has been updated to include more detail about co-morbidities associated with overweight and obesity. The background section has also been updated to include further details of the classification of obesity (in line with NICE CG189). The proposed information about Tier 2 services has not been added because the update to NICE CG189 has not been finalised.

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		Rationale: Previously published literature reviews and a World Health Organization (WHO) report also states sleep apnoea, osteoarthritis, prediabetes and certain types of cancers are associated with obesity (1,2). There is also evidence that suggests that obesity is associated with an increase in all-cause mortality, reduced health related quality of life and that ≥5 percent weight loss has significant health benefits (4-7). Current wording: In adults of European family origin, overweight is typically defined by a BMI of 25 kg/m2 to <30 kg/m2 and obesity by a BMI of 30 kg/m2 or more (an appropriate adjustment of BMI for other ethnic groups is necessary). Suggested new wording: In adults of European family origin, overweight is typically defined by a BMI of 25 kg/m2 to <30 kg/m2 and obesity by a BMI of 30 kg/m2 or more (an appropriate adjustment of BMI for other ethnic groups is necessary). BMI in the range of 30-34.9 is defined as Obesity class I, 35-39.9 as Obesity class II and BMI>40 as obesity class III. Rationale: The categories are defined in NICE clinical guideline 189; adding this additional background makes clear to the reader that treatment cut offs reported in the scope are consistent with disease severity and usual practice.	

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		Current wording: Specialist multi-disciplinary weight management interventions (known as tier 3 interventions) are also used in current practice. Tier 3 interventions include dietary, lifestyle and behaviour modification with or without drug therapy. Tier 3 interventions include dietary, lifestyle and behaviour modification with or without drug therapy. NICE clinical guideline 189 'Obesity: identification, assessment and management' recommends that drug therapy with orlistat should only be considered after dietary, physical activity and behavioural approaches have been started and evaluated. It recommends orlistat for the management of obesity in people with a BMI of 30 kg/m2 or more, and in people with a BMI of 28 kg/m2 or more and significant comorbidities. Suggested new wording: Different tiers of weight management services vary locally but usually both Tier 2 and Tier 3 interventions include dietary, lifestyle and behaviour modification with or without drug therapy. NICE clinical guideline 189 'Obesity: identification, assessment and management' recommends that drug therapy with orlistat should only be considered after dietary, physical activity and behavioural approaches have been started and evaluated. It recommends orlistat for the management of obesity in people with a BMI of 30 kg/m2 or more, and in people with a BMI of 28 kg/m2 or more and significant comorbidities. Rationale:	

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		Tier 2 also includes lifestyle interventions, diets and pharmacotherapy as defined by the British Obesity and Metabolic Surgery Society (BOMSS) 2017 Commissioning guide on weight assessment and management clinics (tier 3) (8). Therefore orlistat may also be offered in Tier 2 services. Following the consultation period for the update to NICE clinical guideline189, NICE has stated that the BOMSS commissioning guide will be taken into account when defining the Tiered structure for obesity management in clinical practice (9).	
	Royal College of Physicians	The background should clearly highlight some of the other conditions that are caused by obesity such as non-alcoholic fatty liver disease (NAFLD) and benign intracranial hypertension in addition to cardiovascular disease, diabetes and sleep apnoea. It should be made clear that tier 3 interventions can be appropriately delivered in either primary or secondary care.	Thank you for your comment. The background section has been updated to reflect these suggestions.
	GlaxoSmithKline	The background information is accurate and appropriate	Thank you for your comment.
	Public Health England	Public Health England (PHE) does not agree with the line 'In adults of European family origin, overweight is typically defined by a BMI of 25 kg/m2 to <30 kg/m2 and obesity by a BMI of 30 kg/m2 or more (an appropriate adjustment of BMI for other ethnic groups is necessary).' While some ethnic groups may be at increased risk of some ill health conditions at lower BMI than Caucasians the definition of overweight/obese does not differ by ethnic origin. This provides an incorrect message as worded.	Thank you for your comment. The scope has been updated to say 'some ethnic groups may be at increased risk of some ill health conditions at lower BMI than people of European family origin'. The description of the classification of overweight and obesity no longer mentions ethnicity.

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The technology/ intervention	Association for the Study of Obesity	Yes	Thank you for your comment.
	Obesity Group of the British Dietetic Association	We have no comments related to this.	Noted.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	Yes	Thank you for your comment.
	Dorset CCG	yes	Thank you for your comment.
	Novo Nordisk	Current wording: Liraglutide (Saxenda, Novo Nordisk Limited) is a glucagon-like peptide-1 (GLP-1) analogue produced by recombinant DNA technology in saccharomyces cerevisiae. It is administered by subcutaneous injection. Liraglutide has a marketing authorisation in the UK as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients with an initial 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 such as dysglycaemia (pre-diabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea.	Thank you for your comment. The appraisal will only appraise liraglutide within its marketing authorisation and within the remit of the scope. It is therefore not necessary to distinguish between doses from other indications.

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		Suggested new wording: Liraglutide is a glucagon-like peptide-1 (GLP-1) analogue produced by recombinant DNA technology in saccharomyces cerevisiae. It is administered by subcutaneous injection. Liraglutide 3.0mg (Saxenda®, Novo Nordisk Limited) has a marketing authorisation in the UK as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients with an initial 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 such as dysglycaemia (pre-diabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea. Treatment with liraglutide 3.0mg 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. In addition, Liraglutide 1.2mg and 1.8mg (Victoza®, Novo Nordisk Ltd) is licensed for adults with insufficiently controlled type 2 diabetes mellitus. This appraisal only considers the use of liraglutide 3.0mg (Saxenda, Novo Nordisk Limited) in a subgroup within its licensed indication for overweight and obesity. Rationale: To include the licensed indication for liraglutide 3.0mg and to differentiate from liraglutide 1.2mg and 1.8mg.	
	Royal College of Physicians	Yes	Thank you for your comment.

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	Royal College of Pathologists	yes	Thank you for your comment.
	Public Health England	Consideration should be made about the nutrient content of the reduced calorie diet – in comparison to government advice and some measurements to assess this should be considered	Thank you for your comment. In order to allow flexibility, the scope will be aligned to marketing authorisation of liraglutide (which does not specify about the nutritional content of the reduced calorie diet).
	GlaxoSmithKline	Yes, the description of the technology is appropriate.	Thank you for your comment.
Population	Association for the Study of Obesity	The population defined appropriately but we suggest having increased focus on patients with obesity-related complications who are likely to gain greater benefits from weight loss; particularly considering the cardiovascular outcomes trials with liraglutide in patients with high risk or established cardiovascular disease. In addition, a focus on patients with significant mental illness is important as this group of patients is prone to the development of obesity-related metabolic complications and liraglutide has been shown to be effective in this group of patients (Larsen et al JAMA Psychiatry 2017;74(7):719-728. doi:10.1001/jamapsychiatry.2017.1220)	Thank you for your comment. The population has been left broad to reflect the full marketing authorisation for liraglutide (Saxenda). The committee will consider how any recommendations it makes may have a differential impact on people with mental

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			illness or learning disability and the relevance of ethnicity when considering BMI thresholds.
	Obesity Group of the British Dietetic Association	We agree that the population is defined appropriately. We suggest that those with type 2 diabetes should be considered separately since weight loss and weight maintenance may be different in those who are overweight or obese with type 2 diabetes compared with other groups. Those who have pre-diabetes or obstructive sleep apnoea might also be considered separately.	Thank you for your comment. The population has been left broad to reflect the full marketing authorisation for liraglutide (Saxenda)
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	1. The population group should explicitly include adults with Type 2 diabetes who are obese but don't necessarily have poor glycaemic control (i.e. they are within their target range). This group will particularly benefit from weight management with a medication like a GLP-1 analogue due to the increased risk of developing complications, such as CVD. There is also added benefit of using GLP-1's in adults with Type 2 diabetes and established CVD as this can help prevent CVD events and cardiovascular deaths.	Thank you for your comment. The population has been left broad to reflect the full marketing authorisation for liraglutide (Saxenda).

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		NICE guideline NG28 - Type 2 diabetes in adults: management should be updated in line with the above for consistency. 2. Should also explicitly include BAME groups at a BMI of ≥ 27 kg/ m2 (classed as obese) without necessarily having the presence of any other co-morbidities.	
	Dorset CCG	An endocrinologist in our area has a concern that it is considering people with BMI of 27-30 with a comorbidity in the scope. “I’m not convinced many clinicians would be happy prescribing at a BMI of 27 with say hypertension as a comorbidity – so it would be unlikely to add to the evaluation”	Thank you for your comment. The population has been left broad to reflect the full marketing authorisation for liraglutide (Saxenda).
	Novo Nordisk	Novo Nordisk recognises the clinical and economic implications of recommending a pharmacotherapy for weight loss, and wants to ensure appropriate prescribing in patients who would most benefit and discontinue therapy in patients based on clinically appropriate stopping rules. In addition, Novo Nordisk wants to align with NICE’s aims of facilitating access for products which are found to offer the best values for patients and the NHS. To support this, Novo Nordisk is seeking a NICE recommendation for a subgroup of patients within the current licensed indication for liraglutide 3.0 mg; in adult patients with a BMI ≥35 with prediabetes (HbA1c measurement	Thank you for your comment. The population has been left broad to reflect the full marketing authorisation for liraglutide (Saxenda). The committee will consider how any recommendations it makes may have a

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		42-47 mmol/mol) and high risk CVD in specialist Tier 3 services. The rationale for this subgroup is discussed below. Rationale for use in specialist Tier 3 services: In NICE clinical guideline 189 for obesity, pharmacological therapy is limited by treatment line (after dietary, exercise and behavioural approaches have been started and evaluated) or for people who have not reached their target weight loss or have reached a plateau on dietary, activity and behavioural changes (Section 5.10.1). Currently in section 1.3.7 of NICE clinical guideline 189 there are several criteria that should be considered when referring patients to Tier 3, which includes assessment of complex patients or when conventional treatments have been unsuccessful (10). Pharmacological therapy can be prescribed for patients with obesity in Tier 2 and Tier 3 services. Orlistat is the only NICE recommended pharmacological treatment option currently available; however, its use is limited by undesirable side effects leading to poor adherence and outcomes. Therefore most patients either do not want to take orlistat or stop treatment after a short time (as stated by clinical experts in section 3.2 of the final appraisal determination for technology appraisal 494 (naltrexone-bupropion; Mysimba®) (11). Therefore, it is expected that patients with obesity will have been unsuccessfully treated on conventional treatment with or without available pharmacotherapy treatment options prior to being referred to Tier 3. Rationale for patients with obesity (BMI ≥35): Based on the latest consultation feedback on clinical guideline 189 (April 2018), best practice states that referral to Tier 3 should align with the BOMSS	differential impact on people with mental illness or learning disability and the relevance of ethnicity when considering BMI thresholds.

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		commissioning guide which considers patients with a BMI >40 or patients with a BMI ≥35 and other obesity-related comorbidities. This is based on input from appropriate specialists (8,9). Rationale for patients with obesity (BMI ≥35) and prediabetes: The BOMSS commissioning guide also suggests to consider offering patients with obesity identified as having prediabetes (HbA1c measurement 42-47 mmol/mol) to be referred to the NHS National Diabetes Prevention programme if clinically appropriate (8). However, the NHS Diabetes Prevention Programme eligibility criteria (2017) suggests that these patients, who also present with comorbidities, should also be eligible for Tier 3 weight management services (12). Therefore, prediabetes is a relevant additional criterion for patients treated with liraglutide 3.0mg. In addition to weight loss, the reversal of prediabetes to normal glucose tolerance has also been shown to reduce the incidence of type 2 diabetes (3) and its associated complications and has a big influence on the cost effectiveness of liraglutide 3.0mg in our cost effectiveness model. Rationale for high risk CVD: BMI is an important risk factor in developing CVD. NICE clinical guideline 181 states that patients with high risk of or with CVD who are obese should be offered appropriate advice and support to work towards achieving and maintaining a healthy weight (13). Liraglutide has been shown to reduce the risk of CVD events, which is reported in the current EMA Summary of Product Characteristics for liraglutide 3.0 mg. (14)	

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		Although the NICE definition of high risk CVD is defined as ≥20% 10 year risk of developing CVD, according to the QRISK2 calculator (13), some of the data required for this (e.g. patient postcode, family history of CVD, rheumatoid arthritis) has not been routinely collected in the liraglutide 3.0mg clinical study programme. Therefore Novo Nordisk has attempted to approximate high risk CVD patients based on key blood pressure and lipid thresholds advised through clinical expert opinion. These thresholds are also supported by the criteria used for key lipid and blood pressure parameters referenced in "support for implementation" paragraph in section 2.1 of NICE clinical guideline 181 (15). Therefore, we intend to explore the cost effectiveness of liraglutide 3.0mg in high risk CVD patients based on patients having at least one of the criteria below: • Total cholesterol > 5mmol/L • Systolic Blood Pressure >140 mmHg • HDL < 1.0 for men and < 1.3 for women Insofar as data are available consideration will also be given to clinical and cost effectiveness in different ethnic groups. Ethnicity impacts BMI definitions and risk of cardiovascular events and diabetes.	
	Royal College of Physicians	• We would suggest that the focus here should be on people with significant obesity-related health conditions, such as prediabetes, type 2 diabetes, and sleep apnoea, those with pre-existing CV disease, non-alcoholic fatty liver disease and benign intracranial hypertension. • People with serious mental illness are a high risk group from metabolic disease and related mortality and Larsen et al JAMA Psychiatry 2017;74(7):719-728. doi:10.1001/jamapsychiatry.2017.1220 showed	Thank you for your comment. The population has been left broad to reflect the full marketing authorisation for liraglutide (Saxenda).

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		liraglutide was effective in this group, so its use should be considered in this high risk group where the outcome is likely to be both clinically and cost effective. • People who meet criteria for bariatric surgery but are to unwell to undergo a surgical procedure.	The committee will consider how any recommendations it makes may have a differential impact on people with mental illness or learning disability and the relevance of ethnicity when considering BMI thresholds.
	Royal College of Pathologists	no comments	Noted.
	Public Health England	It is unclear why the cut off of 'BMI >27 with a comorbidity' has been chosen. PHE is not suggesting this may not be appropriate just that the justification is made.	Thank you for your comment. The population in the scope is aligned to the population indicated in the marketing authorisation.
	GlaxoSmithKline	Yes, the population is defined appropriately. But it would be useful if the differences in populations between the standard treatment (orlistat) and the new technology are highlighted.	Thank you for your comment. Liraglutide (Saxenda) will be appraised within its marketing authorisation.

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Comparators	Association for the Study of Obesity	Liraglutide should always be used in the context of life style intervention which is consistent with design of the SCALE Trials. Standard care should be defined as the provision of tier 2 or tier 3 services. Comparators can include orlistat and low energy diet (LED) or very low calorie diet (VLCD) which should be used in combination with standard care)	Thank you for your comment. The comparators section has been updated.
	Obesity Group of the British Dietetic Association	We agree with the proposed comparators. Standard care should be as defined by NICE (i.e. behaviour change, diet and physical activity as part of a multicomponent approach. This may include a range of dietary options including use of low or very low calorie diets). Standard care is delivered in tiers 2 and 3, and liraglutide would be added to standard care, not offered as an alternative.	Thank you for your comment. The comparators section has been updated.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	We agree with the comparators used. When making comparisons, it will be important to consider the other benefits aside from weight loss of GLP-1's for people with Type 2 diabetes, namely the glycaemic and CVD benefits.	Thank you for your comment.
	Dorset CCG	Yes, standard comparator and best alternative care	Thank you for your comment.
	Novo Nordisk	Novo Nordisk would like to propose the following amendments to the Comparators section: Current wording: • Standard management without liraglutide	Thank you for your comment. Although clinical expert comments in TA494 indicated that orlistat is not widely used, it is listed as an available treatment option in

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		• Orlistat (prescription dose) Suggested wording: • Standard management without liraglutide Rationale: Standard management without liraglutide is the only relevant comparator with which liraglutide 3.0 mg as an adjunct to standard management should be compared. In section 3.4 of the final appraisal determination for technology appraisal 494, the committee heard from the clinical experts and from consultees after consultation on the appraisal consultation document that standard management (lifestyle measures) is the relevant comparator because orlistat is not often used in clinical practice. It concluded that standard management was therefore the main comparator in the appraisal (11). The definition of standard management without liraglutide observed in UK clinical practice falls largely in line with the definition of comparator in our key trial for the appraisal (SCALE obesity and prediabetes).This involved lifestyle measures; every 4 weeks subjects received diet counselling (either in a group or individually) by a qualified dietitian according to local standards. There were 8 trial sites in the United Kingdom. Patients were also put on a hypo-caloric diet and expected to undertake physical activity. The current license recommends the use of liraglutide 3.0mg as an adjunct to diet and exercise (lifestyle measures) and therefore diet and exercise will continue to be a significant component for the ongoing management of obesity.	CG189. For completeness, it has been kept in the scope as a comparator. Bariatric surgery has also been added to the list of comparators for completeness.

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		Orlistat (prescription dose) is therefore not a relevant comparator. In section 3.2 of the final appraisal determination for technology appraisal 494, orlistat was not considered to be widely used by the clinical experts in clinical practice due to undesirable side effects leading to poor adherence and outcomes. As a result most patients do not want to take it or stop treatment after a short time. In section 3.4 of the document it was disregarded as a relevant comparator during the appraisal process by the committee (11). As mentioned above, patients with obesity who are unsuccessful on conventional treatment in Tier 2 are eligible for referral to Tier 3. Given orlistat is also prescribed in Tier 2, patients in our target population would have likely tried orlistat prior to consideration for treatment with liraglutide 3.0mg in Tier 3. Furthermore, most of the trials with orlistat were conducted over 20 years ago, so comparisons using these studies may be not be robust. Therefore, based on this rationale, orlistat should not be considered a relevant comparator. Bariatric surgery should also not be considered a relevant comparator in the appraisal for liraglutide 3.0mg. Although bariatric surgery may be considered a last resort treatment option for patients with obesity with a high BMI (a BMI of 40 kg/m2 or more, or between 35 kg/m2 and 40 kg/m2 and other significant disease) (10), in UK clinical practice it is not realistic that all patients will be offered bariatric surgery.	

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		In section 3.1 of the final appraisal determination for technology appraisal 494, clinical experts stated that only 0.1% of patients eligible for surgery actually have it (11). Furthermore, patients with obesity would be assessed in a Tier 3 service before being referred to Tier 4. (8) Therefore, there is an unmet need for a clinically effective weight loss tool as an adjunct to diet and exercise for these patients in specialist Tier 3 services prior to Tier 4. To account for bariatric surgery in the treatment pathway for obesity, this will be included in the economic model as an event. The rate of surgery would be based on the current incidence in the NHS and modifiable via sensitivity analysis. Mysimba® is not considered a relevant comparator as it is not recommended by NICE as a cost-effective treatment option for the NHS.	
	Royal College of Physicians	Main comparator is standard care defined as multicomponent interventions (as delivered in tier 2 and 3 obesity services). Liraglutide should always be added to the standard or care (it is not an alternative). Standard of care might include total or partial meal replacements.	Thank you for your comment. The comparators section has been updated.
	Royal College of Pathologists	Yes, bariatric surgery is mentioned in the background information and might be another comparator for highest BMI individuals.	Thank you for your comment. Bariatric surgery has been added to the list of comparators for completeness.

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	Public Health England	Issue of the dietary and physical activity components within the comparators may be confounding factors and this needs to be considered carefully when assessing the evidence.	Thank you for your comment. Comparators are chosen to reflect UK clinical practice. The appraisal committee will consider whether the economic model is robust (including assessing confounding).
	GlaxoSmithKline	Since orlistat is the only authorised medicine for obesity treatment in the UK, it is an appropriate comparator. However, only the 120mg prescription dose is approved for long term use; 60mg orlistat is only approved for 6 months. The indication for orlistat 60mg is limited to weight loss whereas the 120mg dose is indicated for the treatment of obese patients, which includes weight loss, maintenance and improvement in weight-related risk factors	Thank you for your comment. The scope specifies that the prescription dose of orlistat is a relevant comparator.
Outcomes	Association for the Study of Obesity	Yes, but in addition outcomes related to non-alcoholic fatty liver disease, idiopathic intracranial hypertension, obstructive sleep apnoea, and fertility should be captured as these are likely to improve significantly with weight loss	Thank you for your comment. Idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added to the scope. We recognise that there are several outcomes related to co-morbidities

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			associated with overweight and obesity that may be relevant to the economic evaluation. However, it is unlikely to be feasible to model all of these outcomes in a way that is informative for the appraisal committee. Mindful of this, the other outcomes included in the scope have been left to be consistent with those used in TA494.
	Obesity Group of the British Dietetic Association	We suggest in addition to those listed existing diabetes, obstructive sleep apnoea, and other risk factors for cardiovascular disease, risk factors for type 2 diabetes e.g. HbA1C. Possibly pre-surgical interventions e.g. orthopaedic, gynaecological, access to fertility treatments (conditions where pre-surgery weight loss is required).	Thank you for your comment. We recognise that there are several outcomes related to co-morbidities associated with overweight and obesity that may be relevant to the economic evaluation. However, it is unlikely to be feasible to model all of these outcomes in a way that is informative for the appraisal committee.

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			Mindful of this, the outcomes included in the scope have been left to be consistent with those used in TA494 and idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	Yes. Better glycaemic control in adults with Type 2 diabetes and therefore lower risk of developing diabetes complications which can affect quality of life.	Thank you for your comment. We recognise that there are several outcomes related to co-morbidities associated with overweight and obesity that may be relevant to the economic evaluation. However, it is unlikely to be feasible to model all of these outcomes in a way that is informative for the appraisal committee. Mindful of this, the

Section	Consultee/ Commentator	Comments [sic]	Action
			outcomes included in the scope have been left to be consistent with those used in TA494. and idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added.
	Dorset CCG	Yes but should the length of treatment course be clarified and explicit for how to proceed if treatment is or is not successful after 12 weeks.	Thank you for your comment. Liraglutide will be appraised within its marketing authorisation.
	Novo Nordisk	The following outcomes were collected as part of the Saxenda clinical development programme:- • Fasting weight change from baseline (%, kg) • BMI change from baseline • Waist circumference • Impact on glycaemic status and prediabetes • Proportion of subjects losing ≥5% of baseline fasting body weight (5% responders) • Proportion of subjects losing >10% of baseline fasting body weight (10% responders)	Thank you for your comment. We recognise that there are several outcomes related to co-morbidities associated with overweight and obesity that may be relevant to the economic evaluation. However, it is unlikely to be feasible to model all of these outcomes in a way that is informative for the

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		• CV risk markers including lipid parameters and CV biomarkers • Modelled outcomes include, life expectancy, health-related quality of life measures, cardiovascular events, incidence of type 2 diabetes, weight progression over time. • The most commonly reported adverse events as a result of treatment will be captured in the submission Proposed change: Percentage body fat (adiposity) should not be included as an outcome. Rationale: Section 1.2.2 of NICE clinical guidelines 189, suggests using BMI as a practical estimate of percentage body fat (adiposity) in adults. In section 1.2.6 it also does not advocate percentage body fat as a measurement of overweight or obesity via bioimpedance (10). This is also supported in section 5.1.3 of the NICE Evidence Review for clinical guideline 43, which states there is a weak association between BMI and percentage adiposity: "Adiposity is defined as the amount of body fat expressed as either the absolute fat mass (in kilograms) or as the percentage of total body mass. Absolute adiposity is highly correlated with body mass, but percentage adiposity is relatively uncorrelated with body mass" (16). Furthermore, percentage body fat is not routinely collected in UK clinical practice and was not collected in the liraglutide 3.0mg clinical trials.	appraisal committee. Mindful of this, the outcomes included in the scope have been left to be consistent with those used in TA494 and idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added.
	Royal College of Physicians	Weight loss, improvement in obesity-related complications such as progression to diabetes in those with impaired glucose regulation, HbA1c in	Thank you for your comment. Idiopathic

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		people with diabetes, Epworth score and apnoea-hypopnea index in those with sleep apnoea. Markers of severity in NAFLD.	intracranial hypertension and non-alcoholic fatty liver disease have been added to the scope. We recognise that there are several outcomes related to co-morbidities associated with overweight and obesity that may be relevant to the economic evaluation. However, it is unlikely to be feasible to model all of these outcomes in a way that is informative for the appraisal committee. Mindful of this, the other outcomes included in the scope have been left to be consistent with those used in TA494.
	Royal College of Pathologists	yes	Thank you for your comment.
		Weight and BMI should be assessed at appropriate time points. Many studies will measure this after a short intervention but PHE suggests that studies should be at 12 months plus to be meaningful.	Thank you for your comment. The appraisal committee will consider

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			all available relevant evidence.
	GlaxoSmithKline	In addition to the outcome measures listed, the following might be considered as surrogate end points: • Total fat mass and % body fat • Estimates of visceral adipose tissue	Thank you for your comment. We recognise that there are several outcomes related to co-morbidities associated with overweight and obesity that may be relevant to the economic evaluation. However, it is unlikely to be feasible to model all of these outcomes in a way that is informative for the appraisal committee. Mindful of this, the outcomes included in the scope have been left to be consistent with those used in TA494, and idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added.

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Economic analysis	Association for the Study of Obesity	Nothing specific, but adequate time to allow the impact on obesity-related complications is essential	Thank you for your comment.
	Obesity Group of the British Dietetic Association	We have no comments.	Noted.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	n/a	Noted.
	Dorset CCG	The appropriate time horizon is not clear	Thank you for your comment. The appraisal committee will consider whether the time horizon in the economic model is appropriate. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the

Section	Consultee/ Commentator	Comments [sic]	Action
			technologies being compared.
	Novo Nordisk	The costs and consequences of liraglutide 3.0mg vs the relevant comparator will be modelled over a lifetime horizon with ability for sensitivity analyses at different time horizons.	Comment noted.
	Royal College of Physicians	No specific comments but time horizon needs to be sufficient to capture long-term outcomes	Comment noted.
	Royal College of Pathologists	none	Noted.
	Public Health England	No comment	Noted.
	GlaxoSmithKline	No additional comment	Noted.
Equality and Diversity	Association for the Study of Obesity	Important to consider appropriate BMI cut-offs for people from ethnic groups where obesity can have adverse impacts at lower BMI than in White European populations. People with significant mental illness should be considered as obesity is particularly difficult to treat in this population and liraglutide showed evidence of efficacy as highlighted above.	Thank you for your comment. These equalities considerations are formally addressed in the Equalities Impact Assessment form.
	Obesity Group of the British Dietetic Association	We note that the cut-off points for BMI and waist circumference used to classify overweight and obesity may differ by ethnicity so some ethnic groups will be at a higher risk of ill-health at lower BMI than others. This potentially disadvantages them unless it is recognised.	Thank you for your comment. These equalities considerations are

Section	Consultee/ Commentator	Comments [sic]	Action
			formally addressed in the Equalities Impact Assessment form.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	No	Thank you for your comment.
	Dorset CCG	Proposed remit and scope do not need changing	Thank you for your comment.
	Novo Nordisk	Socioeconomic status has an influence on the incidence and the impact of obesity. The lack of effective treatment options available on the NHS for the medical management of obesity means that there may be inequity in access to available treatment options. Therefore, Novo Nordisk considers the availability of liraglutide 3.0mg to our proposed target population to be important from an equality standpoint. For BMI an adjustment will be considered for the BMI threshold for treatment in patients from non-European descent. This is in line with the wording used in the background for the scope, which suggests an appropriate adjustment of BMI for other ethnic groups is necessary.	Thank you for your comment. These equalities considerations are formally addressed in the Equalities Impact Assessment form.
	Royal College of Physicians	Important to consider appropriate BMI cut-offs for people from ethnic groups where obesity can have adverse impacts at lower BMI than in White European populations.	Thank you for your comment. These equalities considerations are formally addressed in

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		There is a lack of data in people with learning disability which should be considered as a gap in the evidence base. People with serious mental illness should be considered as highlighted above as there is some evidence of weight loss efficacy in this group.	the Equalities Impact Assessment form.
	Royal College of Pathologists	Not aware of any equality issues	Thank you for your comment.
	Public Health England	No comment	Noted.
	GlaxoSmithKline	No additional comment	Noted.
Other considerations	Obesity Group of the British Dietetic Association	Compliance may be an issue since injections are required.	Thank you for your comment. If the topic is referred, the appraisal committee will consider whether the administration of liraglutide is adequately captured in the economic model.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	n/a	Noted.

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	Dorset CCG	Financial impact for commissioners in the short to medium-term	Thank you for your comment. If the technology is recommended NICE will present a resource impact assessment.
	Novo Nordisk	There is very little data on some ethnic groups (particularly people from Asia) within the trials with liraglutide 3.0mg. However Novo Nordisk will consider adjusting for relevant risk factors to account for any differences.	Thank you for your comment. These equalities considerations are formally addressed in the Equalities Impact Assessment form.
	Royal College of Pathologists	none	Noted.
	Public Health England	Insufficient time to consider	Noted.
	GlaxoSmithKline	No additional comment	Noted.
Innovation	Association for the Study of Obesity	Yes – this is an important innovative technology that addresses an unmet need in the management of patients with obesity. Liraglutide is more effective that other weight loss strategy in terms of weight loss (except bariatric surgery). In addition, it has strong evidence of benefit in terms of cardiovascular outcomes from a well-designed randomised controlled trial (RCT) in patients with Type 2 diabetes. Many studies (including recent RCTs) showed that 10% weight loss has major beneficial impacts in patients with obesity related complications including but not limited to Type 2 diabetes,	Thank you for your comment. The appraisal committee will consider whether there are any innovative aspects of liraglutide.

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		non-alcoholic fatty liver disease and idiopathic intracranial hypertension, subfertility and it also reduces the risk of developing complications such as Type 2 diabetes. Furthermore, emerging evidence suggest benefits in patients with mental health disorders. Hence the use of high dose liraglutide in combination with life style intervention would be expected to have significant health favourable health impacts. The assessment needs to consider that there are clear early stopping rules regarding the use of liraglutide in obesity and these are based on the likelihood of achieving significant weight loss at 12 months. Hence, the efficacy of liraglutide in real life is likely to exceed what reported in the clinical trials. The assessment might want to consider the cost-effectiveness of using a different weight loss stopping rule than what is used currently.	
	Obesity Group of the British Dietetic Association	Yes in terms of weight loss achieved and potential benefits for those who have diabetes and are at high risk of cardiovascular disease.	Thank you for your comment. The appraisal committee will consider whether there are any innovative aspects of liraglutide.
	British Obesity Society	agree	Thank you for your comment.
	Diabetes UK	Yes	Thank you for your comment.
	Dorset CCG	No	Thank you for your comment.
	Novo Nordisk	As noted in the final appraisal determination for technology appraisal 494, there is a lack of available clinically effective treatment options for weight	Thank you for your comment. The appraisal

Section	Consultee/ Commentator	Comments [sic]	Action
		loss. Therefore, Novo Nordisk believes that liraglutide 3.0mg provides an alternative treatment option as an adjunct to diet and exercise in order to help patients lose weight and reduce the rising numbers of Type 2 diabetes and other obesity-related conditions. The merits for weight loss to avoid long term conditions have been demonstrated through the NHS Diabetes Prevention programme and published evidence (3, 12)	committee will consider whether there are any benefits of liraglutide that are not adequately captured by the QALY estimate.
	Royal College of Physicians	Yes – this is an innovative technology that seems more effective than existing non-surgical intervention (lifestyle and other medication). Many of the conditions and groups of people discussed above such as those who are too unwell to have surgery, people with NAFLD, those with learning disability or severe mental illness were not included in the main phase 3 trials yet there is emerging evidence of effectiveness in some of these groups that would be unlikely to be included in generic measures of QALY improvement. Effects on QALYs should consider data on responders as there are built in stopping rules (based on non-response after 16 weeks of treatment) that mean that weight loss at 12 months or longer in 'responders' is likely to be greater than the mean observed in clinical trials. Alternative stricter stopping rules should also be modelled.	Thank you for your comment. The appraisal committee will consider whether there are any innovative aspects of liraglutide or benefits that are not adequately captured by the QALY estimate.
	Royal College of Pathologists	This would be an innovative use of an established treatment.	Thank you for your comment. The appraisal committee will consider whether there are any innovative aspects of liraglutide.
	Public Health England	No comment	Noted.

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	GlaxoSmithKline	Based on the data available, liraglutide provides significant efficacy as compared with placebo but may not have a sustainable impact in the management of obesity or provide additional health-related benefits. Also, Liraglutide is given by subcutaneous injection, which may not be preferable to patients compared with Orlistat. So treatment with liraglutide might not improve the way the current need is met.	Thank you for your comment. The appraisal committee will consider whether there are any benefits of liraglutide or orlistat that are not adequately captured by the QALY estimate.
Questions for consultation	Association for the Study of Obesity	All answered above	Thank you for your comment.
	Obesity Group of the British Dietetic Association	Liraglutide will fit into the existing NICE pathway as an option to Orlistat, as an addition to standard lifestyle care, primarily within tier 3.	Thank you for your comment.
	British Obesity Society	agree	Thank you for your comment.
	Dorset CCG	Should a standardised, validated weight-management program be included as a comparator? 'Standard care without liraglutide' could be defined as weight measurement by and verbal advice from a health professional A barrier to the adoption of this technology into practice could be the short-medium term costs for commissioners without the evidence of longer term benefits.	Thank you for your comment. The comparators section has been updated.

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		We consider that liraglutide would fit in the NICE pathway for obesity alongside other pharmacological interventions e.g.1.8	
	Novo Nordisk	Novo Nordisk agrees with the NICE topic selection committee that liraglutide 3.0mg should be appraised through the single technology appraisal process. Please find below Novo Nordisk's responses to the additional consultation questions. Have all relevant comparators for liraglutide been included in the scope? Which treatments are considered to be established clinical practice in the NHS for overweight and obesity? As above, standard management without liraglutide 3.0 mg should be considered as the only relevant comparator for this appraisal. This is defined as lifestyle measures based on NICE clinical guideline 189 and clinical expert opinion expressed in section 3.8 of the final appraisal determination for technology appraisal 494, which comprises diet and exercise (11). How should 'standard care without liraglutide' be defined? As mentioned above, in section 3.8 of the final appraisal determination for technology appraisal 494, the clinical experts suggested that standard of care is likely to involve general counselling on lifestyle measures, which is defined as diet and physical activity in section 1.3.6 of NICE clinical guideline 189 (10-11). This is in line with the standard management seen in the SCALE obesity and prediabetes trial where patients received diet counselling	Thank you for your comment. The comparators section has been updated. Although clinical expert comments in TA494 indicated that orlistat is not widely used, it is listed as an available treatment option in CG189. For completeness, it has been kept in the scope as a comparator. Bariatric surgery has also been added to the list of comparators for completeness. We recognise that there are several outcomes related to co-morbidities associated with overweight and obesity that may be relevant to the economic evaluation. However, it

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		according to local standard. There were 8 trial sites in the United Kingdom. Patients were also put on a hypo-caloric diet and advised to do exercise. Based on NICE recommendations and clinical expert opinion, this is reflective of standard management without liraglutide in UK clinical practice. Are the outcomes listed appropriate? As mentioned above, percentage body is not considered an appropriate measure for BMI in section 1.2.6 of NICE clinical guideline 189 and should not be listed as an outcome (10). The other outcomes listed are appropriate, however they are not exhaustive. Therefore additional suggested outcomes not listed in the scope e.g. • Impact on glycaemic status and prediabetes will be presented alongside those listed. Are there any subgroups of people in whom liraglutide is expected to be more clinically effective and cost effective or other groups that should be examined separately? As above, Novo Nordisk proposes that liraglutide 3.0mg should be appraised for adult patients with a BMI ≥35 with prediabetes and high risk of CVD in tier 3 services. Based on the clinical and cost effectiveness evidence, Novo Nordisk believes that this subgroup of patients would benefit the most from liraglutide 3.0mg in UK clinical practice.	is unlikely to be feasible to model all of these outcomes in a way that is informative for the appraisal committee. Mindful of this, the outcomes included in the scope have been left to be consistent with those used in TA494 and idiopathic intracranial hypertension and non-alcoholic fatty liver disease have been added In order to allow flexibility, the population in the scope has been kept broad (to cover the whole marketing authorisation). The appraisal committee will consider whether there are any innovative aspects of liraglutide or benefits that are not adequately

Section	Consultee/ Commentator	Comments [sic]	Action
			captured by the QALY estimate.
		Where do you consider liraglutide will fit into the existing NICE pathway, Obesity? Novo Nordisk considers that liraglutide 3.0mg should be considered for use in specialist Tier 3 services when conventional treatment has been unsuccessful. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which liraglutide is licensed; Novo Nordisk does not believe the proposed remit and scope could exclude any people protected by the equality legislation who fall within the patient population for which liraglutide is licensed • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;	

Section	Consultee/ Commentator	Comments [sic]	Action
		Novo Nordisk does not believe the proposed remit and scope could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population • could have any adverse impact on people with a particular disability or disabilities. Novo Nordisk does not believe the proposed remit and scope could have any adverse impact on people with a particular disability or disabilities Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts. N/A Do you consider liraglutide to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Yes Do you consider that the use of liraglutide can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?	

Section	Consultee/ Commentator	Comments [sic]	Action
		Obesity is a complex condition that impacts on a patient's physical, social and psychological wellbeing. Accounting for all of these aspects in an economic model is also complex. Novo Nordisk has developed an obesity model which takes into account conditions which have a strong relationship with obesity according to the WHO (1) and therefore may underestimate health-related benefits associated with all conditions that benefit from weight loss. Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. Novo Nordisk will include a utility value per BMI increment, which can be varied in a sensitivity analysis. A review of relevant epidemiology will be presented to substantiate the association between BMI and longer-term complications not directly measured in the model. To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. There is potential for some patients to be excluded from treatment with liraglutide 3.0mg if patients are not able to access a Tier 3 service. Based on clinical expert opinion in the final appraisal determination for technology appraisal 494, it was suggested that Tier 3 services are being decommissioned or are not widely available (11). However, it is expected that	

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		following positive NICE guidance on the technology, more Tier 3 services will be commissioned to meet local clinical unmet needs for the target population.	
	Public Health England.	PHE agrees that standard care without liraglutide should be noted consistently. – Care must be taken to understand that defining this at outset could impact upon inclusion of evidence an could in effect be seen as another intervention. PHE is unable to comment on the clinical aspects of this consultation as this outside PHE's responsibility.	Thank you for your comment.
	Royal College of Physicians	All questions have been addressed above	Comment noted.
Additional comments on the draft scope	Association for the Study of Obesity	None	Comment noted.
	Dorset CCG	Yes: The causes and treatment of obesity are multifactorial and any use of these type of drugs for obesity outside of the setting of type 2 diabetes would need to be as part of a multi-disciplinary team approach that includes a focus on lifestyle and behaviour modification with a motivational interviewing approach. Drugs will only ever be an adjunct to this and therefore any analysis needs to factor this in.	Thank you for comment.
	Novo Nordisk	References 1. World Health Organisation. WHO. Obesity: Preventing And Managing The Global Epidemic. Report Of A WHO Consultation. World Health	Noted.

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		Organization, 2000. Geneva. http://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/ 2. Holmes M. (2017). Literature review for evidence to populate the Novo obesity model. University of Sheffield. Data on File. 3. Khaodhiar L et al (2010). Treating Diabetes and Prediabetes by Focusing on Obesity Management. Current Diabetes Reports. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2857968/ 4. Flegal et al (2013). Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories. A Systematic Review and Meta-analysis. JAMA. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4855514/ 5. Grover SA et al, (2014). Years of life lost and healthy life-years lost from diabetes and cardiovascular disease in overweight and obese people: a modelling study. Lancet Diabetes Endocrinology. https://www.thelancet.com/journals/landia/article/PIIS2213-8587(14)70229-3/fulltext 6. Ul-Haq Z, et al (2013). Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity (Silver Spring). https://onlinelibrary.wiley.com/doi/full/10.1002/oby.20107 7. Magkos et al (2016). Effects of Moderate and Subsequent Progressive Weight Loss on Metabolic Function and Adipose Tissue Biology in Humans with Obesity. Cell Metabolism. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4833627/ 8. British Obesity and Metabolic Surgery Society (BOMSS) Commissioning guide: weigh assessment and management clinics (tier 3) (2017). http://www.bomss.org.uk/wp-content/uploads/2017/10/Revision-of-Commissioning-guide-Tier-3-clinics-04042017.pdf	

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		9. NICE 2018 surveillance of CG189 Obesity: identification, assessment and management (2014) and PH46 BMI: preventing ill health and premature death in black, Asian and other minority ethnic groups (2013) stakeholder consultation (Appendix B).https://www.nice.org.uk/guidance/cg189/evidence/appendix-b-stakeholder-consultation-comments-table-ph46-and-cg189-pdf-4847559664 10. NICE Clinical Guideline 189. Obesity: identification, assessment and management (2014). https://www.nice.org.uk/guidance/cg189/resources/obesity-identification-assessment-and-management-pdf-35109821097925 11. Final appraisal determination (2017). Naltrexone–bupropion for managing overweight and obesity (TA 494). https://www.nice.org.uk/guidance/ta494/documents/final-appraisal-determination-document 12. NHS Diabetes Prevention Programme and Weight Management Services: Eligibility Criteria (2017). https://www.england.nhs.uk/wp-content/uploads/2016/07/dpp-wm-service.pdf 13. NICE Clinical Guideline 181 (2014). Cardiovascular disease: risk assessment and reduction, including lipid modifification. https://www.nice.org.uk/guidance/cg181/resources/cardiovascular-disease-risk-assessment-and-reduction-including-lipid-modification-pdf-35109807660997 14. Summary of Product Characteristics; Saxenda 6 mg/mL solution for injection in pre-filled pen (2018). https://www.medicines.org.uk/emc/product/2313/smpc 15. AACC Lipid Panel. Labtests online (2018). https://labtestsonline.org/tests/lipid-panel	

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		16. NICE Clinical Guideline 47. Obesity Prevention. Full guideline, section 2 - identification and classification: evidence statements and reviews. (2007). https://www.nice.org.uk/guidance/cg43/evidence/full-guideline-section-2-identification-and-classification-evidence-statements-and-reviews-pdf-195027230	
	Royal College of Physicians	None	Noted.
	GlaxoSmithKline	No additional comments.	Noted.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

None.