ASSESSING A PATIENT'S SUITABILITY

ASSESSING SUITABILITY FOR A GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST (GLP-1 RA)

PEOPLE TO CONSIDER	PRESCRIBE WITH CAUTION	UNSUITABLE PEOPLE
■ People with type 2 diabetes (T2D) who are overweight ■ People with T2D and significant risk of cardiovascular disease (CVD) ■ People with T2D and established CVD ■ People with T2D and high body mass index (BMI), adjusted for ethnicity	■ People in whom weight loss would cause concern (eg frailty) ■ People with a history of gallstones ■ Women of child-bearing age (ensure adequate contraception; GLP-1 RAs may reduce oral contraceptive efficacy) ■ People with irritable bowel syndrome or gastro-oesophageal reflux disease (GORD) ■ Patients with renal (see below) or hepatic impairment	■ People with type 1 diabetes (T1D) ■ Children ■ Pregnant women ■ People with a history of, or risk factors for, pancreatitis* ■ People with a history of medullary thyroid cancer or multiple endocrine neoplasia type 2 ■ Active proliferative or pre-proliferative retinopathy †

* For example: idiopathic, gallstones, alcohol, trauma and hyperlipidaemia

† Non-significant increase in retinopathy with liraglutide versus placebo in LEADER[1] (0.6 vs. 0.5 events per 100 patient-years respectively; hazard ratio, 1.15); Retinopathy complications occurred in 3.0% of the semaglutide group and 1.8% in the placebo group (hazard ratio, 1.76) in SUSTAIN-6[2]

- Consider local and national guidance (see below).
- Review concurrent medications to determine if any drugs can be reduced or stopped: eg stop dipeptidyl peptidase 4 (DPP-4) inhibitor and consider reducing sulphonylurea or insulin dose if hypoglycaemia is a concern.

PRESCRIBING GLP-1 RAs IN PEOPLE WITH RENAL IMPAIRMENT

CKD STAGE (mL/min/1.73m²)	STAGES G1 and G2 eGFR>60	STAGE G3a eGFR 45-59	STAGE G3b eGFR 30-44	STAGE G4 eGFR 15-30	STAGE G5 eGFR <15
Dulaglutide					
Exenatide ER		Not recommended if CrCl <50 mL/min			
Liraglutide					
Lixisenatide					
Semaglutide					

CKD: Chronic kidney disease; CrCl: Creatinine Clearance; eGFR: estimated glomerular filtration rate ER: Extended release.

KEY

No dose adjustment required

Dose adjustment recommended

Not recommended / contraindicated

GLP-1 RA GUIDELINES: STARTING AND STOPPING CRITERIA

NICE NG28 (2015) If triple therapy with metformin and two other oral drugs is ineffective, not tolerated or contraindicated, HCPs should consider combination therapy with metformin, SU and GLP-1 RA as below		SIGN 154 (2017)	
STARTING CRITERIA	**STOPPING CRITERIA**	**STARTING CRITERIA**	**STOPPING CRITERIA**
■ BMI≥35 kg/m² (adjust for ethnicity) and specific psychological or other medical problems associated with obesity ■ BMI<35 kg/m² when insulin would have significant occupational implications or weight loss would benefit other significant obesity-related co-morbidities	■ Only continue GLP-1 RAs if the person has had a beneficial metabolic response: reduction of ≥11 mmol/mol (1.0%) in HbA1c and weight loss of ≥3% of initial body weight in 6 months	■ People with a BMI≥30 kg/m² (or ethnicity-adjusted equivalent) combined with oral glucose-lowering drugs, basal insulin or both as 3rd- or 4th-line treatment, when adequate glycaemic control was not achieved with these drugs ■ As an alternative to insulin in people for whom combinations of oral glucose-lowering drugs did not produce adequate glycaemic control ■ Consider a GLP-1 RA with proven cardiovascular (CV) benefit for people with T2D and established CVD	■ Continue GLP-1 RA at each if either individualised HbA1c target achieved or HbA1c falls more than 5.5 mmol/mol (0.5%) in 3–6 months. ■ Discontinue GLP-1 RA if evidence that it is ineffective

REVIEWING TREATMENT WITH GLP-1 RA

- Review lifestyle and diet and address compliance. Review individualised HbA1c target. Check injection sites for hypertrophy.
- Review renal function and ensure GLP-1 RA and dose is appropriate for eGFR.
- Consider a more potent GLP-1 RA or consider additional therapies, such as basal insulin. Obtain specialist advice as appropriate.
- Blood glucose monitoring may indicate the influence of fasting or prandial glucose on suboptimal HbA1c; such insights can inform next therapeutic steps. Longer-acting GLP-1 RAs appear to benefit fasting and post-prandial glucose control.
- Reinforce sick day rules: temporarily stop GLP-1 RAs during any acute illness to avoid any dehydration or acute kidney injury.

GLP-1 RAS AND INSULIN

- GLP-1 RAs are not substitutes for insulin.
- Exercise caution when reducing insulin after introducing a GLP-1 RA.[3]

TAILORING THE DRUG AND DEVICE TO THE PATIENT

DEVICE	DOSING REGIMEN and AVAILABLE DOSES	HOW TO INITIATE	OTHER INFORMATION
DULAGLUTIDE (TRULICITY)	ONCE WEEKLY 0.75 mg or 1.5 mg in a pen that delivers one of the two doses	INITIAL DOSE 0.75 mg (monotherapy) and 1.5 mg (as add-in therapy) weekly. May increase dose to 1.5 mg weekly for additional glycaemic control	One-use disposable device (pre-filled pen or syringe)
EXTENDED-RELEASE EXENATIDE (BYDUREON)	ONCE WEEKLY 2 mg	FIXED DOSE 2 mg WEEKLY	One-use disposable device with hidden needle
LIXISENATIDE (LYXUMIA)	ONCE DAILY 10 mg or 20 mg in a pen that delivers one of the two doses	INITIAL DOSE 10 mg ONCE DAILY FOR 2 WEEKS THEN INCREASE TO 20 mg Starter kit has both strength pens	Pen device requires attachable needle
LIRAGLUTIDE (VICTOZA)	ONCE DAILY 1 pen delivers 3 different doses: 0.6 mg, 1.2 mg or 1.8 mg	INITIAL DOSE 0.6 mg ONCE DAILY FOR AT LEAST 1 WEEK THEN 1.2 mg DAILY Escalate to 1.8 mg, after at least 1 week, if further glycaemic control required or in people with established CVD*	Pen device requires attachable needle
SEMAGLUTIDE (OZEMPIC)	ONCE WEEKLY 0.25 mg, 0.5 mg or 1 mg in a pen that delivers one of the three doses	INITIAL DOSE 0.25 mg FOR 4 WEEKS THEN 0.5 mg FOR AT LEAST 4 WEEKS Escalate to 1 mg if further glycaemic control required	Pen device requires attachable needle (included with pens)

* Scottish Medicines Consortium has not approve 1.8 mg on grounds of cost-effectiveness

EDUCATION AND COUNSELLING FOR PEOPLE CONSIDERING A GLP-1 RA:

- Educate about the mode of action including expected benefits, eg reductions in HbA1c and weight, and if appropriate, CV risk.
- Explain possible adverse events and management strategies especially postprandial fullness and nausea (suggest the patient eats smaller meals more frequently and stop when they start to feel full) and possible worsening of GORD.
- Show patients the range of devices and assess their understanding and ability to use the agreed device.
- Discuss injection sites and also the importance of rotating the site. Stress the importance of needle safety, including disposal.
- Arrange appropriate monitoring and review.

REFERENCES

1 Marso SP, Daniels GH, Brown-Frandsen K et al N Engl J Med 2016;375:311-322

2 Marso SP, Bain SC, Consoli A et al N Engl J Med 2016;375:1834-1844

3 MHRA Safety Alert, June 2019. GLP-1 receptor agonists: reports of diabetic ketoacidosis when concomitant insulin was rapidly reduced or discontinued

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