



Medicine Supply Notification

MSN/2023/061

GLP-1 receptor agonists* used in the management of type 2 diabetes

*Annex 4 lists individual medicines affected

Tier 3 – high impact*

Date of issue: 27/06/2023

Link: [Medicines Supply Tool](#)

Summary

- There are very limited, intermittent supplies of all glucagon-like peptide-1 receptor agonists (GLP-1 RAs) licensed in the management of Type 2 Diabetes Mellitus (T2DM).
- Supply is not expected to return to normal until at least mid-2024.
- The supply issues have been caused by an increase in demand for these products for licensed and off-label indications.
- Please refer to the SPS Tool for Medicines Shortages for an up-to-date supply stock situation and clinical guidance on alternative treatment options.

Actions Required

Actions for clinicians until supply issues have resolved:

- GLP-1 RAs should only be prescribed for their licensed indication
- Avoid initiating people with type 2 diabetes on GLP-1 RAs for the duration of the GLP1-RA national shortage.
- Review the need for prescribing a GLP-1 RA agent and stop treatment if no longer required due to not achieving desired clinical effect as per [NICE CG28](#).
- Avoid switching between brands of GLP-1 RAs, including between injectable and oral forms.
- Where a higher dose preparation of GLP-1 RA is not available, do not substitute by doubling up a lower dose preparation.
- Where GLP-1 RA therapy is not available, proactively identify patients established on the affected preparation and consider prioritising for review based on the criteria below.
- Where an alternative glucose lowering therapy needs to be considered, use the principles of shared decision making as per [NICE guidelines](#) in conjunction with the **Supporting Information** below.
- Where there is reduced access to GLP-1 RAs, support people with type 2 diabetes to access to structured education and weight management programmes where available.
- Order stocks sensibly in line with demand during this time, limiting prescribing to minimise risk to the supply chain whilst acknowledging the needs of the patient.

*Classification of Tiers can be found at the following link:

<https://www.england.nhs.uk/publication/a-guide-to-managing-medicines-supply-and-shortages/>

Supporting information

This guidance aims to support clinicians in choosing suitable alternative glucose lowering therapies to GLP-1 RAs during this period of national shortage. The advice in annex 1 should be used in conjunction with [NICE NG28 Type 2 Diabetes in Adults: choosing medicines](#).

When prescribing an alternative class of glucose lowering therapy, clinicians are advised to use medicines across the class evenly to mitigate the potential for further national shortages.

This guidance does not override the responsibility of the clinician to make decisions appropriate to the circumstances of the individual, in consultation with them and their carers or guardians.

Clinical supervision is essential for switching between a GLP1-RA and any other treatment for diabetes to avoid detrimental glycaemic events.

Clinical Review

In most cases, the need to consider alternative glucose lowering therapy will arise when a person with T2DM established on GLP-1 RA therapy is unable to source their regular prescription.

Should a particular preparation of GLP-1 RA be unavailable, clinical teams may want to proactively identify people with T2DM established on that preparation to help planning.

Consider prioritising review for people with T2DM on the affected GLP-1 RA preparation where:

- HbA1c greater than 86mmol/mol in the previous 3 to 6 months.
- HbA1c greater than 86mmol/mol prior to starting the GLP1-RA.
- HbA1c not recorded in the previous 6 months.
- Urine albumin creatinine ratio (uACR) greater than 30mg/mmol.
- Self-monitoring glucose readings (or Continuous Glucose Monitoring, where available) are persistently above individualised target range.

Clinical Information

When is a GLP-1 RA normally recommended?

If triple therapy with metformin hydrochloride and two other oral drugs is tried and is not effective, or is not tolerated or contra-indicated, a GLP-1 RA may be considered as part of a triple therapy regimen by switching one of the other drugs for a GLP-1 RA.

These should only be considered for patients who have:

- a BMI of 35 kg/m² or above (adjusted for ethnicity) and who also have specific psychological or medical problems associated with obesity; or
- a BMI lower than 35 kg/m² and for whom insulin therapy would have significant occupational implications or if the weight loss associated with GLP-1 RAs would benefit other significant obesity-related comorbidities.

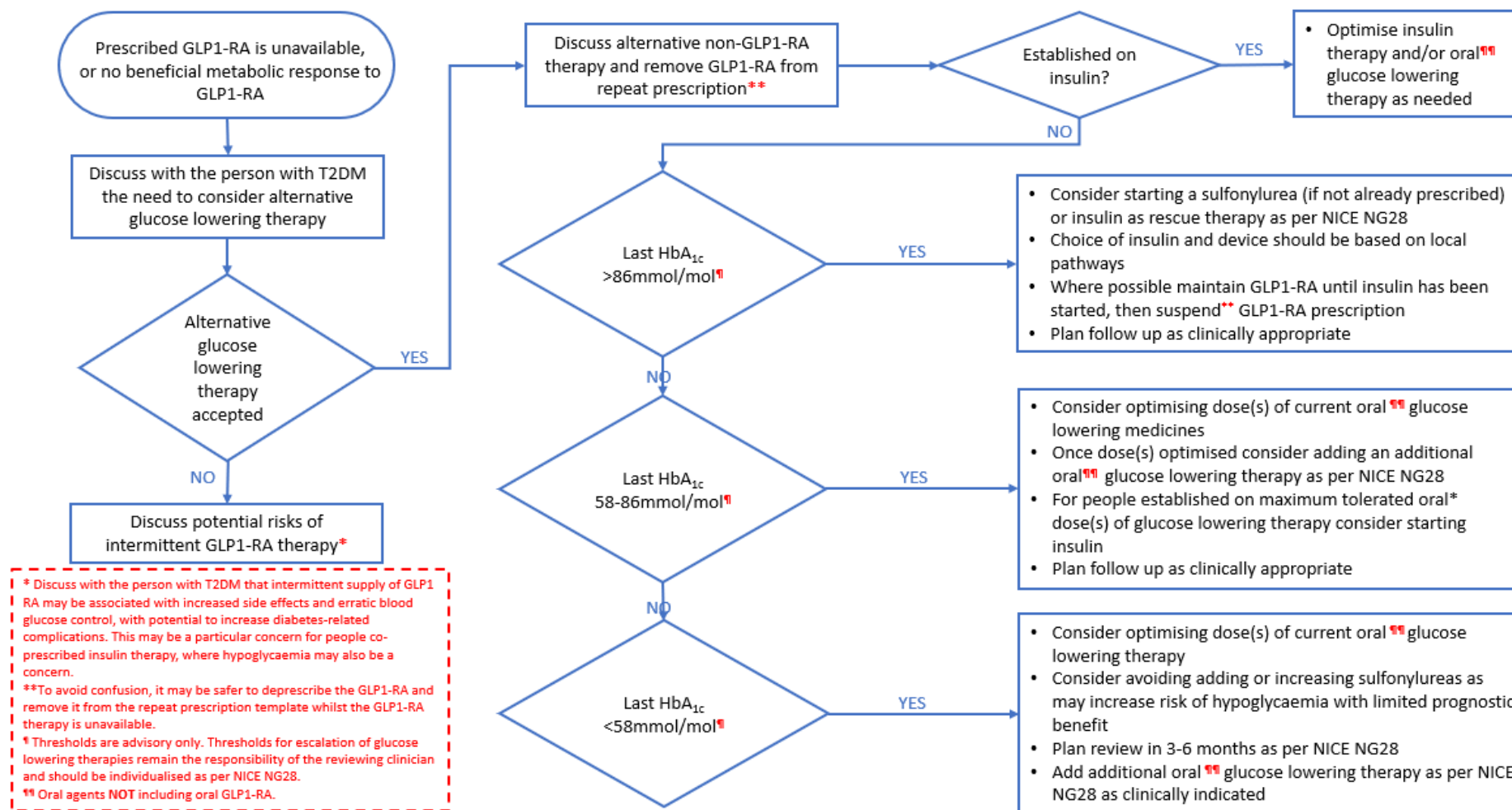
GLP-1 RA therapies with proven cardiovascular benefit (such as liraglutide) should be considered in patients with established cardiovascular disease.

After six months, the GLP-1 RAs should be reviewed and only continued if there has been a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body-weight).

Insulin should only be prescribed in combination with a GLP-1 RA under specialist care advice and with ongoing support from a consultant-led multidisciplinary team.

The below annexes have been developed by PCDS and ABCD – details on contributors are below.

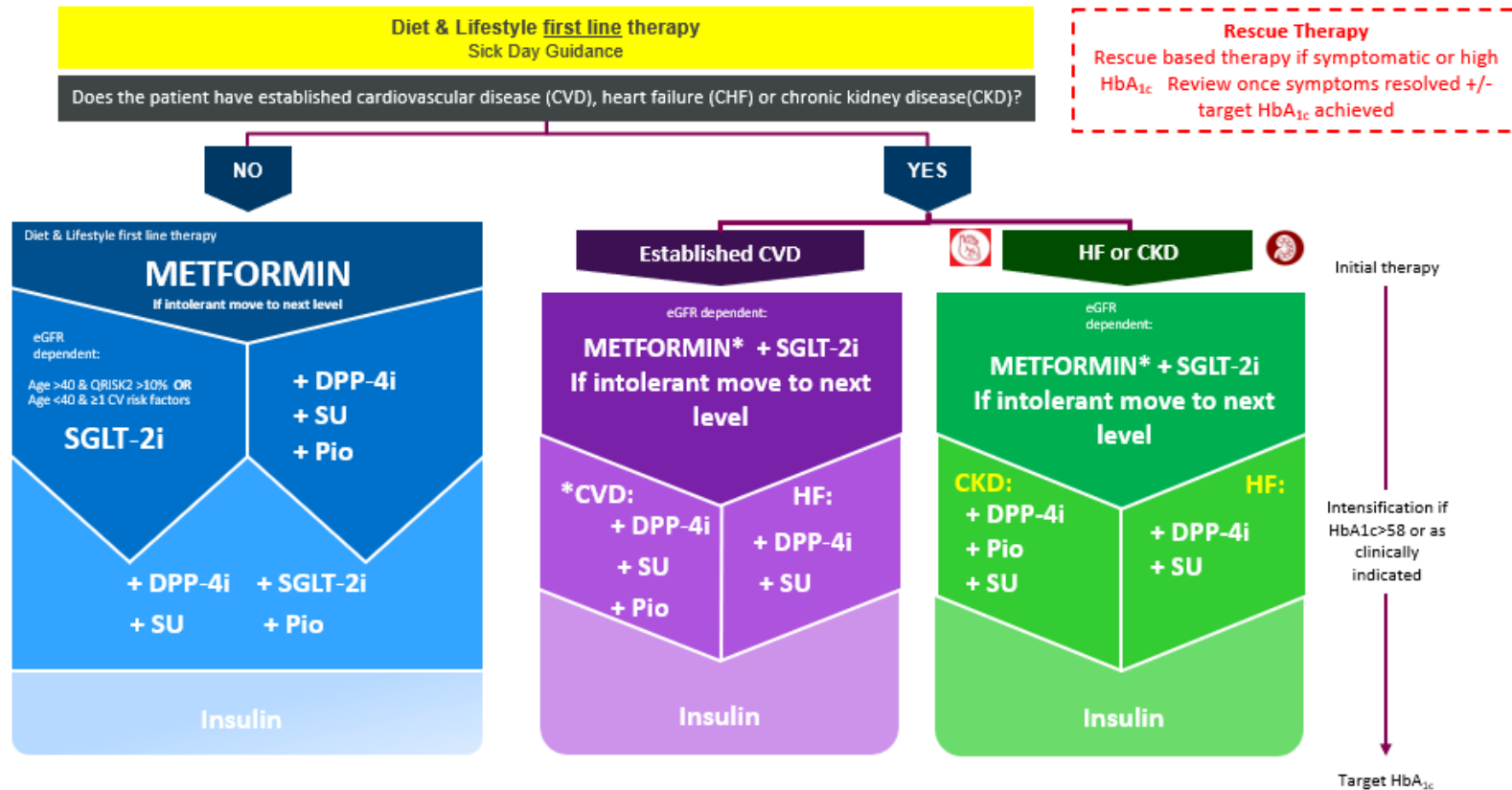
Annex 1: Selecting Alternative Glucose Lowering Therapy for People with T2DM when GLP1-RAs are unavailable



Note: Symptomatic hyperglycaemia may indicate clinical need for insulin therapy. If in doubt, discuss with specialist clinician. Symptoms of hyperglycaemia include polyuria, polydipsia, weight loss and fatigue. Think 4Ts – Thirst, Toilet, Thinner, Tired.

Annex 2: Quick reference guide for selecting oral antidiabetic therapy

Based on NICE NG28, adapted with permission from the North West London Diabetes Glycaemic Management Guideline



* When initiating metformin	Consider 2 weeks of monotherapy before initiating another agent to assess for gastrointestinal side-effects
When initiating a SGLT-2i	Consider a 25% dose reduction in any concomitant SU or Basal insulin & monitor for evidence of hypoglycaemia. If prescribing for Heart Failure (HF) or Chronic Kidney Disease (CKD) ensure licensed product is used.
Definitions	DPP-4i (Dipeptidyl Peptidase-4 Inhibitor), SGLT-2i (Sodium Glucose Co-Transporter-2 Inhibitor), SU (Sulfonylurea), Pio (Pioglitazone)
*CVD	Cardiovascular Disease in the ABSENCE of Heart Failure (HF). DO NOT use Pio (Pioglitazone) if evidence of HF.

Annex 3: Oral Glucose Lowering Therapies by Class

Class	Biguanides	Sodium Glucose Co-Transporter-2 Inhibitors (SGLT2iY "Gliflozins"	Di—tidyl Peptidase 4 Inhibitors (DDP4i) - "Gliptins"	Sulfonylureas	Thiazolidinedione
Medicine	Metformin	Canagliflozin, dapagliflozin, empagliflozin and ertugliflozin	Alogliptin, linagliptin, saxagliptin, sitagliptin and vildagliptin	Gliclazide, glipizide, glimepiride, glibenclamide and tolbutamide	Pioglitazone
When best to use	<ul style="list-style-type: none"> Ensure metformin is taken with food. If gastrointestinal side effects develop consider switching to modified release If hypoglycaemia a concern People concerned about weight gain and wanting an agent that offers some weight loss/weight neutrality 	<ul style="list-style-type: none"> If hypoglycaemia is a concern If the person is at high cardiovascular risk Established heart failure or chronic kidney disease (CKD) consider a SGLT2i licensed for these indications in addition to diabetes People concerned about weight gain and wanting an agent that offers some weight loss/weight neutrality 	<ul style="list-style-type: none"> If hypoglycaemia is a concern 	<ul style="list-style-type: none"> In people with high HbA1c as rescue therapy Symptomatic hyperglycaemia 	<ul style="list-style-type: none"> Fatty liver disease If people have deranged lipid profile it can increase HDL and lower LDL/TG If hypoglycaemia is a concern Can be continued in renal impairment
When to be cautious/not used	<ul style="list-style-type: none"> If eGFR<45ml/min review dose and stop if eGFR <30ml/min/1.73m² 	<ul style="list-style-type: none"> If high HbA1c >86mmol/mol History of DKA If renal function is <45ml/min then the SGLT2i will have minimal effect on blood glucose however effects for heart failure and CKD remain Elderly, risk of volume depletion History of recurrent urinary tract infection/urosepsis/genital infections Use "Sick Day Rules" guidance Preconception/pregnancy Risk of hypoglycaemia if concomitant use with sulfonylurea or basal insulin therapy. Consider reducing dose of sulfonylurea or insulin (c. 25% insulin dose reduction) 	<ul style="list-style-type: none"> Dose adjustments required (except linagliptin). See BNF for dosing instructions by product and eGFR Avoid in patients with a history of pancreatitis Avoid saxagliptin in heart failure Preconception/ pregnancy 	<ul style="list-style-type: none"> Consider alternatives in occupations where hypoglycaemia is likely to cause issues Use cautious dosing and slower titrations in people with renal impairment In the elderly where hypoglycaemia may be more concerning (set higher HbA1c targets and titrate cautiously with appropriate monitoring) Preconception/ pregnancy 	<ul style="list-style-type: none"> Oedema or heart failure Low bone mineral density (incl. post-menopausal women) Avoid if current or history of bladder cancer or unexplained haematuria Be aware of weight gain (lower doses can be used where this is more of an issue) Significant liver impairment Preconception/ pregnancy
HbA1c drop	1-2% (11-22mmol/mol)	1-1.5% (11-17mmol/mol)	0.5-0.8% (6-9mmol/mol)	1-2% (11-22mmol/mol)	0.5-1.4% (5-15 mmol/mol)
For further information please refer to NICE guidelines, British National Formulary and the Electronic Medicines Compendium					

Annex 4 : GLP-1 RAs affected

GLP-1 RA	Brand and formulation	Indication	Ability to uplift
Semaglutide	Ozmepic® 0.25 mg solution for injection in pre-filled pen	Type 2 diabetes mellitus as monotherapy (if metformin inappropriate), or in combination with other antidiabetic drugs (including insulin) if existing treatment fails to achieve adequate glycaemic control	Unable to uplift
	Ozmepic® 0.5mg solution for injection in pre-filled pen		
	Ozmepic® 1mg solution for injection in pre-filled pen		
Semaglutide	Rybelsus 3mg tablets	Oral GLP-1 RA licensed for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise: <ul style="list-style-type: none"> • as monotherapy when metformin is considered inappropriate due to intolerance or contraindications • in addition to other medicinal products for the treatment of diabetes. 	Unable to uplift
	Rybelsus 7mg tablets		
	Rybelsus 14mg tablets		
Dulaglutide	Trulicity® 0.75 mg solution for injection in pre-filled pen	Type 2 diabetes mellitus as monotherapy (if metformin inappropriate)	Unable to uplift
	Trulicity® 1.5 mg solution for injection in pre-filled pen		
	Trulicity® 3 mg solution for injection in pre-filled pen	Type 2 diabetes mellitus in combination with other antidiabetic drugs (including insulin) if existing treatment fails to achieve adequate glycaemic control	
	Trulicity® 4.5 mg solution for injection in pre-filled pen		
Liraglutide	Victoza® 6mg/ml solution for injection in prefilled pen	Type 2 diabetes mellitus as monotherapy (if metformin inappropriate), or in combination with other antidiabetic drugs, (including insulin) if existing treatment fails to achieve adequate glycaemic control	Unable to uplift
	Saxenda® 6mg/ml solution for injection in prefilled pen	Adjunct in weight management [in conjunction with dietary measures and increased physical activity in individuals with a body mass index (BMI) of 30 kg/m ² or more, or in individuals with a BMI of 27 kg/m ² or more in the presence of at least one weight-related co-morbidity]	

Exenatide	Byetta® 5micrograms/0.02ml solution for injection 1.2ml pre-filled pens	Type 2 diabetes mellitus in combination with other antidiabetic drugs (including insulin) if existing treatment fails to achieve adequate glycaemic control	Unable to uplift
	Byetta® 10micrograms/0.04ml solution for injection 1.2ml pre-filled pens		
	Bydureon® 2mg/0.85ml prolonged-release suspension for injection 1.2ml pre-filled pens		

Source: [BNF](#)

The SPS Medicines Supply Tool will be updated for stock position of all GLP1 RAs
 The SPS website will have a dedicated GLP1 RA page
[Medicines Supply Tool – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice](#)

Please refer to the links below for further information:

[NICE NG197 Shared Decision Making](#)

[For all individual GLP1-RA preparations Summary of Product Characteristics Home - electronic medicines compendium \(emc\)](#)

[NICE NG28 Type 2 Diabetes in Adults: choosing medicines. Type 2 diabetes | Treatment summaries | BNF | NICE](#)

Clinical Expertise sought from Hannah Beba¹, Ketan Dhatariya², Jane Diggle³, Clare Hambling⁴, Nicola Milne⁵, Philip Newland-Jones⁶.

1. Consultant Pharmacist, Diabetes, Primary Care Diabetes Society
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3. Diabetes Advance Nurse Practitioner and Co-Vice Chair Primary Care Diabetes Society
4. General Practitioner and Chair, Primary Care Diabetes Society
5. Diabetes Specialist Nurse, Primary Care Diabetes Society
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Full guidance to be published by the above group; link will be supplied on the SPS Tool once available.

[Glucagon-Like-Peptide 1 Receptor Agonist National Shortage](#)

[Guidance from the Primary Care Diabetes Society \(PCDS\) and Association of British Clinical Diabetologists \(ABCD\)](#)

Enquiries

Enquiries from NHS Trusts in England should in the first instance be directed to your Regional Pharmacy Procurement Specialist, who will escalate to national teams if required.

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All other organisations should send enquiries about this notice to the DHSC Medicine Supply Team quoting reference number MSN/2023/061

Email: DHSCmedicinesupplyteam@dhsc.gov.uk.