

Glucagon-Like-Peptide 1 Receptor Agonist National Shortage

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

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Background

There is an ongoing national shortage of glucagon like peptide-1 receptor agonists (GLP-1 RAs) used in the management of Type 2 Diabetes (T2DM). This situation is not expected to resolve until mid-2024. Supplies of some GLP-1 RA preparations may be intermittent or exhausted within this time frame (see [Appendix 1](#) for products affected). Although other GLP-1 RA therapies may be available, it is possible there will be insufficient additional capacity to accommodate switching everyone with T2DM currently prescribed an affected GLP-1 RA to an alternative brand.

Scope

This guidance aims to support clinicians in selecting alternative glucose-lowering therapies when GLP-1 RAs used in the management of T2DM in adults are unavailable during this period of national shortage. This guidance should be used in conjunction with [NICE NG28 Type 2 Diabetes in Adults: choosing medicines](#).

Children and young people with T2DM prescribed GLP-1 RAs under the care of specialist paediatric services should be directed back to specialist services.

The use of GLP-1 RAs in the management of obesity is outside the scope of this guidance.

Target audience:

- Prescribers in all care settings.
- NHS Diabetologists/Endocrinologists.
- Specialist diabetes services and associated health care professionals.
- People with Type 2 Diabetes, their families, or carers.
- Organisations commissioning NHS services.
- Providers of NHS services.

Advice from the Department of Health & Social Care (DHSC)

The following advice has been issued from DHSC for the period of national GLP-1 RA shortages, 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 GLP-1 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 effects as per NICE NG28.
- 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 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.

Advice for prescribers:

This guidance aims to support clinicians in selecting alternative glucose-lowering therapy when the prescribed GLP-1 RA is unavailable. This advice 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 prescribe medications in accordance with the licensed indications.

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 families and carers or guardian.

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 GLP-1 RA prescription.

Should a particular preparation of GLP-1 RA be unavailable and an alternative cannot be sourced, 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:

- HbA_{1c} greater than 86mmol/mol in the previous 3 to 6 months.
- HbA_{1c} greater than 86mmol/mol prior to starting the GLP-1 RA.
- HbA_{1c} not recorded in the previous 6 months.
- Urine albumin:creatinine ratio (uACR) greater than 30mg/mmol.
- Self-monitoring of blood glucose readings (or Continuous Glucose Monitoring, where available) persistently above individualised target range.

In all cases, the need to consider alternative glucose-lowering therapy presents an opportunity for engagement and clinical review.

Advice for people with T2DM

Counterfeit products

People with T2DM should be advised that GLP-1 RAs should only be obtained on prescription from registered pharmacies. It is not legal to obtain GLP-1 RA therapy without a prescription and there is a risk that the medicine may not be genuine. [Please see the government's website for further information](#).

Structured education

People with T2DM requiring a change to their usual medication may welcome an opportunity to access structured education to support self-management. In addition to local services, offer access to structured education at <https://healthyliving.nhs.uk/>.

Weight management

Eligible people with T2DM who would like support with weight management should be signposted to available weight management programmes. In addition to local pathways, there are several nationally available options, including:

- [Adult weight management: short conversations with patients](#)
- [The NHS Digital Weight Management Programme](#)
- [Tier 1 and 2 weight management services](#)
- [NHS Type 2 Diabetes Path to Remission programme](#)
- <https://www.nhs.uk/better-health/lose-weight/>

Reviewing metabolic response to prescribed GLP-1 RA therapy

NICE NG28 guidance advises:

GLP-1 RA therapy should only be continued if the adult with T2DM has had a beneficial metabolic response,

defined as

- **a reduction of at least 11 mmol/mol [1.0%] in HbA_{1c}, and**
- **weight loss of at least 3% of initial body weight in 6 months**

Where the person with T2DM has a confirmed beneficial metabolic response but GLP-1 RA therapy is unavailable, review and discuss options for alternative glucose-lowering therapy (see *Figure 1*).

Where there has been no beneficial metabolic response to GLP-1 RA therapy, it is clinically appropriate to withdraw GLP-1 RA therapy and consider alternative glucose-lowering therapy (see *Figure 1*).

Giving advice when availability of the prescribed GLP-1 RA is intermittent

National supply chain issues for affected GLP-1 RA preparations are anticipated to extend into mid-2024, with risk that supplies will be intermittent or exhausted.

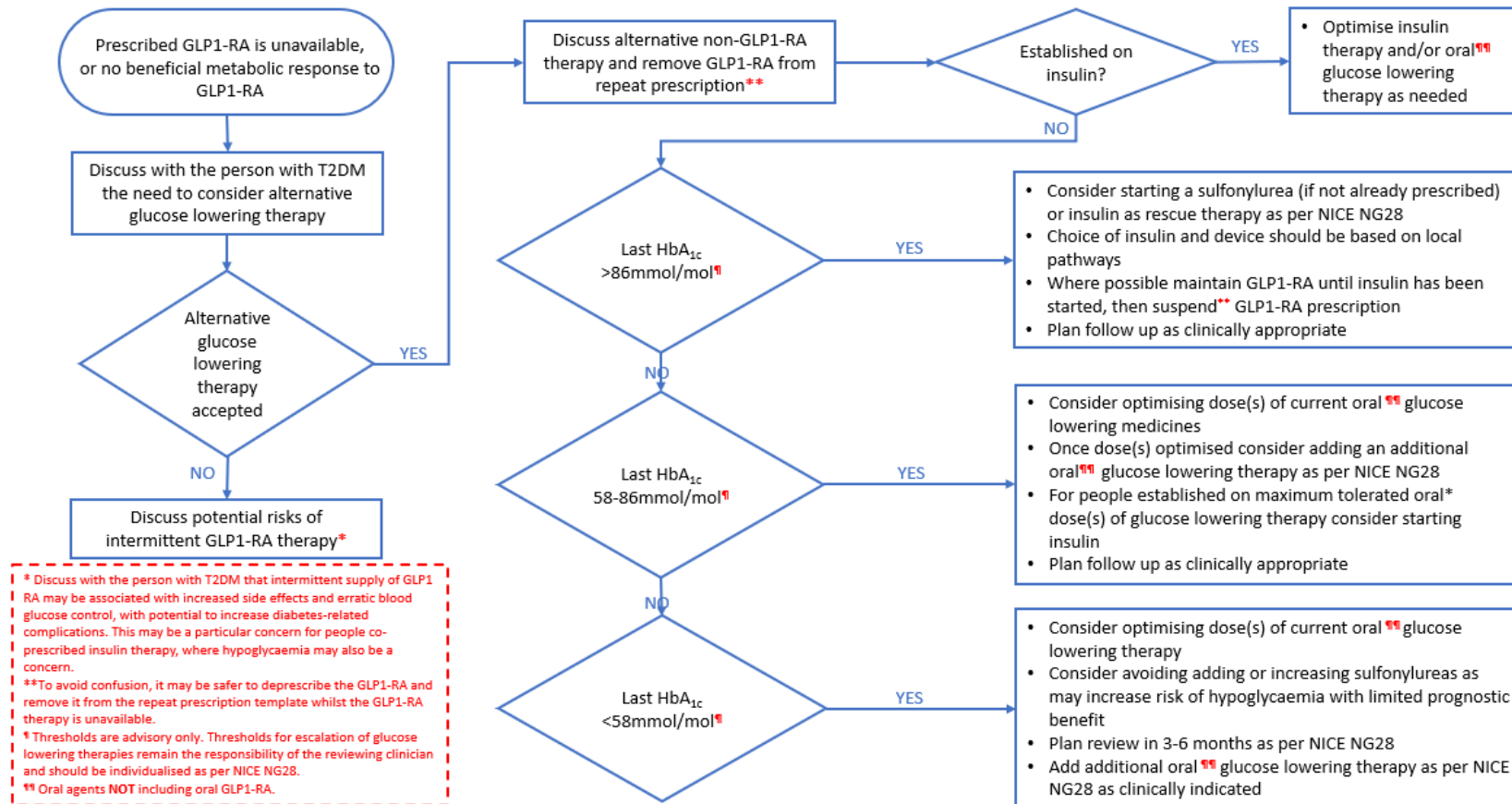
Whilst short delays accessing the usual GLP-1 RA prescription may be considered manageable, longer delays suggest the need to switch to an alternative glucose-lowering therapy.

Even where other GLP-1 RA preparations are intermittently available, there may be insufficient capacity to accommodate switching everyone to an alternative brand. DHSC advises against switching between GLP-1 RA preparations.

Discuss with the person with T2DM that intermittent supply of their GLP-1 RA may be associated with increased side effects and erratic blood glucose control, with potential to increase diabetes-related complications. This may be a particular concern for people co-prescribed insulin therapy, where hypoglycaemia may also be a concern.

Selecting alternative glucose-lowering therapy when GLP-1 RAs are unavailable or where there is no beneficial metabolic response to GLP-1 RA therapy

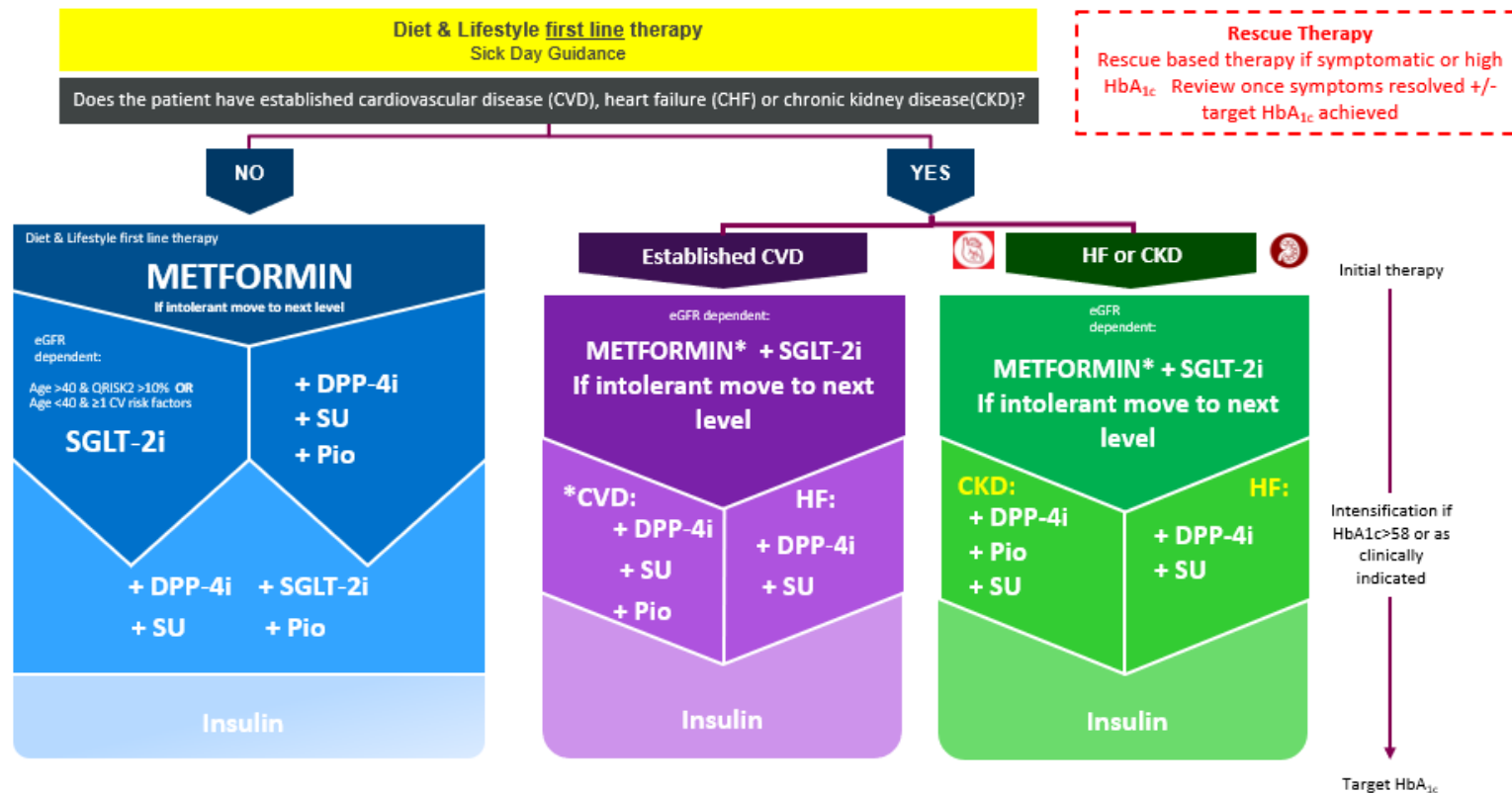
Figure 1. Choosing alternative glucose-lowering therapies in T2DM when GLP-1 RAs are unavailable or there is no beneficial metabolic response.



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

Figure 2. Quick reference guide for selecting oral glucose-lowering 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.

Figure 3. Oral glucose-lowering therapies by class.

Class	Biguanides	Sodium Glucose Co-Transporter-2 Inhibitors (SGLT2i)- "Gliflozins"	Dipeptidyl Peptidase 4 Inhibitors (DDP4i) - "Gliptins"	Sulfonylureas	Thiazolidinedione
Medicines	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 is 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 licenced 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 HbA_{1c} 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 use	<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 HbA_{1c} >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 HbA_{1c} 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
Expected HbA _{1c} 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 Formerly and the Electronic Medicines Compendium					

Where insulin therapy is required

Where insulin therapy is clinically indicated, clinicians are advised to initiate insulin in line with principles of NICE NG28: <https://www.nice.org.uk/guidance/ng28/chapter/recommendations-insulin-based-treatments>. **It is important to note that specific brands of insulin mentioned within NICE NG28 are unlikely to be able to take a large uplift in prescribing, therefore any decisions on insulin brand choice should be based on ongoing insulin availability noted within the SPS supply tool: <https://www.sps.nhs.uk/home/tools/medicines-supply-tool/>.**

The choice of insulin should take account of individual characteristics and the clinical needs of the person with T2DM.

Where possible, utilise the full range of insulins and devices available to reduce the risk of further impacting supply chain issues.

Re-commencing GLP-1 RA therapy when the period of national shortage has passed

The national shortage of GLP-1 RAs is expected to extend into mid-2024.

When GLP-1 RAs are regularly and reliably available again, it will be possible to re-commence prescribing GLP-1 RAs for people with T2DM meeting the eligibility criteria as per NICE NG28. Where a GLP-1 RA has been prescribed previously, review whether a beneficial metabolic response was achieved. Where there was no beneficial therapeutic response, consider alternative glucose-lowering therapies (See Figure 1).

NICE NG28 recommendations

If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug for a GLP-1 mimetic for adults with type 2 diabetes who:

- have a body mass index (BMI) of 35 kg/m² or higher (adjust accordingly for people from Black, Asian and other minority ethnic groups) **and** specific psychological or other medical problems associated with obesity **or**
- have a BMI lower than 35 kg/m² **and**:
 - for whom insulin therapy would have significant occupational implications **or**
 - weight loss would benefit other significant obesity-related comorbidities. **[2015, amended 2022]**

1.7.22 Only continue GLP-1 mimetic therapy if the adult with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA_{1c} and weight loss of at least 3% of initial body weight in 6 months). **[2015]**

1.7.23 For adults with type 2 diabetes, only offer combination therapy with a GLP-1 mimetic and insulin along with specialist care advice and ongoing support from a [consultant-led multidisciplinary team](#). **[2015]**

Appendix 1. List of GLP-1 RAs licensed for use in the management of T2DM in the UK (June 2023)

Brand Name	Generic Name	Oral or subcutaneous administration
Victoza[®]	Liraglutide	Subcutaneous
Xultophy[®]	Liraglutide + Insulin Degludec	Subcutaneous
Ozempic[®]	Semaglutide	Subcutaneous
Rybelsus[®]	Semaglutide	Oral
Trulicity[®]	Dulaglutide	Subcutaneous
Byetta[®]	Exenatide	Subcutaneous
Bydureon[®]	Exenatide	Subcutaneous
Lyxumia[®]	Lixisenatide	Subcutaneous
Suliqua[®]	Lixisenatide + Insulin Glargine	Subcutaneous

For up-to-date information on current availability and supply issues affecting GLP-1 RAs, see <https://www.sps.nhs.uk/home/tools/medicines-supply-tool/> or contact your local Prescribing Advisor/Medicines Optimisation Team.