GLP-1 Shortages

Philip Newland-Jones
Consultant Pharmacist Diabetes & Endocrinology
Clinical Director Diabetes & Endocrinology
University Hospital Southampton NHSFT

GLP-1 Shortages - 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 into mid-2024.

Supplies of some GLP-1 RA preparations may be intermittent or exhausted within this time frame

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.

Which Products are affected…

GLP-1 RA	Brand and formulation	Indication	Ability to uplift
Semaglutide	Ozmepic ®0.25 mg solution for injection in pre-filled pen Ozmepic ®0.5mg solution for injection in pre-filled pen Ozmepic ®1mg 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
Semaglutide	Rybelsus 3mg tablets Rybelsus 7mg tablets Rybelsus 14mg 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: • 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
Dulaglutide	Trulicity® 0.75 mg solution for injection in pre-filled pen Trulicity® 1.5 mg solution for injection in pre-filled pen Trulicity® 3 mg solution for injection in pre-filled pen Trulicity® 4.5 mg solution for injection in pre-filled pen	Type 2 diabetes mellitus as monotherapy (if metformin inappropriate) Type 2 diabetes mellitus in combination with other antidiabetic drugs (including insulin) if existing treatment fails to achieve adequate glycaemic control	Unable to uplift
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/m2 or more, or in individuals with a BMI of 27 kg/m2 or more in the presence of at least one weight-related co-morbidity]	

Which Products are Affected cont…

Exenatide	Byetta® 5micrograms/0.02ml solution for injection 1.2ml pre-filled pens Byetta® 10micrograms/0.04ml 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
	Bydureon® 2mg/0.85ml prolonged-release suspension for injection 1.2ml pre-filled pens		

Where can I find up to date info on stocks…

- 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
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Who do we expect will need to be involved in managing this shortage …

- 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

What does the DHSC say?

- 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
- 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.

Prioritisation for 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 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.

First Line of defence…

- 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 such as:

- 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

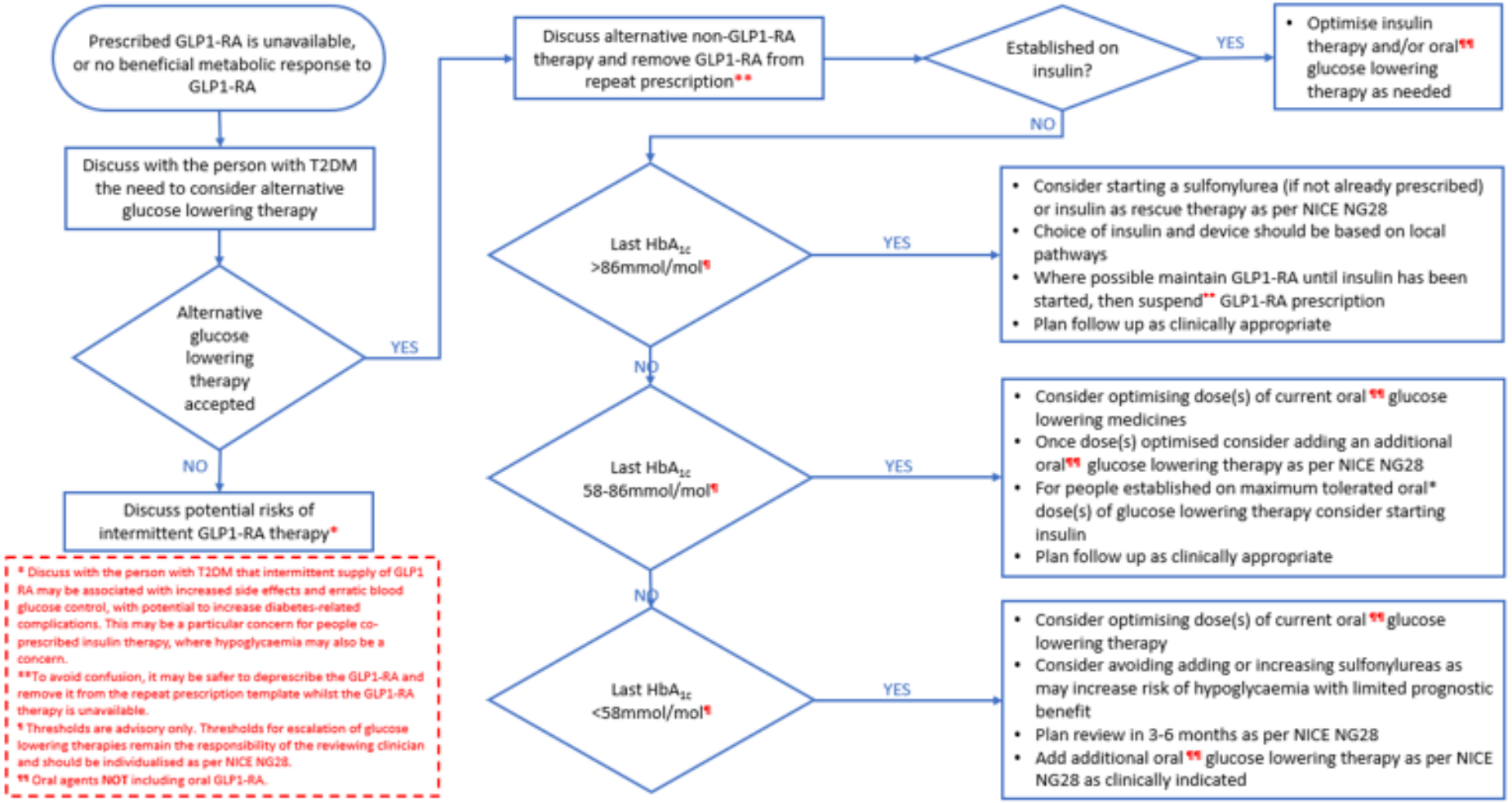
- https://www.nhs.uk/better-health/lose-weight/

Review Response to GLP-1s

- 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} <u>and</u>**
- **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 is unavailable, review and discuss options for alternative glucose lowering therapy
- 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

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

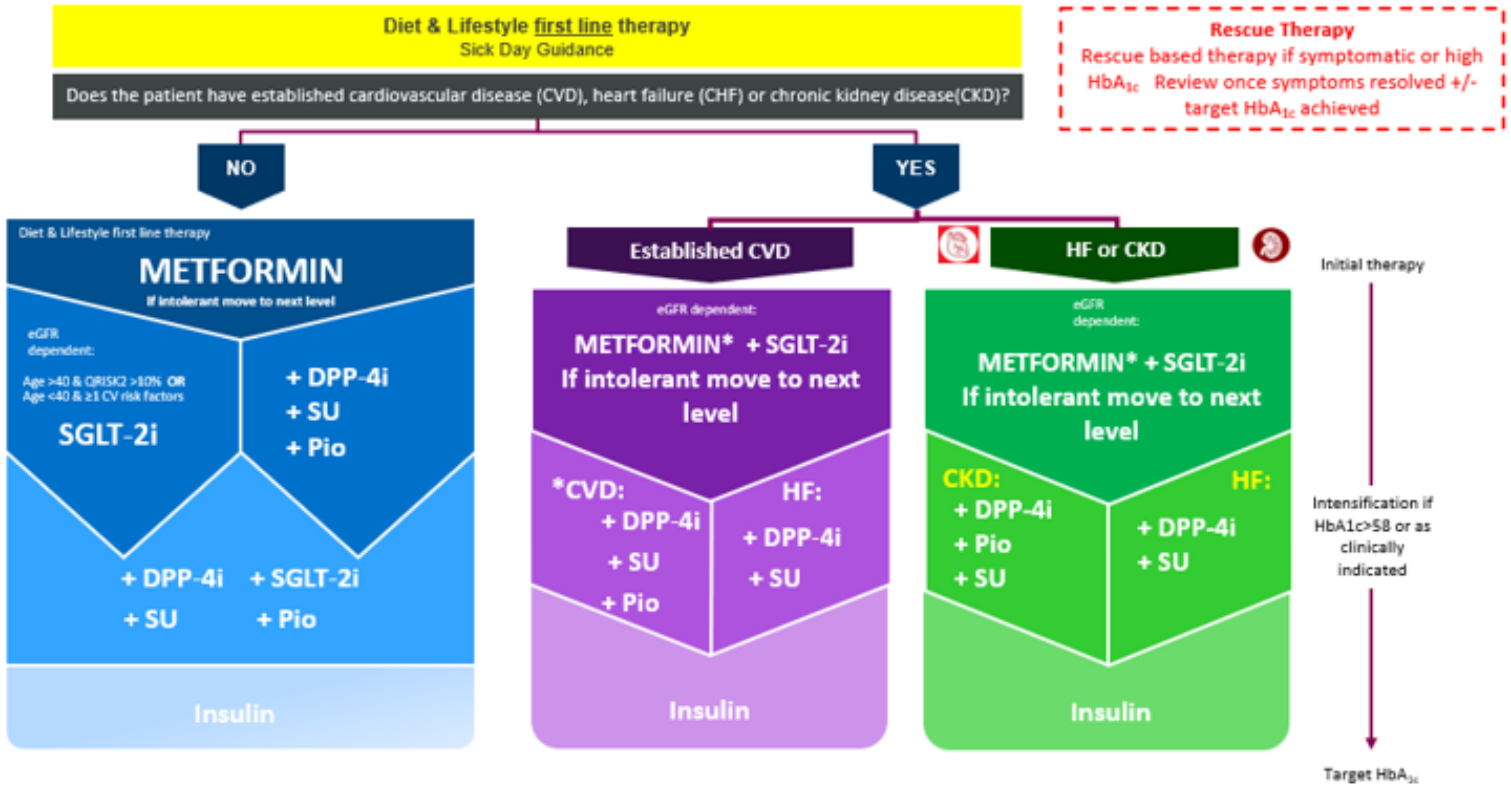
Figure 1. Choosing alternative glucose lowering therapies in T2DM when GLP-1 RAs are unavailable or there is no beneficial metabolic response.



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.

Quick Reference Guide for Oral Glycaemic Agents

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.

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	• 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	• 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	• If hypoglycaemia is a concern	• In people with high HbA_{1c} as rescue therapy • Symptomatic hyperglycaemia	• 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	• If eGFR<45ml/min review dose and stop if eGFR <30ml/min/1.73m^2	• 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)	• 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	• 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	• 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					

When is insulin required?

Where insulin therapy is clinically indicated, clinicians are advised to initiate in accordance with NICE NG28 https://www.nice.org.uk/guidance/ng28/chapter/recommendations - insulin-based-treatments.

- The choice of insulin should take account of individual characteristics and 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.**

Insulin	Uplift
Abasaglar U100 - kwikpen	Small uplift available (2nd Line Basal)
Lantus U100	No uplift beyond normal levels of insulin starts
Levemir U100	No uplift
Toujeo U300 - solostar	Uplift available (1st Line Basal)
Tresiba U100	No uplift
Semglee U100	No uplift
Humulin M3 - kwikpen	Uplift available (1st Line Mixed)
Humalog Mix 25 and Mix 50	No uplift beyond normal levels of insulin starts
Novomix 30	No uplift available
Humulin I - kwikpen	Some uplift (1st Line Intermediate)
Insulatard	No uplift

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 without a prescription and there is a risk that the medicine may not be genuine.

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 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

Any Questions…