Greater Manchester Diabetes Board

NHS Greater Manchester Integrated Care

1. Pathway guidance: Managing GLP1 receptor agonist shortages in adults with type 2 diabetes (supply problems expected until mid-2024 but subject to change)

For persons under the age of 18 years please seek specialist advice from paediatric/transition teams.

TOP TIPS:

1. GLP1RAs should only be prescribed for their licensed indication
2. DO NOT initiate any new GLP1RA (including Rybelsus®)
3. Review the need for prescribing a GLP1RA and stop treatment if no beneficial metabolic response as per NICE NG28 (reduction of HBA1c of at least 11 mmol/mol and weight loss of at least 3%)
4. DO NOT switch between brands
5. DO NOT substitute by doubling up a lower dose preparation
6. Promote access to structured education/ weight management programmes

All GLP1 receptor agonists (GLP1RA) are affected:

Ozempic®, Rybelsus®, Trulicity®, Victoza®, Byetta®, Bydureon®, Lyxumia® and Saxenda® (licensed for weight loss only)

GLP1-RA unavailable

No beneficial metabolic response to GLP1-RA at 6 months ie:
HbA1c reduction < 11mmol/mol and Weight loss < 3% of initial body-weight

Discuss with patient the need to consider alternative therapy in line with joint PCDS ABCD guidance based on current shortages found on page 6: PCDS_ABCD GLP-1 RA shortage_20230710.pdf

Inform the patient that intermittent supply may be associated with erratic blood glucose control, increased side-effects and potential diabetes-related complications

Established on insulin → Optimise insulin (including adding bolus fast acting insulin of choice)/oral agent as appropriate

Not on insulin

Last HbA1c >86 mmol/mol

1. When initiating or adjusting insulin, take into account:
   https://gmmmg.nhs.uk/wp-content/uploads/2021/08/GMMMG-Insulin-Prescribing-Aid-for-Adults-with-Type-2-Diabetes-V-1-1-PaGDSG-approved.pdf

   and
   https://www.sps.nhs.uk/articles/prescribing-available-insulins/

2. Consider sulphonylureas (e.g. gliclazide) if insulin not suitable.

Last HbA1c 58-86 mmol/mol

1. Optimise oral agents and consider additional therapy as per page 6 of:
   PCDS_ABCD GLP-1 RA shortage_20230710.pdf

2. If established on maximum tolerated oral doses, consider initiating insulin taking account of individual patient characteristics, local guidance and availability of products.

NB: Refer to management of hyperglycaemia in T2D (see pages 2a and 2b below).

Last HbA1c <58 mmol/mol

1. Optimise oral agents.

2. Avoid adding or increasing Sulphonylureas due to hypoglycaemia burden.

3. Consider additional therapy as per page 6 of: PCDS_ABCD GLP-1 RA shortage_20230710.pdf

DHSC Medicines Supply Notification MSN/2023/061 MSN_2023_061_GLP1_Receptor_Agonist.pdf (abcd.care)

Prescribing available insulins – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice July 2023

National Patient Safety Alert - DHSC: CAS-ViewAlert (mhra.gov.uk)

Compiled by
Ines Fonseca, Marlon Morais, Anna Swift, Adele Mackellar, Jonathan Schofield, Nicola Milne, Naresh Kanumilli & Ewan Jones
on behalf of
NHS GM Integrated Care

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NHS Greater Manchester Integrated Care

2a. How to manage hyperglycaemia in adults with T2D & minimise risk during GLP1-RA shortages & insulin supply issues (supply problems expected until mid-2024 but subject to change)

For persons under the age of 18 years please seek specialist advice from paediatric/transition teams.

AT DIAGNOSIS

- Offer lifestyle and diet advice. Signpost to diabetes education, either locality provision or GM digital offer, see https://elearning.diabetesmyway.nhs.uk/) for registration information.
- Consider eligibility for referral to the NHS Type 2 Diabetes Path to Remission (low-calorie diet), see https://momentanewcastle.com/hcp-t2dr-gm for referral information.
- Individualised HbA1c target based on patient specific factors, as per **NICE Guidance,** see https://www.nice.org.uk/guidance/ng28 for further information.

If marked osmotic symptoms (thirst, tiredness, nocturia, weight loss) and or HbA1c > 86mmol/mol →

Rescue Therapy: insulin or sulfonylurea:

- Exclude type 1 diabetes.
- Immediately start metformin PLUS insulin or sulfonylurea depending on symptoms, blood glucose levels, and ketone testing.
- When starting insulin, the person with diabetes must receive education and support from an appropriately trained HCP.
- Consider **urgent** discussion with local specialist team.

- Check urine ACR, measure eGFR to assess for any established CKD.
- Assess for any established ASCVD/HF or risk factors for CVD.

→

In the presence of any CKD/ risk factors for CVD (see page 2b), established CVD or heart failure:

- Offer of dual therapy of metformin with an SGLT2i* (see page 3 below) with proven benefit unless contraindicated as soon as practicable/tolerated.
- Use an SGLT2i* (see page 3 below) as monotherapy if Metformin to include MR is not tolerated/contraindicated.

HbA1c remains above individualised target despite appropriate monotherapy. →

Initiate metformin therapy:

- (If metformin contraindicated /not tolerated consider SGLT2i, DPP4i (taking into account cost-effectiveness), sulfonylureas, or pioglitazone, based on patient factors).
- Monitor HbA1c after 3 months.
- Target HbA1c <48mmol/mol **or Individualised.**

HbA1c above individualised target level and not at high CVD risk/no established ASCVD/heart failure or CKD →

DUAL THERAPY: lifestyle management +/- metformin + additional agent:

- Choose second agent after consideration of the presence of Established CVD, heart failure and/or CKD, specific drug effects and person-specific factors.
- e.g., SGLT2i (see prescribing tool on page 3 below),GLP1-RA*, DPP4i**, sulfonylureas or pioglitazone. Monitor HbA1c after 3 months.
- Target HbA1c 58 mmol/mol **or individualised**: If at target, continue to monitor every 3-6 months.

* *When supplies are regularly available.*

** *Saxagliptin & Algogliptin: Studies show a potential increased risk of heart failure*

HbA1c remains above individualised target despite appropriate dual therapy →

TRIPLE THERAPY: lifestyle management +/- metformin + two additional agents:

Add a third agent after consideration of the presence of CVD risk, established CVD, Heart failure and/or CKD and patient factors such as age, eGFR and BMI.

If CVD risk/established CVD heart failure and/or CKD, then SGLT2i should be considered.

Monitor HbA1c after 3months - target HbA1c <53mmol/mol **or individualised:**

- If at target, continue to monitor every 3-6 months.
- If not at target, assess medication adherence .
- Consider trial of an alternative medication.

2b. How to manage hyperglycaemia in adults with T2D & minimise risk during GLP1-RA shortages & insulin supply issues *[continued]* (supply problems expected to mid-2024 - subject to change)

For persons under the age of 18 years please seek specialist advice from paediatric/transition teams.

Definition of high risk of developing cardiovascular disease (CVD)

Adults with Type 2 Diabetes (T2D) who have:

- QRISK >10% and aged >40yrs.
- Clinical judgement of an elevated lifetime risk of cardiovascular disease (CVD) - defined as the presence of one or more of the below CVD in someone <40yrs:
  - Hypertension;
  - Dyslipidaemia;
  - Smoking;
  - Obesity;
  - family history (in a first degree relative) of premature CVD;
  - Proteinuria: ACR >30 mg/mmol.

Primary Prevention

High Risk of CVD/Heart Failure (HF) Prevention

Initiate metformin +

SGLT2i – with proven benefit* (see prescribing tool on page 3 below).

* *Dapaglflozin has the strongest evidence in primary prevention.*

Secondary Prevention

ASCVD (Prior MI, Stroke, Revascularization (CABG or PCI), peripheral arterial disease)

Initiate metformin +

- SGLT2i – **canagliflozin** and **empagliflozin** have evidence for a reduction in MACE (Major Adverse Cardiovascular Events) **canagliflozin, dapagliflozin** and **empagliflozin** reduced the risk of HF in those with established ASCVD

Heart Failure

Standard care + licensed SGLT2-I (see prescribing tool on page 3 below)
NICE has approved:

- **dapagliflozin 10mg** for treating symptomatic chronic heart failure with and without T2D.
- **empagliflozin 10mg** is licensed to treat symptomatic chronic heart failure with and without T2D.

CKD – standard care + licensed SGLT2-i

- **dapagliflozin 10mg** for the treatment of CKD with or without T2D.
- **canagliflozin 100mg** for the treatment of CKD in T2D only.
- **empagliflozin 10mg** for the treatment of CKD with or without T2D.

3. Choosing who to initiate on SGLT2 inhibitors for glucose control

(please refer to individual SPCs for current information on product licences)

Safe to prescribe	• First-line if Metformin intolerant/contraindicated AND HF/CVD OR QRISK2 ≥10%. Also if Pioglitazone and Sulphonylurea inappropriate • Second-line with Metformin OR third-line as add-on to other agents including insulin and GLP1RA • Established CVD or High risk of CVD (QRISK2 ≥ 10%) • History of HF (including receiving loop diuretics) • Prior stroke • Established CKD / DKD (check individual SPC for renal advice) • Overweight (BMI ≥25 Kg/m2) • Need to minimise hypoglycaemia • No history of LLA or PAD • Osteoporosis or history of fractures
Prescribe with caution * Please discuss with specialist team (can refer to practice/PCN clinician with specialist interest in diabetes if applicable or contact the hospital diabetes team)	• Long duration of diabetes (>10 years from diagnosis) • Recurrent UTIs or recurrent genital mycotic infections • Long-term catheter • Frail/ elderly (age >75 years)/ cognitive impairment • Adherence problems • Use of a medication compliance aid e.g., MDS * HbA1c >86 mmol/mol * BMI <25 Kg/m2 * Ketogenic/ low carbohydrate diets/ low calorie diet (do not * prescribe if in total diet replacement phase of the NHS Low Calorie * Diet Programme) * Previous LLA * Active or history of diabetic foot ulcers * History of PAD * Long term or recurrent courses of steroids
Do not prescribe ** NB Can be used in eFGR <45mL/min/1,73m2 if for CKD/heart failure.	• Acute illness (wait at least a few days after illness resolved and ensure person is eating and drinking normally again before considering initiation) • Recent major surgery • DKA or history of DKA • Excessive alcohol intake (binge drinking and >14 units/week on a regular basis) • IVDU • Eating disorders • Rapid Progression to insulin (within 1 year of diagnosis) • Age <18 years /Type 1 Diabetes / LADA / genetic diabetes • Diabetes due to pancreatic disease • Ketosis-prone Type 2 Diabetes • History of Fournier's Gangrene • Pregnancy, planning pregnancy or breastfeeding • eGFR <45mL/min/1.73m2 ** • Severe liver impairment (Child-Pugh score C)

SPC: Summary Product Characteristics; **GLP1RA:** Glucagon-like Peptide-1 Receptor Agonists; **CVD:** Cardiovascular Disease; **HF:** Heart Failure; **BMI:** Body Mass Index; **CKD:** Chronic Kidney Disease; **DKD:** Diabetic Kidney Disease; LLA: Lower Limb Amputation; **PAD:** Peripheral Arterial Disease; **HbA1c:** Glycated Haemoglobin; **UTI:** Urinary Tract Infection; **MDS:** Monitored Dosage System; **DKA:** Diabetic Ketoacidosis; **IVDU:** Intravenous Drug Usage; LADA: Latent Autoimmune Diabetes of Adults; **eGFR:** Estimated glomerular filtration rate; **ACR:** Albumin to Creatinine Ratio.