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

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

TOP TIPS:

1. GLP1-RAs should only be prescribed for their licensed indication.
2. **Prescribe Rybelsus® (Semaglutide tablets) OR Mounjaro® (Tirzepatide) for new initiations. DO NOT initiate other GLP1-RAs.**
3. **Switch people on Byetta® and Victoza® to Rybelsus® tablets OR Mounjaro®.**
4. **Consider Rybelsus® tablets OR Mounjaro® for people on Trulicity® and Ozempic® who unable to obtain supply for over 2 weeks. DO NOT interchange with other GLP1-RAs for short periods of time.**
5. **DO NOT switch between Victoza® and Saxenda® (different indications).**
6. Review the need for prescribing a GLP1-RA and stop treatment if no beneficial metabolic response (NICE NG28: reduction of HbA1c of at least 11 mmol/mol and weight loss of at least 3% in 6 months).
7. **DO NOT substitute by doubling up a lower dose preparation.**
8. **DO NOT switch between strengths.**
9. Continue to promote T2DM lifestyle/remission and education.

SUPPLY UPDATE:

Rybelsus® - available in sufficient quantities to support initiations/switches in T2DM
Mounjaro® - available in sufficient quantities to support initiations/switches in T2DM
Byetta® - will be discontinued March 24
Bydureon® - limited supply
Victoza® - out of stock until end of 2024
Trulicity® - limited supply
Ozempic® - limited supply

***Saxenda® and Wegovy®** - licensed for weight loss only via Tier 3 weight management services

Initiations for people with T2DM

Refer to Page 2a for decision making tool

People with T2DM on Byetta® and Victoza®

1. Start Rybelsus® (Semaglutide tablets) - see **Page 1c** for initiation checklist and counsel on administration instructions below.

OR

2. Start Mounjaro® (Tirzepatide) - see **Page 1d** for initiation checklist and separate guidance *Mounjaro® (Tirzepatide) for Type 2 Diabetes in Greater Manchester ICB .*

People with T2DM on Trulicity® and Ozempic®

Do not initiate Trulicity® and Ozempic®.
If unable to obtain supply for over 2 weeks, consider switching to:

1. Rybelsus® (Semaglutide tablets) - see **Page 1c** for initiation checklist and counsel on administration instructions below.

OR

2. Mounjaro® (Tirzepatide) - see **Page 1d** for initiation checklist and separate guidance *Mounjaro® (Tirzepatide) for Type 2 Diabetes in Greater Manchester ICB.*

Refer to Page 1b for advice on missed doses and re-starting after period of withholding

How to take Rybelsus® tablets:

1. Take Rybelsus® tablets on an empty stomach (at least 6 hours from last oral intake) at any time of the day.
2. Swallow Rybelsus® tablets whole with no more than half a glass of water (up to 120 ml). Do not split, crush, or chew the tablet, as it is not known if it affects absorption.
3. After taking Rybelsus® tablets wait at least 30 minutes before having the first meal or drink of the day or taking other oral medicines. Waiting less than 30 minutes lowers the absorption.

Prescribing considerations:

Sick day rules: ensure adequate fluid intake through any acute dehydrating illness (e.g. diarrhoea, vomiting or unable to eat and drink). and when to seek advice.
Pregnancy and Breastfeeding: contraindicated.
Severe GI disease: caution in gastroparesis.
Pancreatitis: caution in history of pancreatitis. Counsel patient on how to recognise signs/symptoms of acute pancreatitis and advise to seek medical attention if persistent, severe abdominal pain.
Hypoglycaemia: caution in use with insulin and sulphonylureas.

Refer to individual SPCs for full prescribing considerations https://www.medicines.org.uk/emc.

Dhsc Medicines Supply Notification: MSN/2023/061MSN_2023_061_GLP1_Receptor_Agonist.pdf (abcd.care)
National Patient Safety Alert – DHSC Jul-2023: CAS-ViewAlert (mhra.gov.uk)
National Patient Safety Alert – DHSC Jan-2024: CAS-ViewAlert (mhra.gov.uk)
Prescribing available insulins – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice July 2023

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on behalf of
NHS GM Integrated Care

Version 2, January 2024,
Ratified by GM Diabetes Board

1b. GLP1 Receptor Agonists: Missed dose and re-starting after period of withholding

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

Rybelsus® (Semaglutide daily oral tablets)	
3 mg	Resume dosing with next scheduled dose.
7 mg **14 mg**	If a morning dose is missed, the missed dose should be skipped and the next dose should be taken the following day. If a patient misses multiple days, clinical judgement should be used to determine the need for potential dose reductions. The half-life (~1 week), and time to steady-state (4-5 weeks) can inform decision and suggests that in established use, several weeks can be missed before full dose titration is required.
Trulicity® (Dulaglutide weekly subcutaneous injection)	
0.75 mg **1.5 mg**	Missed dose can be taken up to 3 days (72 hours) before next scheduled dose. If two or more consecutive doses are missed, restart dulaglutide at the same dose, and then titrate if required.
3 mg **4.5 mg**	Missed dose can be taken up to 3 days (72 hours) before next scheduled dose. If two or more consecutive doses are missed, restart dulaglutide at 1.5mg weekly, and then titrate as required.
Ozempic® (Semaglutide weekly subcutaneous injection)	
0.25 mg	Missed dose can be taken within 5 days after missed dose.
0.5 mg	Missed dose can be taken within 5 days after missed dose. If 2 doses missed, continue with 0.5 mg once weekly. If 3 or more doses missed, re-start with 0.25 mg once weekly for 4 weeks and then titrate as required.
1 mg	Missed dose can be taken within 5 days after missed dose. If 2 doses missed, continue with 1 mg once weekly. If 3 or more doses missed, re-start with 0.25 mg once-weekly for 4 weeks and then titrate as required.
Mounjaro® (Tirzepatide weekly subcutaneous injection)	
2.5 mg	Missed dose can be taken within 4 days after missed dose.
5 mg	Missed dose can be taken within 4 days after missed dose. If 2 doses missed, continue with 5 mg once weekly. If 3 or more doses missed, re-start with 2.5 mg once weekly for 4 weeks and then titrate as required.

1c. Rybelsus® Initiation Checklist

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

- ☐ Continue to promote T2DM lifestyle/remission and education
- ☐ Review the need for prescribing a GLP1-RA 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% in 6 months).
- ☐ Review medical history (e.g. pancreatitis or risk factors)
- ☐ Assess for any contraindications or cautions (e.g. severe GI disease, pancreatitis, women of childbearing potential)
- ☐ Consider renal and hepatic impairment - consult www.medicines.org.uk/emc for product license
- ☐ Explain the rationale for recommending therapy
- ☐ Explain the mode of action including GI effects such as reduced appetite and weight loss
- ☐ Advise on daily dosing regimen and how to take **(see boxes 1 and 2)**
- ☐ Consider the timing of other medications which may need to be taken on an empty stomach e.g. thyroxine
- ☐ Discuss potential side-effects and how to manage these – reassure they are mostly mild and transient **(see box 3)**
- ☐ Ensure robust contraception for use in women of childbearing potential
- ☐ Review and adjust other therapies (e.g. stop DPP4-inhibitors, consider dose reduction of sulphonylurea or insulin)
- ☐ Discuss self-monitoring of blood glucose if on insulin and/or sulphonylureas and look to empower self-titration of therapies
- ☐ Provide sick day guidance - ensure adequate fluid intake through any acute dehydrating illness (e.g. diarrhoea, vomiting or unable to eat and drink) and when to seek advice
- ☐ Agree realistic blood glucose and weight loss targets
- ☐ Arrange appropriate monitoring of response and a review date

Box 1: Initiation or switching to Rybelsus® - Dosing regimen:

3 mg once daily for 1 month.
Then, 7 mg once daily for at least 1 month.
Can be increased to 14 mg once daily to further improve glycaemic control.
Do not use two 7mg tablets to achieve the 14mg dose.

Box 2: Counsel on administration instructions:

1. Take Rybelsus® tablets on an empty stomach (at least 6 hours from last oral intake) at any time of the day.

2. Swallow Rybelsus® tablets whole with no more than half a glass of water (up to 120 ml). Do not split, crush, or chew the tablet, as it is not known if it affects absorption.

3. After taking Rybelsus® tablets wait at least 30 minutes before having the first meal or drink of the day or taking other oral medicines. Waiting less than 30 minutes lowers the absorption.

Box 3: Minimising side-effects:

- Eat smaller meals
- Stop eating when sensation of fullness starts
- Avoid fried or fatty foods
- Maintain adequate fluid intake
- Reassure that these symptoms are mostly mild and transient
- Most people are able to continue despite initial nausea

1d. Tirzepatide (Mounjaro®) Initiation Checklist

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

- ☐ Continue to promote T2DM lifestyle/remission and education
- ☐ Review the need for prescribing a dual GIP and GLP-1 receptor agonist 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% in 6 months).
- ☐ Review medical history (e.g. pancreatitis, active diabetic retinopathy or risk factors)
- ☐ Assess for any contraindications or cautions (e.g. severe GI disease, pancreatitis, women of childbearing potential)
- ☐ Consider severe hepatic impairment - consult www.medicines.org.uk/emc for product license
- ☐ Explain the rationale for recommending therapy
- ☐ Explain the mode of action including GI effects such as reduced appetite and weight loss
- ☐ Advise on weekly dosing regimen **(consult separate guidance *Tirzepatide (Mounjaro) for Type 2 Diabetes in Greater Manchester ICB*)**
- ☐ Advise on method of administration and injection technique (e.g. air shot is required before each injection) - **consult separate guidance *Tirzepatide (Mounjaro) for Type 2 Diabetes in Greater Manchester ICB***
- ☐ Ensure 4mm needles (32 gauge) are prescribed separately
- ☐ Consider effect on absorption of warfarin and other drugs with a narrow therapeutic index (e.g. digoxin) due to slow gastric emptying and monitor when initiating or increasing Tirzepatide
- ☐ Discuss potential side-effects and how to manage these – reassure they are mostly mild and transient **(see box 1)**
- ☐ Ensure robust contraception for use in women of childbearing potential. In overweight/ obese women, switch to a non-oral contraceptive method or add a barrier method to oral contraceptive when initiating or increasing Tirzepatide (for 4 weeks)
- ☐ Review and adjust other therapies (e.g. stop DPP4-inhibitors, consider dose reduction of sulphonylurea or insulin)
- ☐ Discuss self-monitoring of blood glucose if on insulin and/or sulphonylureas and look to empower self-titration of therapies
- ☐ Provide sick day guidance - ensure adequate fluid intake through any acute dehydrating illness (e.g. diarrhoea, vomiting or unable to eat and drink) and when to seek advice
- ☐ Agree realistic blood glucose and weight loss targets
- ☐ Arrange appropriate monitoring of response and a review date

Box 1: Minimising side-effects:

- Eat smaller meals
- Stop eating when sensation of fullness starts
- Avoid fried or fatty foods
- Maintain adequate fluid intake
- Reassure that these symptoms are mostly mild and transient
- Most people are able to continue despite initial nausea

2a. How to manage hyperglycaemia in adults with T2DM & minimise risk during GLP1-RA shortages & insulin supply issues (supply problems expected until end-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 or 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 T2DM & minimise risk during GLP1-RA shortages & insulin supply issues *[continued]*

(supply problems expected until end-2024 but 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 (T2DM) 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 SGLT2i (see prescribing tool on page 3 below)
NICE has approved:
dapagliflozin 10mg for treating symptomatic chronic heart failure with and without T2DM.
empagliflozin 10mg is licensed to treat symptomatic chronic heart failure with and without T2DM.

CKD – standard care + licensed SGLT2-i

dapagliflozin 10mg for the treatment of CKD with or without T2DM.
canagliflozin 100mg for the treatment of CKD in T2DM only.
empagliflozin 10mg for the treatment of CKD with or without T2DM.

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 GLP1-RA • 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.