DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Management of Type 2 Diabetes in adults

Key messages:

- Asses a person's cardiovascular status to determine whether the person with type 2 diabetes (T2DM) has chronic heart failure, established atherosclerotic cardiovascular disease or are at high risk of developing cardiovascular disease.

- Mangement strategies include
  - Adopt an individualised approach to diabetes care, which is tailored to the needs of the patient.
  - Offer structured education to adults with type 2 diabetes and their family members/carers

- Target HbA1c level should be agreed on an individual basis and people need to be encouraged and supported to achieve the target and maintain it. Measure HbA1c levels every three to six months until stable, then measure HbA1c six monthly.

- When starting oral hypoglycaemic therapy, base choice on effectiveness, safety, tolerability, monitoring requirements, licensed indications, cost, individual clinical circumstances, preferences and needs.

- **Metformin remains first line** drug treatment choice for adults with T2DM.

- For people with type 2 diabetes who have chronic HF or established atherosclerotic CVD **OFFER** an SGLT2i (see algorithm 1 for prefered local choice) with proven CV benefit in **addition** to metformin.

- For people with type 2 diabetes who have high risk of CVD (QRISK2 ≥10%) **CONSIDER** an SGLT2i (see algorthim 1 for prefered local choice) with proven CV benefit in **addition** to metformin.

- For people with type 2 diabetes who have an elevated lifetime risk of cardiovascular disease (defined as the presence of ≥1 cardiovascular risk factor* in someone aged <40 years), **CONSIDER** adding an SGLT2i

- Check and address modifiable risks for diabetic ketoacidosis before starting treatment with an SGLT2i

- When starting an insulin for which a biosimilar is available, use the product with the lowest acquistion cost.

- For patients with diabetes with significant osmotic symptoms (e.g., weight loss, polyuria, and polydipsia) or ketosis or age <50 years or a family or personal history of autoimmune disease, the diagnosis may be Type 1 diabetes, which requires insulin therapy. Please refer urgently to a specialist team for advice, assessment and/or treatment. **Do not start SGLT2i in those with possible Type 1 diabetes**.

*cardiovascular disease risk factors include hypertension, dyslipidaemia, smoking, obesity, and family history (in a first degree relative) of premature CVD)

- Do not routinely offer self-monitoring of capillary blood glucose (SMBG) to adults with type 2 diabetes unless in-line with NICE guidance.

- Do not offer antiplatelet therapy for adults with type 2 diabetes mellitus without cardiovascular disease.

- Driving advice: this should be an individualised decision by the clinician, using the DVLA guidance (https://www.gov.uk/government/publications/at-a-glance) and advice from diabetes.org.uk.

- Patient decision aids can help patients think about their options for controlling their blood glucose to try to reduce the long-term risks of diabetes. NICE patient decision aids can be found here

NICE defines
Interventions that should be used - strong recommendation

- **'Offer'** as an intervention which will does more good than harm and be cost effective, for the vast majority of patients.

Interventions that could be used:
- **'Consider'** as an intervention which will does more good than harm for most patients and be cost effective, but other options may be similarly cost effective.

Key

BMI	body mass index
DPP4i	Dipeptidyl peptidase-4 inhibitor ('gliptin')
DVLA	Driver and Vehicle Licensing Agency
eGFR	Estimated glomerular filtration rate
GI	gastro-intestinal
GLP1	Glucagon-like peptide-1 mimetic
HbA1c	Glycated haemoglobin
HF	heart failure
Met	metformin
NG	National guidance
Pio	pioglitazone
SGLT2i	sodium-glucose cotransporter 2 inhibitors
T2DM	Type 2 diabetes mellitus

Reference

- NICE NG28 Type 2 diabetes in adults: management (2015)

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Document updates	Date updated
Removal of insuman (human insulin) products due to discontinuation of the range	Jan 2023
Add message to prescribe GLP1s by brand	Feb 2023
Update preferred BGT choice; update insulin table following endocrine chapter update	June 2023
Admelog (insulin lispro biosimilar) inserted into table p.29	June 2023
Sitagliptin recommended as 1st line DPP4i	July 2023
Continuation criteria updated on page 19 to be in line with NICE criteria	August 2023
Reference to lixisenatide removed due to discontinuation of drug	December 2023
Toujeo (Insulin Glargine) classification changed from Specialist Initiation to Specialist Recommendation (Decision date Aug 2023)	December 2023
Rybelsus updated to Green and added to daily GLP1 table	Jan 2024
Tirzepatide (Mounjaro) addition	July 24
Byetta (exenatide) removed as discontinued product	July 24
Amendment to Appendix 6 tirzepatide (Mounjaro) to include prescribing information	October 2024
Amendment to Appendix 4 – Removed mention of liraglutide (Victoza) due to discontinuation and add in semaglutide tablets (Rybelsus)	Jan 2025
Liraglutide (Victoza) discontinued Brand replaced by liraglutide (Zegluxen), liraglutide (Zegluxen) also added to Appendix 4. Amendment to Rybelsus GREEN if needle phobic. Wavesense Jazz test strips added to preferred formulary choice list	March 2025

Management of diabetes requires a multifactorial approach in its management
Diabetes is a complex condition which requires regular monitoring. NICE recommend that patients with diabetes should receive the following nine key tests/processes done at least once a year:

- **Blood pressure** (aim: <140/90mmHg. See local hypertension guideline)
- **Cholesterol** (see local lipid modification guideline)
- Weight (aim: health weight between a BMI of 18.5 – 24.9kg/m^2). Overweight patients should aim for a 5-10% target loss.
- Smoking status
- HbA1c (tailored to individual needs)
- Urinary albumin (Aim: <2.5mg/mol for men, <3.5mg/mmol for women)
- Serum Creatinine (>150 micromol/L – discontinue metformin)
- Eye examination
- Foot examination (Risk scored as low, moderate and high)

The relative benefit of different treatments.
People with diabetes have a greater chance of developing a variety of complications and health problems, especially if their blood glucose is not well managed. Good glycaemic control will reduce the incidence of micro and macrovascular complications such as blindness, kidney failure and lower limb amputation.

However, **lifestyle advice, blood pressure monitoring and control of cholesterol level are essential components in the management of type 2 diabetes**; blood glucose control is less effective in reducing cardiovascular disease when compared to blood pressure or cholesterol lowering.

Young adults
It should be noted that young adults who develop type 2 diabetes have significantly elevated mortality, up to six times higher than age matched controls and double that of age matched peers with type 1 diabetes. Anyone with diabetes, whether type 1 or type 2, under the age of 25 years should be referred into the young adult diabetes clinic.

Management strategies

Individualised care
Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences, comorbidities and risks from polypharmacy and their likelihood of benefiting from long-term interventions.
An example of individualised treatment options is to consider the ABCD approach -

- **A**ge – less stringent HbA1c targets with decreasing life expectancy.
- **B**ody weight. Be aware of which drugs affect body weight – weight neutral – metformin and DPP4i (gliptins), weight gain – insulins, pioglitazone, sulphonylureas, weight loss – SGLT I and GLP1.
- **C**omplications – co-incident complications will impact drug selection e.g., patient with eGFR< 30ml/min/1.73m^2 should avoid metformin.
- **D**uration – disease duration is a consideration when setting HbA1c levels. The shorter the disease duration the greater the cardiovascular protection offered by strict glycaemic control. Once disease duration is 10-12 years the beneficial effects of strict glycaemic control may be lost or reversed.

- Reassess the person's needs and circumstances at each review and consider discontinuing any medicines that are not effective.
- Be aware of AKI, diabetes and sick day rules. See also think kidney .

Patient education
Offer therapy (lifestyle and medication) to help achieve and maintain the HbA1c target level.

- Offer structured education to adults with type 2 diabetes and/or their family members/carers (as appropriate) at diagnosis, with annual reinforcement and review. Explain that structured education is an integral part of diabetes care. Further details - NICE NG28

Dietary advice
Provide individualised and on-going nutritional advice from a healthcare professional with specific expertise and competencies in nutrition.

- Integrate dietary advice with a personalised diabetes management plan, including other aspects of lifestyle modification, such as increasing physical activity and losing weight.
- For recommendations on lifestyle advice see NICE guidelines on: preventing excess weight gain, weight management, obesity, physical activity, smoking: brief interventions and referrals, stop smoking services, smoking: harm reduction and smoking: acute, maternity and mental health services.

Physical Activity
Exercise is associated with improved glucose control and lower cardiovascular mortality. Individuals should be encouraged to perform at least 150 minutes (2.5 hours) of moderate intensity physical activity in bouts of 10 minutes or more over a week.

- Individuals should be encouraged to minimise the amount of time spent being sedentary (sitting) for extended periods. (NICE PH44).

Bariatric surgery
Consider bariatric surgery as an option for people with a BMI ≥35 and significant co-morbidities as long as they are also receiving assessment through a tier 3 service (or equivalent).

Blood Pressure (BP) management
Diagnosis, treatment and monitoring of hypertension is broadly the same for people with type 2 diabetes as for other people. See local hypertension guideline

Lipid management
Patients with Type 2 diabetes are considered to be at high risk of cardiovascular disease, requiring prevention therapies. Risk assess the patient for eligibility for statin therapy using QRISK 2. See Lipid modification guidance for further details.

Anti-platelet therapy
Do not offer antiplatelet therapy (aspirin or clopidogrel) for adults with type 2 diabetes without cardiovascular disease.

HbA1c measurement
NICE recommends the following frequencies for the measurement of HbA1c; however local advice is to tailor measurements according to the individual's needs.

In adults with type 2 diabetes measure $HbA1_c$ levels at:	
• 3-6 monthly intervals (Tailored to individual needs)	until the HbA1c is stable on unchanging therapy
• 6 monthly intervals	once the HbA1c level and blood glucose lowering therapy are stable

If HbA1c remains above target levels, but pre-meal self-monitored glucose levels are well controlled, consider self-monitoring to detect postprandial hyperglycaemia and manage this if detected.

If HbA1c monitoring is suspected to be inaccurate (because of disturbed erythrocyte turnover or abnormal haemoglobin type), seek advice from a diabetologist, clinical biochemistry or appropriate specialist if required.

Individualised targets
NICE have produced a patient decision aid on agreeing HbA1c targets, which also covers factors to weigh up when discussing HbA1c targets with patients.

When setting a target HbA1c level, NICE recommends to:

- Involve patients with type 2 diabetes in the decision regarding individual HbA1c targets. Encourage them to achieve and maintain their targets unless any resulting adverse effects or their efforts to achieve their target impair their quality of life.

Management of T2DM (adults)	**Support to aim for HbA1c level**
Lifestyle and diet, or lifestyle and diet + single drug not associated with hypoglycaemia	48 mmol/mol (6.5%).
Adults on a drug associated with hypoglycaemia	53 mmol/mol (7.0%).
If HbA1c levels are not adequately controlled by a single drug and ≥ 58 mmol/mol (7.5%): ➢ reinforce advice about diet, lifestyle and adherence to drug treatment and ➢ intensify drug treatment	53 mmol/mol (7.0%)

- Consider relaxing target HbA1c level on a case-by-case basis, with particular consideration for patients who are older or frail.

- Inform a person with a higher HbA1c that any reduction in HbA1c towards the agreed target is advantageous to future health.

- If adults achieve a HbA1c level below target and if you are certain that the patient is not experiencing hypoglycaemia, encourage them to maintain it.

- Avoid pursuing highly intensive management to levels below 42mmol/mol (6.0%).

Self-monitoring of blood glucose (SMBG)
NICE recommendations
Do not routinely offer SMBG for adults with type 2 diabetes unless:

- the person is on insulin or
- there is evidence of hypoglycaemic episodes or
- the person is on oral medication (e.g sulphonylurea) that may increase their risk of hypoglycaemia while driving or operating machinery or
- the person is pregnant or is planning to become pregnant.

Consider short-term SMBG levels (and review treatment as necessary):

- When starting treatment with oral or intravenous corticosteroids or
- To confirm suspected hypoglycaemia

Be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia and review their treatment as necessary.

Preferred formulary choices
See Blood glucose and ketone meters, testing strips and lancets formulary

- On Call Extra Mobile
- GlucoRx Q
- WaveSense Jazz (only for patients requiring extra functionality)

If none of the above is suitable for clinical reasons, then any meter with blood glucose test strips costing less than £9 for 50 are recommended for patients with type 2 diabetes and corresponding lancets costing less than £4 per 100 are suitable for prescribing.

Blood glucose testing for people with diabetes who drive
See chapter 3 "Assessing fitness to drive - guide for medical professionals" for further guidance.

Preconception advice
NICE recommend all women of childbearing age should regularly be informed that establishing good glycaemic control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. It is important to explain that risks can be reduced but not eliminated. https://www.nice.org.uk/guidance/ng3

PROCEED
Any women with any type of diabetes planning pregnancy should be referred to secondary care for pre-conception advice to get their diabetes under tight control. Please refer as soon as possible and up to a year ahead of the plans to conceive.:

- South Derbyshire - referral via task on SystmOne or admin 01332 258119 or email to dhft.ids@nhs.net
- North Derbyshire - referral to preconception clinic in CRH

For HbA1c targets for women with T2DM who are pregnant or planning to be pregnant see NICE guideline on diabetes in pregnancy.

Algorithm 1 - Treatment algorithm for Type 2 diabetes in adults – first line drug treatment

Initiation of **lifestyle and diet intervention.** Offer **structured education** (See appendix 5 for further details). **Reinforce** dietary and lifestyle advice and adherence to drug treatment at each step and consider discontinuing any medicines that are not effective**. Rescue Therapy** - For **symptomatic hyperglycaemia consider** insulin or a sulfonylurea and review when blood glucose control has been achieved.
JAPC recommend using the most cost-effective treatment. (See oral hypoglycaemic section for local choices p14)

First-line treatment **Assess HbA1c, cardiovascular risk and kidney function**

Chronic Kidney Disease

For people with type 2 diabetes and chronic kidney disease see NICE NG203 – chronic kidney disease: assessment and management

Not at high CVD risk

Offer
Metformin or
Metformin MR if GI disturbance
Prescribe generically

If metformin contraindicated

Consider
+Sulfonylurea (*Preferred: gliclazide)* or
+Gliptin (*Preferred: sitagliptin)* or
+Pioglitazone or
+an SGLT2 inhibitor for people who meet NICE criteria:

- Empagliflozin TA390*
- Dapagliflozin TA390*
- Canagliflozin TA390*
- Ertugliflozin TA572*

***NICE TA390/572**
Canagliflozin, dapagliflozin and empagliflozin as monotherapies are recommended as options when metformin CI or not tolerated, and diet/exercise alone do not provide adequate glycaemic control, only if SU or Pio is not appropriate, and gliptin would otherwise be prescribed

Using ertugliflozin to reduce CV risk when blood glucose is well controlled is off label (Feb 2022)

CHF or established atherosclerotic CVD

Offer
Metformin or
Metformin MR if GI disturbance
Prescribe generically

& as soon as metformin tolerability is confirmed

Offer
SGLT2 inhibitor
With proven cardiovascular benefit as soon as metformin tolerability is confirmed

Preferred: ***Empagliflozin***
Alternative: ***Dapagliflozin***

If metformin contraindicated
Offer - SGLT2 inhibitor alone

High risk of CVD
QRISK2 ≥ 10% or have an elevated lifetime risk of CVD (defined as the presence of ≥1 CV risk factor in someone aged <40 years

Offer
Metformin or
Metformin MR if GI disturbance
Prescribe generically

& as soon as metformin tolerability is confirmed

Consider
SGLT2 inhibitor
With proven cardiovascular as soon as metformin tolerability is confirmed benefit

Preferred: ***Empagliflozin***
Alternative: ***Dapagliflozin***

If metformin contraindicated
Consider - SGLT2 inhibitor alone

At any point - person's HbA1c not controlled below individual threshold, or the person develops CVD or a high risk of CVD

See algorithm 2 for treatment options if further interventions are needed

Prescribing note - When starting an adult with T2DM on metformin and an SGLT2i as 1st line therapy, introduce the **drugs sequentially**, starting with metformin and checking tolerability. Start the SGLT2i as soon as metformin tolerability is confirmed.

Rescue Therapy - For symptomatic hyperglycaemia, consider insulin or a sulfonylurea and review when blood glucose control has been achieved. Monitor the patients HbA1c and CVD status and risk

Algorithm 2 - Treatment options if further interventions are needed

At any point – HbA1c not controlled below individually agreed threshold

Switch or add further treatment options

If **monotherapy** has not reduced HbA1c below individually agreed target,

Consider:

+Sulfonylurea (*Preferred: gliclazide)* or
+Gliptin (*Preferred: sitagliptin)* or
+Pioglitazone or
+an SGLT2 inhibitor may also be an option if they meet the criteria in NICE technology appraisal for:

- **dual therapy or**
- **triple therapy**

GLP-1 mimetic treatments

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 BMI of ≥35 kg/m^2 (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 < 35 kg/m^2 and:
  – for whom insulin therapy would have significant occupational implications or
  – weight loss would benefit other significant obesity related comorbidities.

GLP-1s only be continued if the person has had a beneficial metabolic response (defined as a reduction of at least 11 mmol/mol [1.0%] in HbA1c and weight loss of at least 3% of initial body weight in 6 months.

Insulin therapy

When dual therapy has not continued to control HbA1c to below the persons individually agreed threshold, also consider insulin-based therapy (with or without other drugs)

Only offer combination therapy with a **GLP-1 agonist and insulin** along with specialist care advice and ongoing support from a consultant-led multidisciplinary team.

At any point – Cardiovascular risk or status changes

If patient has or develops CHF or established atherosclerotic CVD

If patient has or develops high risk of CVD (QRISK2≥10%)

Switch or add further treatment options

Switch or add further treatment options

Offer – an **SGLT2 inhibitor**
(If not already prescribed)

Preferred: Empagliflozin
Alternative: Dapagliflozin

Consider – an **SGLT2 inhibitor**
(If not already prescribed)

Preferred: Empagliflozin
Alternative: Dapagliflozin

Definition of atherosclerotic CVD and high risk of developing CVD

Atherosclerotic cardiovascular disease

- Includes coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, previous coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and transient ischaemic attack), and peripheral arterial disease

High risk of developing cardiovascular disease

- Defined as adults with type 2 diabetes who have:
  - QRISK2 cardiovascular risk score >10% in adults aged ≥40 years *or*
  - Elevated lifetime risk of cardiovascular disease (defined as the presence of ≥1 cardiovascular risk factor* in someone aged <40 years)
  - Chronic kidney disease, microalbuminuria, proteinuria, declining GFR (included by UHDB specialist)

* Cardiovascular disease risk factors: hypertension, dyslipidaemia, smoking, obesity, family history (in a first degree relative) of premature cardiovascular disease

Comparison of efficacy, hypoglycaemia, weight, side effects and cost for metformin- based combinations.

	Efficacy (↓HbA1c)	Hypoglycaemia	Weight	Side effects	Costs
Metformin	High	Low risk	None	GI, lactic acidosis	Low
Met + SGLT2	Intermediate	Low risk	Loss (~ 2kg)	GU infections, dehydration	High
Met + Gli	High	Moderate risk	Gain (~ 1.5 -2kg)	Hypoglycaemia	Low
Met + Pio	High	Low risk	Gain (~ 4- 5kg)	Oedema, HF, fractures	Low
Met + DPP4i (Gliptin)	Intermediate	Low risk	Neutral	Rare	High
Met + GLP1	High	Low risk	Loss (~1 - 3kg)	GI	High
Met + insulin	Highest	High risk	Gain (~ 4 - 5kg)	Hypoglycaemia	Variable

Comparison of efficacy, hypoglycaemia, weight, side effects and cost for Gliclazide-based combinations.

	Efficacy (↓HbA1c)	Hypoglycaemia	Weight	Side effects	Costs
Gliclazide	High	Moderate risk	Gain (~1.5 – 2kg)	Hypoglycaemia	Low
Glic + met	High	Moderate risk	Gain (~ 1.5 -2kg)	Hypoglycaemia	Low
Glic + DPP4i (gliptin)	Mid	Moderate risk	Neutral	Rare	High
Glic + pio	High	Moderate risk	Gain (~ 4- 5kg)	Oedema, HF, fractures	Low
Glic + GLP1	High	Moderate risk	Loss (~1 - 3kg)	GI	High
Glic + insulin	Highest	High risk	Gain (~ 4 - 5kg)	Hypoglycaemia	Variable

Alternative to NPH insulin:

- Insulin detemir or glargine if person needs assistance to inject insulin, lifestyle restricted by recurrent symptomatic hypoglycaemia or would otherwise need twice daily NPH insulin + oral hypoglycaemics.
- Offer insulin + GLP1 agonist only with specialist advice and consultant-led multidisciplinary support.
- An SGLT2 inhibitor + insulin +/- other antidiabetic drugs is an option after consultant/specialist initiation and assessment.

Scope of guideline

This guideline primarily considers drug treatments used in type 2 diabetes. It does not address the management of impaired glucose tolerance, impaired fasting glucose, type 1 diabetes or diabetes in pregnancy.

Choosing treatments

The choice of medicine should be based on:

- the person's individual clinical circumstances, for example comorbidities, contraindications, weight, and risks from polypharmacy
- the person's individual preferences and needs
- the effectiveness of the drug treatments in terms of metabolic response and cardiovascular and renal protection
- safety (see MHRA guidance, the BNF and individual SPCs) and tolerability of the drug treatment monitoring requirements
- the licensed indications or combinations available
- cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost)

NICE recommend assessing a person's cardiovascular status and risk to determine whether they have

- chronic heart failure or
- established CV disease, (includes CHD, ACS, previous MI, stable angina, previous coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and TIA) and PAD; or
- are at high risk of developing CV disease (risk factors include hypertension, dyslipidaemia, smoking, obesity, and family history (in a first-degree relative) of premature cardiovascular disease).

Use **QRISK2 tool** in adults with type 2 diabetes to assess the risk of developing CV disease.

1. **First-line drug treatment** If no chronic heart failure, established atherosclerotic CV disease or not at high risk.

    - **Offer Metformin -** standard release remains **first-line drug treatment** for adults with type 2 diabetes.
    - For individuals who experience gastrointestinal side effects with standard release metformin, consider a trial with modified release metformin. (For further see details on metformin prescribing see p14).

- If metformin is contraindicated, consider:
  - gliptins' or
  - pioglitazone or
  - a sulfonylurea or
  - SGLT2i for people who meet the criteria in NICE TA390 or NICE TA572

2. First line drug treatment options for type 2 diabetes based on CV assessment

	Metformin tolerated	**Metformin contra-indicated**
CHF or established atherosclerotic CVD	**Offer:** Met + SGLT2i*	**Offer:** SGLT2i*
High risk of developing CVD (QRISK2 ≥10%)	**Consider:** Met + SGLT2i*	**Consider:** SGLT2i*
T2DM adults at any stage if they develop CHF or established atherosclerotic CVD	**Offer:** SGLT2i in addition to current treatment or replace an existing drug with the SGLT2i*	
T2DM adults at any stage if they become at high risk of CVD	**Consider:** SGLT2i in addition to current treatment or replace an existing drug with the SGLT2i*	

*SGLT2i with proven cardiovascular benefit. See prescribing note for SGLT2i

Further treatment options:

Dual therapy

If the monotherapy has not controlled HbA1c to below the persons individually agreed threshold, consider adding:

- Gliclazide or
- Pioglitazone or
- Sitagliptin or
- an SGLT2i if patients meet NICE criteria for combination therapy (NICE TA315, NICE TA572, NICE TA288, NICE TA336)

Triple therapy

If dual therapy with metformin and another oral dug has not controlled HbA1c to below the persons individually agreed threshold, consider adding:

- Gliclazide or
- Pioglitazone or
- Sitagliptin or
- an SGLT2i if patients meet NICE criteria for combination therapy
- insulin-based treatment (see p27 for insulin therapy in type 2 diabetes)

If dual therapy with 2 oral drugs has not controlled HbA1c to below the persons individually agreed threshold, (and metformin is CI or not tolerated) consider adding insulin-based treatment (see p27 for insulin therapy in type 2 diabetes)

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

- have a body mass index (BMI) ≥ 35 kg/m^2 (adjust accordingly for people from Black, Asian and other minority ethnic groups) and

- specific psychological or
- other medical problems associated with obesity

- have a BMI < 35 kg/m^2 and:
  - for whom insulin therapy would have significant occupational implications or
  - weight loss would benefit other significant obesity-related comorbidities.

GLP1 + insulin
Only offer combination therapy with a GLP-1 agonist and insulin along with specialist care advice and ongoing support from a **consultant-led multidisciplinary team.**

Prescribing note 1 - reviewing and changing treatments:
At each point, think about and discuss the following with the person:

- stopping medicines that are not tolerated
- stopping medicines that have had no impact on glycaemic control or weight, unless there is an additional clinical benefit, such as cardiovascular or renal protection, from continued treatment
- For continued therapy, sitagliptin (DPP4i) /pioglitazone must show HbA1c reduction ≥5.5 mmol/mol (0.5%) in 6 months [local consensus based on previous NICE recommendation]
- how to optimise their current treatment regimen before thinking about changing treatments, considering factors such as:
  - adverse effects
  - adherence to existing medicines
  - the need to revisit advice about diet and lifestyle
  - prescribed doses and formulations
- whether **switching rather than adding drugs** could be effective

Prescribing note 2 - SGLT2i
SGLT2i are an established class of medications for the treatment of T2DM, HF, and CKD. They act be preventing the absorption of glucose and sodium, mainly form the proximal renal tubule in the kidney. Glucose and sodium are therefore, lost in urine.

Clinical trials using SGLT2i have provided strong evidence in the trial populations for reduced risk of major cardiovascular, renal and heart failure events. There are many benefits to these agents to people living with diabetes:

Benefits	Risks
↓ HbA1c levels (6-11mmol/mol (0.5-1%))	↑ Genitourinary infections
↑ Weight loss (typically 2-3kg)	↑ Diabetic ketoacidosis
↓ in blood pressure (4/2mmHg)	↑ Acute kidney injury
↑ High-density lipoprotein cholesterol	↑ Risk for amputation (seen with canagliflozin)
↓ Intestinal absorption of LDL-C	↑ Hypotension
↑ Faecal excretion of LDL-C	↑ Bone fractures
↓ Albuminuria	
↔Once-daily, oral agent	

Ref: Pittampalli S, Upadyayula S, Mekala HM, Lippmann S. Risks vs Benefits for SGLT2 Inhibitor Medications. Fed Pract. 2018;35(7):45-48.

Only three SGLT2i within the class have positive CV data - empagliflozin, dapagliflozin and canagliflozin. Currently there is greater uncertainty around the CV benefits associated with ertugliflozin.

Prescribing information

Please check full specific product characteristics for more detailed and current information. https://www.medicines.org.uk/emc/

BIGUANIDES – METFORMIN

Decreases gluconeogenesis and increases peripheral utilisation of glucose

<table>
<tr><td>Traffic light status</td><td colspan="3">Standard release
GREEN 1st line</td><td>Modified release
GREEN 2nd line
If standard-release metformin is not tolerated due to GI side effects, consider a trial of modified-release metformin tablets</td></tr>
<tr><td>Regimen</td><td colspan="3">Take with meals and start low and go slow.
500mg OD for at least 1 week, then increase in 500mg steps at weekly intervals to highest tolerated dose or maximum dose.

Maximum dose in BNF is 2g/day.

Titrate dose over several weeks to minimise risk of gastro-intestinal side effects. N.B. often side effects settle after approximately 1 week.</td><td>Initially 500 mg once daily, then increased if necessary up to 2 g once daily with meals. Dose increased gradually, every 10–15 days.</td></tr>
<tr><td>Place in therapy</td><td colspan="4">First line choice for all patients</td></tr>
<tr><td>Advantages</td><td colspan="4">Long-term safety data -strong evidence for the beneficial cardiovascular effect of metformin; Low risk of hypoglycaemia; moderate weight loss</td></tr>
<tr><td rowspan="8">Renal impairment</td><td colspan="4">A GFR should be assessed before initiation of treatment with metformin and at least annually thereafter. In patients at an increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g., every 3-6 months.</td></tr>
<tr><td>GFR (ml/min)</td><td>Total maximum daily dose
(To be divided into 2-3 daily doses)</td><td colspan="2">Additional considerations</td></tr>
<tr><td>60-89</td><td>2000 mg</td><td colspan="2">Dose reduction may be considered in relation to declining renal function.</td></tr>
<tr><td>45-59</td><td>2000 mg</td><td colspan="2" rowspan="2">Factors that may increase the risk of lactic acidosis should be reviewed before initiation of metformin. The starting dose is at most half of the maximum dose</td></tr>
<tr><td>30-44</td><td>1000 mg</td></tr>
<tr><td><30</td><td>-</td><td colspan="2">Metformin is contraindicated.</td></tr>
<tr><td colspan="4">• Review metformin dose if the eGFR is below 45 ml/min/1.73-m^2
• Stop the metformin if the eGFR is below 30 ml/minute/1.73-m^2.
• Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/min/1.73-m^2.</td></tr>
<tr><td>Hepatic impairment</td><td colspan="4">Withdraw if tissue hypoxia likely</td></tr>
<tr><td>Warning</td><td colspan="4">Lactic acidosis is a rare, but serious (high mortality in the absence of prompt treatment) metabolic complication that can occur due to metformin accumulation. Reported cases of lactic acidosis in patients on metformin have occurred primarily in diabetic patients with significant renal failure.
Metformin and reduced vitamin B12 levels see MHRA June 2022 and also local advice in formulary endocrine chapter.</td></tr>
</table>

SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITOR **Reversibly inhibits sodium-glucose co-transporter-2 (SGLT2) in the renal proximal convoluted tubule to reduce glucose reabsorption and increase urinary glucose excretion**				
	Empagliflozin	**Dapagliflozin**	**Canagliflozin**	**Ertugliflozin**
Traffic light status				
T2DM ***without*** *CKD*	**GREEN** *NICE TA336 & TA390*	**GREEN** *NICE TA288, TA390 & TA418*	**GREY** *NICE TA315 & TA390*	**GREY** *NICE TA572*
T2DM ***with CKD*** as per NICE NG28	**GREEN**	**GREEN**	**GREY**	-
Regimen	Starting dose: **10mg od** Can be increased to: **25mg od*** (*if eGFR ≥60 ml/min/1.73m^2 and tighter glycaemic control is needed)	Recommended dose:10mg od	Starting dose: **100mg od** Can be increased to: **300mg od*** (*if eGFR ≥60 mL/min/1.73m^2 or CrCl ≥60 mL/min and tighter glycaemic control is needed)	Starting dose: 5mg od Can be increased to: 15mg od if additional glycaemic control is needed.
Place in therapy as per NICE				
Advantages	Low hypoglycaemia, weight loss (~2kg stabilising over 6-12 months) and lowering of systolic and diastolic blood pressure in the order of ~ 2-4 / ~ 1-2mmgHg. (Silvio E. Inzucchi et al. Dia Care 2015; 38:140-149)			In the pool of placebo-controlled studies, the incidence of documented hypoglycaemia was increased for 5mg &15mg (5% & 4.5%) compared to placebo (2.9%).
Before commencing an SGLT2i	➢ Check whether the patient maybe at increased risk of diabetic ketoacidosis (DKA): • had a previous episode of DKA • unwell due to intercurrent illness • following a very low carbohydrate or ketogenic diet ➢ Address modifiable risks for DKA before starting an SGLT2I. For example, for people who are following a **very low carbohydrate or ketogenic diet**, they may need to delay treatment until they have changed their diet. ➢ Advise people with type 2 diabetes who are taking an SGLT2 inhibitor about the need to minimise their risk of DKA by **not starting a very low carbohydrate or ketogenic diet** without discussing it with their healthcare professional, because they may need to suspend SGLT2 inhibitor treatment. *(A very low carbohydrate diet has 20 to 50 grams per day of carbohydrate or less than 10% of a 2000 kcal/day diet. A ketogenic diet is a very low carbohydrate, high fat diet that is designed to induce ketosis*). Educate the patient about sick day rules. Links to patient information leaflets are includes below: 1. ABCD_A4_Leaflet_Final (002).jpg (848×1200) 2. Diabetes and being ill | Managing when you're sick | Diabetes UK Medicines_and_your_kidneys.pdf (derbyshiremedicinesmanagement.nhs.uk)			

	Empagliflozin		Dapagliflozin		Canagliflozin		Ertugliflozin
Contraindications	Diabetic ketoacidosis		Ketoacidosis		Ketoacidosis		Ketoacidosis
Renal function	**eGFR (mL/min/1.73m^2) or CrCl (mL/min)**	**Total daily dose of empagliflozin**	**eGFR (mL/min/1.73m^2) or CrCl (mL/min)**	**Total daily dose of dapagliflozin**	**eGFR (mL/min/1.73m^2) or CrCl (mL/min)**	**Total daily dose of canagliflozin**	Ertugliflozin should **not be initiated** in patients with eGFR <60ml/min/1.73m^2 or CrCl <60ml/min. Discontinued when eGFR is persistently <45 ml/min/1.73 m^2 or CrCl is persistently <45 ml/min. Not to be used in patients with severe renal impairment, with end-stage renal disease (ESRD), or receiving dialysis.
	≥60	**Initiate 10mg.** Can be increased to 25mg	≥60	**Initiate 10mg.**	≥60	**Initiate 100mg.** The dose can be increased to 300mg	
	45 to < 60	**Initiate 10mg.** Continue 10mg for patients already taking empagliflozin	45 to < 60	**Initiate 10mg.** Continue with 10mg for patients already taking dapagliflozin	45 to < 60	**Initiate 100mg** Continue 100mg for patients already taking canagliflozin	
	30 to < 45 (Patients with T2DM and established CVD)	**Initiate 10mg.** Continue 10mg for patients already taking empagliflozin	< 45	GFR falls below 45 mL/min/1.73m^2 additional glucose lowering treatment should be considered	30 to < 45 **and** urinary albumin/creatinine ratio > 300mg/g	**Initiate 100mg** Continue 100mg for patients already taking canagliflozin	
	< 30 For HF in patients with or without T2DM continued down to an eGFR of 20 ml/min/1.73 m^2	**Empagliflozin is not recommended**	< 15	**Not recommended** in patients with eGFR < 15 mL/min/1.73m^2	< 30 **and** urinary albumin/creatinine ratio > 300mg/g	Canagliflozin **should not be initiated** Continue 100mg for patients already taking canagliflozin	
Hepatic function	Avoid use in severe hepatic impairment		Initial dose 5mg daily in severe impairment, increased according to response.		Avoid use in severe hepatic impairment		No dosage adjustment necessary in patients with mild or moderate hepatic impairment. Avoid use in severe hepatic impairment.
Adverse effects	Hypoglycaemia in combination with insulin or a sulfonylurea, vulvovaginal candidiasis, urinary tract infection and polyuria or pollakiuria, genital infection		Hypoglycaemia (when used with a sulfonylurea or insulin), urinary tract and genital infection, back pain, dysuria, polyuria, dyslipidaemia and elevated haematocrit. **UTIs-** the incidence of UTIs is increased in patients taking dapagliflozin, however, these infections can be managed in the usual way.		Hypoglycaemia in combination with insulin or a sulfonylurea, vulvovaginal candidiasis, UTI, polyuria, genital infections and nausea.		Hypoglycaemia, vulvovaginal mycotic infection and other female and male genital mycotic infections. Volume depletion, increased urination, vulvovaginal pruritus, thirst, serum lipid changes, haemoglobin increased.

Long-term data	Long-term safety data – concerns about diabetic ketoacidosis at only moderately elevated blood sugars, limited long-term data.			
Monitoring (SPC advice on <u>renal function</u>)	• Prior to empagliflozin initiation and periodically during treatment, i.e., at least yearly. • Prior to initiation of any concomitant medicinal product that may have a negative impact on renal function.	• Prior to initiation of dapagliflozin and at least yearly, thereafter. • prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter	• Prior to initiation of canagliflozin and at least annually, thereafter • Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter. • For renal function approaching moderate renal impairment, at least 2 times to 4 times per year. (CKS)	• Prior to initiation and periodically thereafter • More frequently in patients with an eGFR <60ml/min/1.73m2 or a CrCl <60ml/min
Use SGLT2i with caution in the following situations[1]	• Person adhering to a ketogenic diet • Body mass index under 25 kg/m^2 (under 23 kg/m^2 in South Asian patients) • Person considered at high risk of acute effects of hyperglycaemia (such as dehydration due to non-adherence to medication) • Person with very high level of HbA1c >86 mmol/mol (~10% in old HbA1c units) • People diagnosed with or at risk of frailty • Cognitive impairment as it may interfere with the adequate understanding to take action to prevent and identify DKA • On chronic oral steroids • Long duration of diabetes (generally over 10 years from diagnosis)			
Avoid use of SGLT2I in the following situations[1]	• Past history of diabetic ketoacidosis • Eating disorder • eGFR lower than allowed in the up-to-date licensing of the medication being considered • Person with excess alcohol consumption or Intravenous drug users • Unwell person (acute medical illness including COVID-19, surgery or planned medical procedure) • Any diagnosis or suspicion of diabetes due to other causes, including T1D, latent autoimmune diabetes (LADA), other genetic causes of diabetes, known pancreatic disease or injury, or people who rapidly progressed to needing insulin within 1 year of diagnosis • Pregnant, breast feeding, female in the child-bearing years and sexually active without contraception • Age <18 years			
Warning	MHRA, April 2016- SGLT2 inhibitors (canagliflozin, dapagliflozin and empagliflozin) used in type 2 diabetes, may lead to **ketoacidosis**, a serious condition where the body produces high levels of blood acids – ketones that may require hospitalisation. When treating patients who are taking an SGLT2 inhibitors: • Test for raised blood ketones in patients with symptoms of diabetic ketoacidosis (DKA); omitting this test could delay diagnosis of DKA. • If you suspect DKA, stop SGLT2 inhibitor treatment. • Do not restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use unless another cause for DKA was identified and resolved. • If DKA is confirmed, take appropriate measures to correct the DKA and to monitor glucose levels. • Inform patients of the symptoms and signs of DKA (e.g., nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness); advise them to get immediate medical help if these occur			

	• Interrupt treatment with the SGLT2 inhibitor in patients who are hospitalised for major surgery or acute serious illnesses; treatment may be restarted once the patient's condition has stabilised. MHRA, June 2016- increased **lower limb amputation** (primarily of the toe) in people taking **canagliflozin** compared with placebo. Advice for healthcare professionals • As a precaution, consider stopping canagliflozin if a patient develops a significant lower limb complication (e.g., skin ulcer, osteomyelitis, or gangrene), at least until the condition has resolved, and continue to monitor the patient closely. • carefully monitor patients receiving canagliflozin who have risk factors for amputation (e.g., previous amputations, existing peripheral vascular disease, or neuropathy) • monitor all patients for signs and symptoms of water or salt loss; ensure patients stay sufficiently hydrated to prevent volume depletion in line with recommendations in the product information; note that diuretics can exacerbate dehydration • advise patients to stay well hydrated, carry out routine preventive foot care; seek medical advice promptly if they develop skin ulceration, discolouration, or new pain or tenderness – this should be adopted when using any SGLT2i (local specialist advice) Start treatment for foot problems (e.g., ulceration, infection, or new pain or tenderness) as early as possible. MHRA, Feb 2019- SGLT2 inhibitors: **reports of Fournier's gangrene** (necrotising fasciitis of the genitalia or perineum) Advice for healthcare professionals • Fournier's gangrene is a rare but serious and potentially life-threatening infection • if Fournier's gangrene is suspected, stop the SGLT2 inhibitor and urgently start treatment (including antibiotics and surgical debridement as required) • urogenital infection or perineal abscess may precede necrotising fasciitis • advise patients to seek urgent medical attention if they experience severe pain, tenderness, erythema, or swelling in the genital or perineal area, accompanied by fever or malaise MHRA, March 2020- SGLT2 inhibitors: **monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness** Advice for healthcare professionals • interrupt sodium-glucose co-transporter 2 (SGLT2) inhibitor treatment in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. • monitor ketones during this period – measurement of blood ketone levels is preferred to urine • restart treatment with the SGLT2 inhibitor once ketone values are normal and the patient's condition has stabilised

[1]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8140708/pdf/clinmed-21-3-204.pdf

SULFONYLUREAS- GLICLAZIDE Augments insulin secretion and consequently is only effective when some residual pancreatic beta-cell activity is present	
Traffic light status	**GREEN 1st line** (*Gliclazide MR is classified as **GREY**. This preparation is more costly than the immediate release preparation. The MR preparation may be beneficial for patients with compliance problems requiring once daily dosing.)*
Regimen	Initially, 40-80mg daily, adjusted according to response; up to 160mg as a single dose with breakfast. Maximum dose 320mg daily. Increase the dose every 4-6 weeks to achieve glycaemic target or maximal dose is reached.
Place in therapy	Consider a sulfonylurea as an option for first-line glucose lowering therapy if: • the person is underweight (unusual in T2DM. Discuss with specialist team to exclude Type 1 diabetes/other types of diabetes) • the person does not tolerate metformin (or it is contraindicated) **or** • a rapid response to therapy is required because of hyperglycaemic symptoms. Consider adding a sulfonylurea at the first intensification when blood glucose control remains or becomes inadequate with metformin. Continue with a sulfonylurea if blood glucose control remains or becomes inadequate and another oral glucose-lowering medication is added.
Advantages	Long-term safety data - no significant concerns identified
Renal impairment	Used with care in those with mild to moderate renal impairment due to hazard of hypoglycaemia. Avoid win severe renal impairment.
Hepatic impairment	Manufacturers advise to avoid in severe impairment (increased risk of hypoglycaemia)
Adverse effects	**Risk of hypoglycaemia, High risk in older people**; **Weight gain** (a few kilograms)
Warning	Drivers need to be particularly careful to avoid hypoglycaemia and should be warned of the problems. See Fitness to drive document and http://www.diabetes.org.uk/ website for the latest recommendations. Group 1 drivers (car/motorcycle) - it may be appropriate to monitor blood glucose at times relevant to driving to enable the detection of hypoglycaemia. Group 2 drivers (bus/lorry) are required to monitor glucose level at least twice daily and at times relevant to driving.

Daily GLP-1 (Glucagon-like peptide-1) Agonists Increase insulin secretion, suppress glucagon secretion, slow gastric emptying and reducing appetite and food intake See appendices 1-5 for further information regarding GLP-1 agonist Prescribe by brand			
	Liraglutide (Zegluxen)	**Oral semaglutide (Rybelsus)**	
Traffic light status	**Liraglutide - GREEN 1st line GLP1**	**GREEN if needle phobic**	

NICE guidance	**NICE NG28 - 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 BMI of ≥35kg/m^2 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 <35kg/m^2 and
	  ○ For whom insulin therapy would have significant occupational implications or
	  ○ Weight loss would benefit other significant obesity-related co-morbidities.
	
	Therapy must be reviewed at 6 and 12 months. **Criteria for continuing therapy:**
	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 HbA1c and weight loss of at least 3% of initial body weight in 6 months)		

	NICE NG28 recommends GLP-1 in combination with insulin with specialist care advice and on-going support from a consultant-led multidisciplinary team. Suliqua (insulin glargine + lixisenatide) has been classified **GREY** specialist initiation and stabilisation of dosage, restricted for those patients struggling to manage multiple injections. Ongoing specialist support should be maintained for patients on this treatment. Prescriber must ensure the correct strength and number of dose steps are stated on the prescription.		
Regimen	Initially 0.6mg od for at least 7 days, then increased to 1.2mg od for at least 7 days, administered by subcut injection.	Initially 3 mg once daily for 1 month, then increased to 7 mg once daily for at least 1 month, then increased if necessary to 14 mg once daily, one 14 mg tablet should be used to achieve a 14 mg dose; use of two 7 mg tablets to achieve a 14 mg dose has not been studied and is therefore not recommended.	
Advantages	Weight loss - which can be modest in most patients, but significant in some, low hypoglycaemia, liraglutide, dulaglutide and semaglutide have significant CV benefits.		
Contraindications	Type 1 diabetes, pregnancy and lactation	Uncontrolled diabetic retinopathy Pregnancy and lactation	
	Diabetic ketoacidosis has been reported in patients with type 2 diabetes on a combination of a GLP-1 receptor agonist and insulin who had doses of concomitant insulin rapidly reduced or discontinued. GLP-1 receptor agonists are not substitutes for insulin, and any reduction of insulin should be done in a stepwise manner with careful glucose self-monitoring. See MHRA June 2019		
Renal function	Not recommended for use in patients with a CrCl<15ml/min	No dose adjustment is required for patients with mild, moderate or severe renal impairment. Not recommended for use in patients with end-stage renal disease	
Hepatic function	No dose adjustment is necessary for patients with hepatic impairment		
Adverse effects	Nausea and diarrhoea, vomiting, constipation, abdominal pain, and dyspepsia	Hypoglycaemia, GI upset, anorexia, dizziness, diabetic retinopathy complications	.

Monitoring	Criteria for continuing therapy:
	• a weight reduction of ≥3% (of initial body weight) in those with a BMI≥ 35kg/m^2 and
	  • a reduction of ≥11mmol/mol (1%) by 6 months, with stable renal function.
	  • Monitor for hypoglycaemias and consider a reduction in dose of sulfonylurea or insulin if used in combination.		

Warnings	**MHRA March 2009**-There have been reports of **necrotising and haemorrhagic pancreatitis** with GLP-1 agonists, some of which were fatal. If pancreatitis is suspected, treatment with the GLP-1 agonist should be suspended immediately; if pancreatitis is diagnosed, the GLP-1 agonist should be permanently discontinued. Routine monitoring of blood glucose levels is only required if the GLP-1 agonist is given in combination with another agent likely to cause hypoglycaemia e.g., sulfonylurea. This has implications for drivers holding Group 2 (LCV or PCV) licences and will require individual DVLA assessment.		

Weekly GLP-1 (Glucagon-like peptide-1) AGONISTS Increase insulin secretion, suppress glucagon secretion, slow gastric emptying and reducing appetite and food intake See appendices 1-5 for further information regarding GLP-1 agonist Prescribe by brand			
	Dulaglutide prolonged release (Trulicity)	**Semaglutide (Ozempic)**	**Exenatide prolonged release (Bydureon)**
NICE guidance	Not included in NG28	Not included in NG28 (ESNM59: June 2015)	As per NICE NG28 Exenatide MR can be considered if tolerability and compliance remain a major issue with conventional GLP-1 agonist
Traffic light status	**GREEN** (When weekly preparation is indicated)	**GREEN** (Subcut)- when weekly preparation is indicated	**GREY** - when weekly preparation is indicated
Product	Pre-filled pen available as: • 750mcg/0.5ml pre-filled pen • 1.5mg/0.5ml pre-filled pen • 3mg & 4.5 mg pre-filled pen	Pre-filled pen available as: • 250 micrograms pre-filled pen • 500 micrograms pre-filled pen • 1mg pre-filled pen	Dual chamber pre-filled pen which requires mixing before injection: • 2mg pre-filled pen
Regimen	**Monotherapy:** the750microgram by subcut injection once weekly. **Add on therapy:** 1.5mg by subcut injection once weekly. 750 micrograms once weekly may be considered in vulnerable patients. Increase, if necessary, after ≥4 weeks to 3mg once weekly and after a further ≥4 weeks to max 4.5mg once weekly.	**Subcut dose:** 250microgram by subcut injection once weekly, increasing to 500microgram once weekly after 4 weeks. The dose can be increased to 1 mg once weekly, if necessary, after a further 4 weeks. **Oral dose**: Initially 3 mg once daily for 1 month, then increased to 7 mg once daily for at least 1 month, then increased if necessary to 14 mg once daily, dose to be taken on an empty stomach. (BNF)	2mg by subcut injection once weekly.
Advantages	Weight loss - which can be modest in most patients, but significant in some, low hypoglycaemia, liraglutide, dulaglutide and semaglutide have significant CV benefits. Advantage of a weekly preparation • if compliance is an issue or the patient requires regular visits from a nursing team to administer the drug.		
Contraindications	Type 1 diabetes, pregnancy and breastfeeding, severe gastro-intestinal disease	Type 1 diabetes, pregnancy and breast feeding. Not recommended in patients with congestive heart failure NYHA class IV. Diabetic ketoacidosis. Women of childbearing potential are recommended to use contraception when treated with semaglutide.	Type 1 diabetes, pregnancy and breastfeeding, Bydureon should be discontinued at least 3 months before a planned pregnancy
Renal function	Not recommended for use in patients with end-stage renal disease (<15ml/min/ 1.73m^2)	No dose adjustment is required for patients with mild, moderate or severe renal impairment. Not recommended for use in patients with end-stage renal disease	Not recommended for use in patients with an eGFR 30 - 50ml/min
Hepatic function	No dosage adjustment is recommended for patients with hepatic impairment		
Adverse effects	Acute pancreatitis serious but rare Nausea, vomiting, diarrhoea.	Acute pancreatitis serious but rare Common AE include nausea, diarrhoea and vomiting.	Acute pancreatitis serious but rare

		Caution should be exercised when using semaglutide in patients with diabetic retinopathy treated with insulin as there is an increased risk of developing diabetic retinopathy complications.	Common AE include diarrhoea, nausea, and injection site rash.
Monitoring	Criteria for continuing therapy: • a weight reduction of ≥3% (of initial body weight) in those with a BMI≥ 35kg/m2 and • a reduction in HbA1c of ≥11mmol/mol (1%) by 6 months, with stable renal function. • Risk of diabetic retinopathy with semaglutide - monitor closely. 2mg dose is not recommended in patient with uncontrolled or unstable diabetic retinopathy • Monitor for hypos and consider reducing dose of other anti-diabetic's (e.g., insulin /sulfonylurea) if started in combination, see individual SPCs for further details.		
Warning	See warning in GLP1 section above		

Weekly GIP (Glucose-dependent insulinotropic polypeptide) and GLP-1 (Glucagon-like peptide-1) AGONIST
Increase insulin sensitivity and secretion, suppress glucagon secretion, slow gastric emptying and reducing appetite and food intake
See appendices 1-6 for further information regarding GIP GLP-1 agonist
Prescribe by brand

	Tirzepatide (Mounjaro)
NICE guidance	NICE TA924 (Oct 23) Not included in NG28
Traffic light status	**GREY -** Alternative to GLP-1 mimetics at the level of triple therapy for patients with type 2 diabetes in line with its licensed indication if GLP-1 is not well tolerated by patient, not efficacious or not available due to stock issues.
Product	Pre-filled pen available as: • 2.5mg in 0.6ml multiple dose Kwikpen • 5mg in 0.6ml multiple dose Kwikpen • 7.5mg in 0.6ml multiple dose Kwikpen • 10mg in 0.6ml multiple dose pen • 12.5mg in 0.6ml multiple dose Kwikpen • 15mg in 0.6ml multiple dose Kwikpen
Regimen	2.5mg by subcutaneous injection once weekly, increasing to 5mg once weekly after 4 weeks. If improvement in HbA1c is not reached after 6 months at this dose, refer to specialist for advice before escalating dose.
Advantages	Weight loss - which can be modest in most patients, but significant in some, low hypoglycaemia, liraglutide, dulaglutide and semaglutide have significant CV benefits. Advantage of a weekly preparation • if compliance is an issue or the patient requires regular visits from a nursing team to administer the drug.
Contraindications	Pregnancy and breastfeeding, type 1 diabetes, females of child-bearing potential without contraception Preparation contains Benzyl Alcohol. • Tirzepatide has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy or diabetic macular oedema, and should be used with caution in these patients with appropriate monitoring
Renal function	No dose adjustment is required for patients with renal impairment including end stage renal disease (ESRD).

	Experience with the use of tirzepatide in patients with severe renal impairment and ESRD is limited. Caution should be exercised when treating these patients with tirzepatide. Patients with renal impairment should be informed of the potential risk of metabolic acidosis due to accumulation of benzyl alcohol over time.
Hepatic function	No dosage adjustment is recommended for patients with hepatic impairment. Patients with hepatic impairment should be informed of the potential risk of metabolic acidosis due to accumulation of benzyl alcohol over time.
Adverse effects	Acute pancreatitis serious but rare Common AE include nausea, vomiting, diarrhoea, & constipation
Monitoring	Criteria for continuing therapy: • a weight reduction of ≥3% (of initial body weight) in those with a BMI≥ 35kg/m2 and • a reduction in HbA1c of ≥11mmol/mol (1%) by 6 months, with stable renal function. • Monitor for hypos and consider reducing dose of other anti-diabetic's (e.g., insulin /sulfonylurea) if started in combination, see SPC for further details.
Warning	See warning in daily GLP1 section above

THIAZOLIDINEDIONE- PIOGLITAZONE Reduces peripheral insulin resistance, leading to a reduction of blood glucose concentration	
Traffic light status	**GREEN**
Regimen	Initially 15-30mg once daily, adjusted according to response to 45mg once daily. In elderly patients, initiate with lowest possible dose and increase gradually; review treatment after 3-6 months and regularly thereafter.
Place in therapy	NICE NG28 Recommends use of pioglitazone in patients as an option: • initial drug treatment (if metformin is contraindicated or not tolerated) • as an addition to monotherapy (dual therapy) if HbA1c not controlled to below individually agreed threshold or • as an addition to dual therapy (triple therapy) if HbA1c not controlled to below individually agreed threshold **Continue pioglitazone therapy only if there is a reduction of ≥ 5.5mmol/mol (0.5% points) in HbA1c in 6 months**
C/I	Do NOT start or continue pioglitazone in people who: • have heart failure (NYHA class I-IV) or a history of heart failure • diabetic ketoacidosis • are at a higher risk of fracture • macula oedema • hepatic impairment • current bladder cancer or a history of **bladder cancer.** See MHRA safety update • patients with un-investigated macroscopic or microscopic haematuria
Renal impairment	No dosage adjustment is necessary in patients with impaired renal function (CrCl >4ml/min)
Adverse effects	Risk of hypoglycaemia – rare Weight change - gain
Monitoring	Baseline - weight and LFTs
Warning	**Long-term safety data -** concerns about bladder cancer, heart failure and fractures (use with caution in elderly where these issues are all more common) (See pioglitazone prescribing statement)

	Lack of outcome data Discuss the potential benefits and risks of treatment with pioglitazone with the person to enable them to make an informed decision. Warn a person prescribed pioglitazone about the possibility of significant oedema and advise on what action to take if it develops. Pioglitazone should be used in patients at significant risk of hypoglycaemia or who are intolerant or contra-indicated to metformin or a sulfonylurea when used in combination**.** Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for the development of cardiac failure. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain, and oedema. See MHRA risk of cardiac failure when combined with insulin.

PP-4 INHIBITORS (GLIPTINS)
Inhibit dipeptidylpeptidase-4 to increase insulin secretion and lower glucagon secretion

	Sitagliptin	Alogliptin	Linagliptin	Saxagliptin	Vildagliptin
Traffic light status	**GREEN** *preferred 1st line DPP-4i*	**GREY**	**GREY**	**GREY**	**GREY**
		By exceptionality defined as intolerance to the preferred first line choices or restricted by their licensing.			
Regimen	100mg od	25mg od	5mg od	5mg od	50mg bd
Place in therapy	NICE NG28 recommends DPP4i as monotherapy, dual therapy (DPP4i + met or SU or Pio) and triple therapy (DPP4i +Met + SU). **HOWEVER, JAPC ADVICE:** There is a lack of outcome data for these drugs; circumstances for use of DPP4i should follow as per diabetes management flowchart on page 8 and 9. Potential exceptions include: • When the aim of treatment is to control symptoms of hyperglycaemia in the short term and in whom prevention of long-term diabetes complications is not an issue (e.g., a symptomatic elderly patient, for whom hypoglycaemia is a problem and where insulin is impracticable) • Treatment with a thiazolidinedione is not ideal due to risk of further weight gain; thiazolidinedione contraindicated or not tolerated. **DPP4i should only be continued if there is a reduction of ≥5.5mmol/mol (0.5% points) in HbA1c in 6 months.**				
Advantages	Low risk of hypoglycaemia, (however hypoglycaemia may occur when used in combination with sulphonylurea therapy), generally DPP4i are weight neutral and similar HbA1c reduction to pioglitazone.				
Contraindications	Ketoacidosis	Ketoacidosis, moderate to severe Congestive HF of NYHA, class III-IV, due to limited experience in this population	Ketoacidosis	Ketoacidosis see FDA warning below	Ketoacidosis Avoid in severe heart failure
Renal function	Reduce dose - 50 mg od if GFR 30-45 mL/min	Reduce dose - 12.5mg od if CrCl 30 - 50ml/min/1.73m^2	In renal impairment**, no dose adjustment** is required	Reduce dose – 2.5mg od in moderate to severe renal impairment (GFR<45ml/min)	Reduce dose – 50mg od if eGFR<50ml/min/1.73m^2

	Reduce dose 25mg od if GFR<30ml/min or with end-stage renal disease (GFR<15mL/min)	Reduce dose to 6.25mg od if CrCl<30ml/min/1.73m^2.			
Hepatic function	Not studied in severe hepatic impairment therefore care should be exercised	Avoid in severe hepatic impairment (Child-Pugh score>9)	**No dose adjustment** is required for patients with hepatic impairment	Use with caution in moderate impairment. Avoid in severe impairment	Avoid in hepatic impairment
Adverse effects	GI disturbances, pain, peripheral oedema and upper respiratory tract infection	Abdominal pain, gastro-oesophageal reflux and upper respiratory tract infection.	Nasopharyngitis and cough	Dizziness, dyspepsia, gastroenteritis, upper respiratory tract infection and UTI	Rare reports of liver dysfunction discontinue if jaundice or other signs of liver dysfunction occur.
Monitoring	Baseline renal function before commencing treatment and periodically thereafter is recommended.	Baseline renal before commencing treatment and periodically thereafter is recommended.	NA	Baseline renal before commencing treatment and periodically thereafter is recommended.	Monitor liver function before treatment and every 3months for the first year and periodically thereafter.
Warning	The FDA, August 2015 have issued a warning that DPP- 4 inhibitors may cause joint pain that can be severe and disabling. Health care professionals should consider discontinuation of therapy with this class of drugs if severe and persistent joint pain occurs. The MHRA, (Sept 2012) have issued a warning that DPP-4 inhibitors and risk of acute pancreatitis. Discontinue treatment if symptoms of acute pancreatitis occur (persistent, severe abdominal pain) The FDA, April 2016 has added warnings about heart failure risk to labels of medicines containing saxagliptin and alogliptin as a safety review they conducted found that they may increase the risk in patients with heart/kidney disease. Use saxagliptin with caution if moderate-to-severe heart failure (limited experience)				

Drug therapy and renal and hepatic impairment for type 2 diabetes mellitus

	Worsening renal function (eGFR in ml/min)					Hepatic impairment		
Drug	**CKD 1 & 2 eGFR >60**	**3a (45-59)**	**3b (30-44)**	**4 (15-29)**	**5 (< 15)**	**Mild**	**Moderate**	**Severe**
Metformin / Metformin MR	✓	✓	✓ (Review regularly)	x	x	x Contraindicated in hepatic insufficiency		
Gliclazide	✓	✓	✓	✓ (Use lowest effective dose)	x	✓	✓	x contraindicated
Pioglitazone	✓	✓	✓	✓	✓ (But not with dialysis)	x contraindicated	x contraindicated	x contraindicated
Dapagliflozin	✓		*Consider additional glucose-lowering treatment (reduced efficacy)*	*Limited experience if eGFR<25ml/min/ 1.73m²*	X Do not initiate	✓	✓	✓ starting dose 5mg, increase to 10mg if well tolerated
Canagliflozin	✓	✓ 100mg	✓ 100mg	Do not initiate Continue 100 mg* for patients already taking until dialysis or renal transplantation	Do not initiate Continue 100 mg* for patients already taking until dialysis or renal transplantation	✓	✓	x not recommended
Empagliflozin	✓	10mg Continue 10mg in pts already taking	10mg Continue 10mg in pts already taking	x	x	✓	✓	x not recommended
Ertugliflozin	✓	Start 5mg and increase to 15mg as needed	X	X Discontinue if eGFR persistently <30ml/min/1.73m²	X	✓	✓	x not recommended
Liraglutide	✓	✓	✓	✓	x No experience	✓	✓	x not recommended

Worsening renal function (eGFR in ml/min)						Hepatic impairment		
Drug	**CKD 1 & 2 eGFR >60**	**3a (59-45)**	**3b (44-30)**	**4 (29-15**	**5 (< 15)**	**Mild**	**Moderate**	**Severe**
Exenatide MR	✓	**x (not recommended if GFR between 30-50ml/min)**	**x**	**x**	**x**	✓	✓	✓
Dulaglutide	✓	✓	✓	✓	**x**	✓	✓	✓
Semaglutide	✓	✓	✓	✓	**x**	✓	✓	✓
Tirzepatide	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Limited experience Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*	Use with caution (potential risk of metabolic acidosis due to accumulation of benzyl alcohol excipient over time)*
Albiglutide	✓	✓	✓	**x**	**x**	✓	✓	✓
Insulin	✓	✓	✓	**dose adjustment required**	**dose adjustment required**	✓ **requirements may be altered in hepatic impairment - monitor and adjust dose accordingly.**		
Sitagliptin	✓	✓	**50mg**	**25mg**	**25mg**	✓	✓	**x no studies in severe hepatic impairment**
Linagliptin	✓	✓	✓	✓	✓	✓	✓	✓
Saxagliptin	✓	**5mg**	**2.5mg**	**2.5mg (Use with caution)**	**x (not recommended)**	✓	**use with caution**	**x not recommended**

Worsening renal function (eGFR in ml/min)						Hepatic impairment		
Drug	CKD 1 & 2 eGFR >60	3a (59-45)	3b (44-30)	4 (29-15	5 (< 15)	Mild	Moderate	Severe
Vildagliptin	✓	50mg (GFR<50ml/min)	50mg (GFR<50ml/min)	50mg (GFR<50ml/min)	50mg (Limited experience)	x not recommended	x not recommended	x not recommended
Alogliptin	✓	12.5mg (GFR<50ml/min)	12.5mg	6.25mg (Limited experience)	6.25mg (Limited experience)	✓	✓	x not recommended
Repaglinide	✓	✓	✓	✓ use with caution	✓ use with caution	no studies in hepatic insufficiency	no studies in hepatic insufficiency	x contraindicated

N.B. In patients at extremes of weight (BMI<18.5kg/m2 or >30kg/m^2) or age (>70 yrs), calculate renal function using Cockcroft and Gault equation

- **Reference https://bnf.nice.org.uk/drugs/tirzepatide**

Insulin Therapy in Type 2 Diabetes
Insulin treatment initiation

Insulin indicated
- Structured education programme
- Optimised oral medicines
- Individual target

Once-daily basal insulin	Twice daily bi-phasic insulin	Basal bolus insulin
Intermediate or long-acting, usually at bedtime, in addition to oral hypoglycaemic drugs Commonly initiated after oral medication fails to control blood glucose concentrations or symptoms **Advantages:** • Relatively easy to initiate and titrate. • Involves only one injection a day. • Achieves reasonable glycaemic control with low risk of hypoglycaemia. **Disadvantages:** • May not be enough to maintain control, or good control may be achieved only at the expense of hypoglycaemia. **Choice of insulin** Isophane (NPH) insulin (**Insulatard, Humulin I**)	Premixed biphasic human insulin or analogues are commonly used in twice daily regimens given before or at the time of eating. **Advantages:** • Better glycaemic control than once daily basal insulin. **Disadvantages:** • Need to eat lunch and a bedtime snack to balance the insulin peaks produced. • Greater likelihood of weight gain and hypoglycaemia. • Not suitable for every patient (e.g., people who do shift work) **Choice of insulin** Biphasic isophane insulin (Soluble insulin 30%+isophane insulin 70%; **Humulin M3**)	Involves both basal and prandial insulins Recommended regimen for intensification of treatment if glycaemic or symptoms control is not achieved or maintained on basal insulin alone **Advantages:** • Greater flexibility of patient over when and what to eat. **Disadvantages:** • Multiple injections • Measurement of blood glucose concentrations to titrate insulin dose. • Poor adherence • Bedtime snack to prevent hypoglycaemia. **Choice of Insulin** **Bolus** Soluble insulin (e.g.**, Humulin S,**) **Basal** Isophane (NPH) insulin (**Insulatard, Humulin I**)

- If other measures do not keep HbA1c to individualised target (NICE CG87), discuss benefits and risk of insulin treatment.
- When starting an insulin for which a biosimilar is available, use the product with the lowest acquisition cost.
- When people are already using an insulin for which a lower cost biosimilar is available, discuss the possibility of switching to the biosimilar. Make a shared decision with the person after discussing their preferences.
- Use insulin ALONGSIDE metformin (if there are no contraindications or intolerance). Also review the continued need for other oral hypoglycaemic drugs.
- When starting insulin therapy, use a structured programme employing active insulin titration that encompasses:
    - Injection technique, including rotating injection sites and avoiding repeated injections at same point within sites,
    - Continuing telephone support
    - Self-monitoring
    - Dose titration to target levels
    - Dietary understanding
    - DVLA guidance
    - Management of hypoglycaemia
    - Management of acute changes in plasma glucose control,
    - Support from an appropriately trained and experienced healthcare professional.
- Insulin therapy should be initiated from a choice of a number of insulin types and regimens by a practitioner with the appropriate knowledge, competencies and experience to choose the most appropriate starting regimen tailored to each patient.

- Begin with human NPH insulin (Isophane insulin e.g., Insulatard®, Humulin I®,) taken at bedtime or twice daily according to need. *Human NPH (isophane) insulin is used routinely in preference to a long-acting human insulin analogue, at bedtime or twice a day.*
  It is the preferred first choice insulin recommended by NICE based on cost effectiveness and its safety profile. There is limited evidence of a clinical benefit of insulin analogues over human NPH insulin for type 2 diabetes and they are considerably more expensive.

- However, a long-acting human insulin analogue (as an alternative to NPH insulin) may be considered in patients (after education and lifestyle advice) if:
  - The person requires assistance from a carer or health care professional to administer insulin and in whom use of a long-acting insulin analogue would reduce the frequency from twice to once a day; or
  - The persons' lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes; or
  - The person would otherwise need twice daily isophane insulin (intermediate-acting) in combination with hypoglycaemic drugs; or
  - who are unable to use the device to inject isophane insulin.

- Consider twice-daily, as a pre-mixed – biphasic human insulin regimens in particular where HbA1c >75 mmol/mol (9.0%). A once-daily regimen may be an option when initiating this therapy.

- Insulin analogues rather than pre-mixed human insulin preparations should only be considered when:
  - immediate injection before a meal is needed, or
  - hypoglycaemia is a problem, or
  - there are marked postprandial blood glucose rises.

- Recurrent symptomatic hypoglycaemia should prompt a re-examination of the current insulin regimen, injection sites, a search for other comorbidities (such as liver or renal disease) and a review of the agreed HbA1c target. If tight control is still required, then consider a trial of analogue insulin.
- Monitor a person using a basal insulin regimen (NPH or a long-acting insulin analogue [insulin glargine/detemir]) for the need for mealtime insulin (or a pre-mixed insulin preparation). If blood glucose control remains inadequate (not to agreed target levels without problematic hypoglycaemia), move to a more intensive, twice/three times daily mixed insulin or mealtime plus basal insulin regimen.
- Human insulin's (such as Humulin S®, Isophane insulin, biphasic isophane insulin) should be considered as first line therapy before moving to analogue or analogue mixtures. Insulin analogues should only be considered if one of the criteria described above is met.
- Monitor a person using pre-mixed insulin once or twice daily for the need for a further pre-prandial injection or for an eventual change to a mealtime plus basal insulin regimen, based on human or analogue insulins, if blood glucose control remains inadequate.
- New insulin analogue biosimilars have been launched, with Abasaglar being the preferred 1st line glargine choice over Lantus. In new patients needing an insulin analogue or in existing patients on Lantus who are poorly controlled, Abasaglar is an appropriate alternative. Switching stable patients is not advised.

Keep it simple and safe whenever possible
Health professionals should continue to follow NICE guidance and agree individual HbA1c targets with the patient, taking account of the patient's own preferences and the balance of likely benefits and burden of treatment.

Insulin preparations may vary from the previously standardised strength of 100 iu/ml. If insulin extracted from a pen or cartridge is of higher strength and that is not considered in determining the volume required, it can lead to significant and potentially fatal overdose. **Patient safety alert, Nov 2016** warns against withdrawing insulin from pen devices due to risk of severe harm or death.

MHRA Sept 2020 Injection of insulin (all types) can lead to deposits of amyloid protein under the skin (cutaneous amyloidosis) at the injection site which interferes with insulin absorption thus it is important to rotate injection site. There is a risk of hypoglycaemia in patients that suddenly change injection site from an area with cutaneous amyloidosis to an unaffected area (for example, changing the injection site from the torso to the leg). Patients should therefore carefully monitor blood glucose after changing injection site and consider adjusting the dose of insulin or antidiabetic medication to avoid hypoglycaemia, as needed.

see Derbyshire formulary **chapter 6 endocrine**.

	Insulin (100units/ml)	Notes	Timing of injection	Onset of action	Peak	Duration of action
Mealtime insulins	**Short-acting human insulins**					
	Actrapid (soluble insulin)		Within 30 mins before meal	Within 30 mins	1.5-3.5 hrs	7-8 hrs
	Humulin S (soluble insulin)		Within 30 mins before meal	30min-1h	1-6 hrs	6-12 hrs
	Rapid-acting analogues *Preferred option for type 1 diabetes (NG17)*					
	Insulin aspart & biosimilar					
	Trurapi (insulin aspart biosimilar)	**GREEN** - *Preferred cost-effective brand.*	Immediately before meal	10-20 mins	1-3 hrs	3-5 hrs
	Novo Rapid (insulin aspart)	**GREY** - *New patient should consider Trurapi as the cost-effective brand.*	Immediately before meal	10-20 mins	1-3 hrs	3-5 hrs
	Fiasp (insulin aspart)	**GREEN** - *Specialist recommendation. An option for type 1 diabetes (NG17) in new adult patients.*	Within 0-15 mins of meal	4 mins	1-3 hrs	3-5 hrs
	Insulin lispro & biosimilar					
	Admelog (insulin lispro biosimilar)	**GREEN** - *Preferred cost-effective brand*	Within 0-15 mins of meal	15 mins	1.5hr	2-5 hrs
	Humalog* (insulin lispro)	**GREY**- *New patient should consider Admelog as the cost-effective brand.*	Within 0-15 mins of meal	15 mins	1.5hr	2-5 hrs
	Lyumjev* (insulin lispro)	**GREEN** - *Slightly different releasing profile – used in adults in whom a more rapid acting mealtime insulin is desirable.*	Upto 2min before or 20min after starting meal	20min	1-3 hrs	5 hrs
	Insulin glulisine					
	Apidra (insulin glulisine)	**GREEN**	Within 0-15 mins of meal	10-20 mins	55min	1.5-4 hrs
Basal insulins	**Intermediate-acting human insulin (NPH)** *first line for most patients with type 2 diabetes*					
	Insulatard (isophane (NPH) insulin)		At bedtime or 12 hourly	Within 1.5 hrs	4 -12 hrs	24 hrs
	Humulin I (isophane (NPH) insulin)		At bedtime or 12 hourly	30min-1hr	1-8 hrs	22 hrs
	Long-acting analogues					
	Levemir (insulin detemir)	**GREEN** - *preferred choice for adult type 1 diabetes (NG17)*	Once/twice daily	0.5-1 hr	3-14 hrs	Up to 24 hrs
	Insulin glargine & biosimilar					
	Semglee (insulin glargine biosimilar)	**GREEN** - *Preferred cost-effective brand*	Once daily	0.5-1 hr	No peak	Up to 24 hrs
	Lantus (insulin glargine)	**GREEN** 2nd line *for patients needing cartridge/ vial. New patient should consider Semglee as the cost-effective brand.*	Once daily	0.5-1 hr	No peak	Up to 24 hrs
	Abasaglar (insulin glargine biosimilar)	**GREY** - *New patient should consider Semglee as the cost-effective brand.*	Once daily	0.5-1 hr	No peak	Up to 24 hrs
	Insulin degludec					
	Tresiba* (insulin degludec)	**GREY** *consultant/specialist initiation- restricted to those with documented nocturnal hypoglycaemia or loss of hypoglycaemia awareness despite using long-acting insulin analogue, who would otherwise have been started on an insulin pump in type 1 diabetes; or for people who need help from a carer or healthcare professional to administer injections (NG17)*	Once daily	0.5 –1.5 hrs	No peak	>42 hrs
Biphasic insulins	**Pre-mixed human insulin** *(commonly used in twice daily regimens in type 2 diabetes)*					
	Biphasic isophane insulin **Humulin M3** (soluble insulin 30%+isophane insulin 70%;)		Within 30 mins before meal	Within 30 mins	2 and 8hrs	Up to 24hrs
	Pre-mixed analogues *(an option in type 2 diabetes if a person prefers to inject insulin immediately before a meal)*					
	Biphasic insulin aspart **Novomix 30** (insulin aspart 30%+ insulin aspart protamine 70%)		Within 0-10 mins of meal	Within 10-20 mins	1-4 hrs	up to 24hrs
	Biphasic insulin lispro **Humalog Mix 25** (insulin lispro 25%+insulin lispro protamine75%) **Humalog Mix 50**(insulin lispro 50%+insulin lispro protamine 50%)		Within 0-15 mins of meal	About 15 mins	About 2 hrs	up to 24hrs

Timings of action of insulin's are approximate as they vary between individuals, and with injection sites, blood supply, temperature and physical activity.

Long-acting insulin analogues are designed not to have a peak action as such but to release insulin consistently over their duration of activity.

High strength insulins

Insulin/strength	Traffic light status	Timing of injection	Onset of action	Peak	Duration of action
Rapid-acting analogues (meal time insulin)					
Humalog (Insulin lispro 200units/ml)	**Grey**. See MHRA April 2015, High strength, fixed combination and biosimilar insulin products to minimise the risk of medication error.	Within 0-15 mins of meal	15 mins	1.5hr	2-5 hrs
Lyumjev (insulin lispro 200units/ml)	**Grey**. See MHRA April 2015, High strength, fixed combination and biosimilar insulin products to minimise the risk of medication error.	Up to 2min before or 20min after starting meal	20min	1-3 hrs	5 hrs
Long-acting analogues (basal insulin)					
Toujeo (Insulin glargine 300units/ml)	**GREY** after consultant/specialist recommendation: • for patients on insulin Degludec or • for patients being considered for insulin pump therapy or • for patients currently on high dose of insulin (>150units/day) who would otherwise have been started with Humulin R U-500 or degludec.	Once daily	0.5-1 hr	No peak	24-36 hrs
Tresiba (Insulin degludec 200units/ml)	**GREY** after consultant/specialist initiation for patients currently on high dose of insulin (>150units/day) after consideration of Toujeo.	Once daily	0.5 –1.5 hrs	No peak	>42 hrs

Insupen original (4mm/32/33g, 5mm/31g, 6mm/31/32g, 8mm/30/31/32g,); **GlucoRx Carepoint pen needles** (4mm/31g, 5mm/31g, 6mm/31g, 8mm/31g) and **GlucoRx Carepoint Ultra** (4mm/32g) are the formulary choice of insulin pen needles. If this is unsuitable consider other brands costing less than £5 per 100 needles. All other insulin pen needles with acquisition cost > £5 per 100 are classified as **Do Not Prescribe (DNP)**.

Safety needles should NOT be used by patients who self-administer insulin. If safety needles are indicated GlucoRx Safety Pen Needle (5mm/30g, 8mm/30g) is the preferred brand. If this is unsuitable consider other safety needles with an acquisition cost <£20 per 100. All other insulin safety needles with acquisition cost > £20 per 100 are classified as **Do Not Prescribe (DNP).**

Appendix 1

Reporting units for HbA1c

Glycated haemoglobin (HbA1c) is the recommended method of measuring long term control of blood glucose in people with both type 1 and type 2 diabetes. Previously the results were reported as a percentage (%). This has changed to millimoles/mole (mmol/mol) where people with diabetes will receive their HbA1c measurement in mmol/mol only.

HbA1c (New units)	HbA1c (Old units)
mmol/mol	%
20	4.0
31	5.0
42	6.0
48	6.5
53	7.0
59	7.5
64	8.0
75	9.0
86	10.0

A 0.5% difference in HbA1c is equivalent to a difference of about 5.5mmol/mol, and a 1% difference is equivalent to a difference of about 11mmol/mol. Note these are rounded equivalents.

Appendix 2 - STAR (Stop Think Assess Review)

Titrating insulin doses

This strategy provides a guide for increasing insulin and should be supported by the expertise of suitably experienced clinicians. To prevent excessive doses clinicians, need to be competent in understanding the variations in insulin delivery by the products and interpreting glycaemic control in relation of food and timing. Each patient should have a care management plan

Diabetes specialists have produced this systematic approach to the initiation of insulin in type II diabetes and subsequent management based upon currently available evidence. It is intended as a guide to management, and as such will be appropriate to most groups of people starting insulin in primary care.

It is intended to:

1. Provide a standardised systematic approach.
2. To use a personalised care planning approach to support goals and actions, using a discovery diary to support people starting on insulin.
3. Introducing appropriate educational program addressing knowledge and lifestyle issues prior to the commencement of insulin.
4. Achieve glycaemic control using the least possible amount of insulin to prevent the consequences of hyper-insulinaemia such as weight gain, hypoglycaemia, adverse lipids, and raised blood pressure.
5. Provide a cost-effective program for insulin management with appropriate choice of insulin matched to clinical need.
6. Enhanced self-management, self-awareness of lifestyle, and patient self-adjustment of doses of insulin.
7. Make effective use of blood glucose monitoring.

At each stage explain insulin initiation will occur in a series of stages, each increase in insulin will happen over 2 to 3 weeks followed by a period of stabilisation.

The person will need to monitor their blood glucose during each increase in insulin and discuss their results with their health care professional at the next appointment

Monitor blood glucose before breakfast and before bedtime, plus pre meals to see if OHA are working.

Phone call support from the initiating clinician is recommended during this period.

Stage 1 **0-20 units**

Initiate Human NPH (isophane) insulin 10 units at night-time (or teatime if more convenient). Increase insulin by 2 to 4 units every three days up to 20 units.

At 20 units complete two-day discovery diary (record of insulin, blood glucose 4 times each day, weight, and any episode of hypoglycaemia)

Starting Insulin of choice will be dependent on individual patient see regimen of choice in guidelines

Stage 2 **20- 40 units (2 weeks after commencing insulin)**

Stop Think assess review

Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.

- Review personalised care plan what has happened to the person during this time. What questions do they have?
- Review the person's own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals

Consider:

- if the person is putting on weight
- have they had any hypoglycaemia?
- review blood glucose, has insulin made any difference?

If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.

Consider hypoglycaemia risk.

Seek advice from the local DSN if required.

If some response of blood glucose to insulin, continue with Human NPH (isophane) insulin until target reached or 40 units whichever is lower, increasing in 4 units every 3 or 4 days.
If sugars dropping overnight but steady all day, consider split dose (Human NPH (isophane) insulin)
If no response, consider change to mixed human insulin, or a basal bolus regimen.
(See insulin charts)

Education is key at all stages to support in self-management.

Increase insulin further as part of agreed plan with the patient.
Increase insulin by 4 units every 3 days, up to 40 units or until fasting blood glucose target is reached without overnight drop, or any signs of hypoglycaemia.
At 40 units complete two-day discovery diary (record of insulin, blood glucose 4 times each day, weight, and hypoglycaemia)

Stage 3 40-60 units (6 to 8 weeks after commencing insulin)
Stop think assess review
Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.

- Review personalised care plan, what has happened to the person during this time? What questions do they have?
- Review the person's own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals.

Consider:

- If the person is putting on weight
- Have they had any hypoglycaemia?
- Review blood glucose, has insulin made any difference?

If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.
Consider hypoglycaemia risk, see checklist/screening tool
Seek advice from the local DSN if required.
If some response of blood glucose to insulin, continue with Human NPH (isophane) insulin until target reached 60 units whichever is lower, increasing in 4 units every 3 or 4 days.
If still only on long-acting insulin, change to mixed insulin or basal bolus. (BBR) (Consider reducing dose by approximately 10% while changing insulin).
Increase twice daily insulin by 2 units each morning or evening every 3 or 4 days depending on blood test results. **ONLY CHANGE ONE AT A TIME TO SEE KNOCK ON EFFECT**. (Unless having HYPOS)
Stop increasing insulin if blood glucose test before the next meal has reached target. Sometimes one test may be at target and another not if on a fixed mix of insulin, the mix of insulin or regimen will need to be reviewed.
At 60 units complete two-day discovery diary (record of insulin, blood glucose 4 times each day, weight and hypoglycaemia**).**

Stage 4 60-80 units
Stop think assess review. Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.

- Review personalised care plan, what has happened to the person during this time? What questions do they have?
- Review the person's own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals.

Consider:

- If the person is putting on weight
- Have they had any hypoglycaemia?
- Review blood glucose, has insulin made any difference?

If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.

Consider hypoglycaemia risk, see checklist/screening tool.
Seek advice from the local DSN if required.
If some response of blood glucose to insulin, continue with MIX/ BBR until target reached or 80 units whichever is lower, increasing in 4 units every 3 or 4 days.

Stage 5
Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.

- Review personalised care plan, what has happened to the person during this time? What questions do they have?
- Review the person's own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals.

Consider:

- If the person is putting on weight
- Have they had any hypoglycaemia?
- Review blood glucose, has insulin made any difference?

If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.
Consider hypoglycaemia risk**,** **http://www.trend-uk.org/resources.php**
Seek advice from the local DSN if required.

Stop think and review
Consider reducing insulin, the useful effective dose may already have been passed.
Consider adding other agents e.g., pioglitazone to reduce insulin resistance.
Consider seeking further advice, or referral to insulin support group.

Hypoglycaemia
Hypoglycaemia is more frequent in patients taking insulin with impaired renal function compared to those with normal renal function.
Patients should be questioned closely about hypoglycaemia (frequency, severity and awareness) and consideration given to reduce the doses of insulin and if necessary, change the insulin regimen order to reduce the risks of hypoglycaemia.
Patients experiencing severe episodes of hypoglycaemia, defined as requiring help from a third party should be referred to the specialist diabetes team.

Oral agent combination therapy with insulin
When starting basal insulin therapy, continue with metformin and gliclazide (and acarbose, if used)
However, review sulfonylureas:

I. If hypoglycaemia occurs
II. When mealtime quick acting insulin injections or mixed insulins are started, sulfonylureas should be discontinued, or tapered and then discontinued, since they are not considered synergistic with these insulin types

When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):

I. Continue with metformin
II. Consider combining pioglitazone with insulin therapy if patient:
    a) has previously had a marked glucose-lowering response to thiazolidinedione therapy
    b) on high-dose insulin therapy and blood glucose is inadequately controlled. This may need specialist guidance.

Warn the person to discontinue pioglitazone if clinically significant fluid retention develops.

Insulin delivery devices

- Offer education to patients or carers about using an injection device that they and/or their carer find easy to use
- Appropriate local arrangements should be in place for the disposal of sharps.
- Only Insulatard® and insulin detemir (Levemir®) can be used with the InnoLet® device.
- InnoLet device is useful for patients with dexterity and visual impairment problems.
- Consider any manual or visual disability a patient may have that affects their ability to use a device. Offer a device or adaptation that:

- Takes into account the patients individual needs
- The patient can use successfully.

Advice for the safe administration of insulin (NPSA/ 2010/ RRR013)

- All regular and single insulin (bolus) doses are measured and administered using an insulin syringe or commercial insulin pen device. Intravenous syringes must never be used for insulin administration.
- The term 'units' is used in all contexts. Abbreviations, such as 'U' or 'IU', are never used.
- All clinical areas and community staff treating patients with insulin have adequate supplies of insulin syringes and subcutaneous needles, which staff can obtain at all times.
- A training programme should be put in place for all healthcare staff (including medical staff) expected to prescribe, prepare and administer insulin. An e-learning programme is available from: **www.diabetes.nhs.uk/safe_use_of_insulin**

Adult patients' passport to safer insulin use (NPSA/2011/PSA003) 30 March 2011

- Adult patients on insulin therapy receive a patient information booklet and an Insulin Passport to help provide accurate identification of their current insulin products and provide essential information across healthcare sectors.
- Healthcare professionals and patients are informed how the Insulin Passport and associated patient information can be used to improve safety.
- When prescriptions of insulin are prescribed, dispensed or administered, healthcare professionals cross-reference available information to confirm the correct identity of insulin products.
- Systems are in place to enable hospital inpatients to self-administer insulin where feasible and safe.

More detailed information to support the implementation of this guidance is available at**:**
www.nrls.npsa.nhs.uk/alerts
Email: medicationteam@npsa.nhs.uk

Supplies of the Insulin Passport and patient booklet will be obtained from Primary Care Support England (PCSE) through the following link **http://pcse.england.nhs.uk/** using your practice log in details.

If you have access to the electronic ordering system, you can place your orders via **www.nhsforms.co.uk**

Appendix 3 – Cost comparison chart (Doses given do not imply therapeutic equivalence)

Drug and usual maintenance dose	Daily dose regimen	Cost per 28 days	Cost per year	Current Derbyshire traffic light
Metformin 500mg tabs	2g per day	£3.36	£43.68	**GREEN**
Metformin 1g tabs	**2g per day**	**£80.58**	**£1,047.54**	**GREEN**
Metformin MR 500mg tabs	2g per day	£3.94	£51.22	**GREEN**
Metformin MR 1g tabs	2g per day	£2.95	£38.35	**GREEN**
Dapagliflozin 5mg or 10mg tabs	10mg daily (using 10mg tabs)	£36.59	£476	T2DM with CKD – **GREEN** T2DM without CKD - **GREEN**
Empagliflozin 10mg or 25mg tabs	10mg daily ↑25mg daily	£36.59 £36.59	£476 £476	T2DM with CKD – **GREEN** T2DM without CKD - **GREEN**
Canagliflozin 100mg or 300mg tabs	100mg daily ↑300mg daily	£36.59 £36.59	£476 £476	T2DM with CKD – **GREY** T2DM without CKD – **GREY**
Ertugliflozin 5mg or 15 mg tabs	5mg daily ↑15mg daily	£29.40 £29.40	£382 £382	T2DM without CKD - **GREY**
Sitagliptin 25mg or 50mg or 100mg tabs	100mg daily (using 100mg tabs)	£3.12	£40.56	**GREEN** 1st line DPP4i
Alogliptin 6.25mg or 12.5mg or 25mg tabs	25mg daily (using 25mg tabs)	£26.60	£346	**GREY**
Vildagliptin 50mg tabs	50mg BD	£28.23	£367	**GREY**
Saxagliptin 2.5mg or 5mg tabs	5mg daily (using 5mg tabs)	£31.60	£411	**GREY**
Linagliptin 5mg tabs	5mg daily	£33.26	£432	**GREY**
Pioglitazone 15mg, 30mg or 45mg tabs	15-30mg daily ↑45mg daily	£1.15 - £1.47↑ £2.02	£14.95 - £19↑ £26	**GREEN**
Gliclazide 40mg or 80mg tabs	80-320mg daily (using 80mg tabs)	£0.99 - £3.96	£12.87 - £51.48	**GREEN**
Gliclazide MR 30mg or 60mg tabs	30mg daily ↑120mg daily (using 30mg tabs)	£2.81 -£11.24	£36.53 -£146	**GREY**
Semaglutide (Ozempic) • 0.25mg/0.19ml injection pre-filled pen, • 0.5mg/0.37ml injection pre-filled pen, • 1mg/0.74ml injection pre-filled pen	250microg once weekly ↑1mg once weekly	£73.25	£952	**GREEN** weekly GLP1 (weekly preparation; positive cardiovascular outcomes in clinical trials
Dulaglutide (Trulicity) • 0.75mg/0.5ml injection pre-filled pen • 1.5mg/0.5ml injection pre-filled pen • 3mg/0.5ml injection pre-filled pen • 4.5mg/0.5ml injection pre-filled pen	750microg once weekly ↑Max. 4.5mg once weekly	£73.25	£952	**GREEN** weekly GLP1, (when weekly preparation is indicated)
Exenatide (Bydureon BCise) 2mg powder and solvent for prolonged-release suspension for injection	2mg once weekly	£73.36	£954	**GREY** (when weekly preparation is indicated)
Semaglutide oral (Rybelsus) 3mg,7mg or 14mg tabs	3mg daily increasing to max.14mg daily	£73.25	£952	**GREEN** by exceptionality defined as intolerance to the preferred 1st line choice or restricted by their licensing or needle phobic patients
Liraglutide (Zegluxen) 6mg/ml injection (3ml pre-filled pen)	600microg once daily ↑1.2mg once daily ↑ 1.8mg once daily	£25.51 ↑ £51.01 ↑£76.52	£332 ↑ £664 ↑ £996	**GREEN 1st line GLP1**
Tirzepatide (Mounjaro Kwikpen) • 2.5mg/0.6ml solution for injection 2.4ml pre-filled disposable devices • 5mg/0.6ml solution for injection 2.4ml pre-filled disposable devices • 7.5mg/0.6ml solution for injection 2.4ml pre-filled disposable devices	2.5mg once weekly ↑10mg or 15mg once weekly	£92 ↑ £107 ↑ £122	£1,196 ↑ £1,391 ↑ £1,586	**GREY** Alternative to GLP-1 agonist for patients with type 2 diabetes who require triple therapy if alternative GLP-1s are not tolerated by patient, not efficacious or not available due to stock issues. **D**ose over 5mg

• 10mg/0.6ml solution for injection 2.4ml pre-filled disposable devices • 12.5mg/0.6ml solution for injection 2.4ml pre-filled disposable devices • 15mg/0.6ml solution for injection 2.4ml pre-filled disposable devices				after Specialist recommendation only.

Prices as per Drug tariff & MIMS Online July 2024.

Appendix 4 - Patient agreement form – GLP-1 agonists for Type 2 diabetes

At your appointment today we have agreed to start treatment with one of the following medicines to help manage your type 2 diabetes:

- Dulaglutide (Trulicity)
- Exenatide MR (Bydureon)
- Semaglutide injection (Ozempic)
- Semaglutide tablets (Rybelsus)
- Liraglutide (Zegluxen)
- Tirzepatide (Mounjaro)

These medicines all work in a very similar way and are sometimes known as GLP-1 agonists. Further information on how to use the device or take the tablets and any side-effects you should be aware of is included in the patient information provided with your medicine supply.

These medicines are given as an injection or tablets, and they work in a different way to insulin. However, they should help reduce your blood glucose levels and may also help you lose weight, especially if you follow a healthy diet and take regular exercise.

Please ask your diabetes nurse if you would like further information on the use of these medicines to treat type 2 diabetes or help and support with losing weight.

These injections and tablets do not work for everyone and if left unchecked may not be the best use of NHS resources. We therefore need to regularly monitor whether they are being effective.

In order to do this, we follow the guidance from the National Institute of Health and Clinical Excellence (NICE). This states that treatment with these medicines should only be continued after 6 months if a patient sees a reduction in their HbA1c (measurement of long-term blood sugar control) of 11mmol/mol (in the old number system that is about 1% HbA1c) and a reduction in their weight of 3% or more.

If the GLP-1 agonist we have agreed to start today does not provide these beneficial outcomes after 6 months, we will need to consider alternative options to manage your condition and stop the GLP1 agonist. If treatment is continued after 6 months, we will continue to monitor your HbA1c and weight on a regular basis. If the beneficial effects are not maintained, then again, we will need to consider alternative options to manage your condition and then stop the GLP 1 agonist.

PATIENT AGREEMENT:

The information overleaf has been explained to me and I understand that treatment with GLP1 agonist will be stopped, and alternative options considered if the beneficial effects on my weight and HbA1c are not achieved after 6 months or continued long-term.

	Today	6 month's target
Weight (3% loss needed by 6 months)		
HbA1c (11mmol/mol (1%) reduction needed by 6 months)		
eGFR (To check your kidney function)		To be measured in 6 months

Patient Name: _____ Patient Signature: _____

Clinician Name: _____ Clinician Signature: _____

Date: ___/___/_____ Date of 6-month review: ___/___/_____

If you have any questions or problems with your treatment, please contact:

Name: _____

Contact number: _____

Please give a copy to the patient and keep a copy in the patient's record. If treatment is started by hospital clinicians, please also send a copy to the patient's GP

Appendix 5 – structured education programmes - further resources

Structured Diabetes Education Programme for patients across Derby & Derbyshire ICB.

This includes the following education options:

- Xpert Online,
- Xpert Face-to Face and
- Diabetes & You.

Contact details
Tel no: 01773 525029
Email: dchst.diabetest2education@nhs.net
Post: Diabetes Type 2 Education Team, Babington Hospital, Derby Road, Belper DE56 1WH.

Patients must be referred to this service via their GP/Diabetic Nurse/Health professional. Self-referrals from patients will not be accepted.

Resources and referral forms can be accessed from DCHS Diabetes website:
Diabetes Education Derbyshire (dchs.nhs.uk)

NHS
Derbyshire Community Health Services
NHS Foundation Trust

Diabetes Structured Education Referral Form (including X-PERT and Diabetes & You)

Diabetes Structured Education for people diagnosed with Type 2 Diabetes

Please return the fully completed form by email to DCHST.DiabetesT2Education@nhs.net

Tel: 01773 525029 for more information

Section 1 - Client Details					
Title		Full Name		NHS No.	
D.O.B		Gender	Female ☐ Male ☐	Postcode	
Home Address					
Email address			Home phone		
Mobile phone			Consent to leave voicemail Consent to receive SMS	Yes ☐ No ☐ Yes ☐ No ☐	
GP Name & Surgery Address (or practice stamp)					
Type 2 Diabetes Diagnosis Date			HbA1c at time of diagnosis		
Please provide details of any reasonable adjustments required for this person to access this programme e.g. disability & access, information & communication needs, or in terms of culture, religion, sexuality or gender:					

Section 2 – Health Data – Reading and Date Recorded					
HbA1c	/	Triglycerides	/	Height	/
Blood Pressure	/	HDL Cholesterol	/	Weight	/
Waist Size	/	Total Cholesterol	/	BMI	/

Section 3 – Consent and Referrers Details:			
I can confirm that I have discussed the service with this person and they have agreed consent to be contacted by DCHS Diabetes Structured Education service			Yes ☐
I can confirm that this person has consented to share this health data with the Diabetes Structured Education Service and the National Diabetes Audit for monitoring purposes			Yes ☐
Referrer Name		Position	
Place of Work		Preferred Contact Details	
		Referral Date	
This information will be treated as private and confidential and will be collected by DCHS for the delivery of lifestyle interventions. This information will be held by DCHS and processed in accordance with the Data Protection Act 2018. This information will only be shared with services that the patient has consented to share with.			

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Appendix 6 - Tirzepatide (Mounjaro) treatment algorithm

Before considering Tirzepatide (Mounjaro)

- Consider eligibility for referral to the NHS Type 2 Diabetes Pathway to Remission (low-calorie diet)
- Offer diabetes education Programme
- Offer Stop Smoking advice via Local Authority services if appropriate
- Offer Weight Management programme through Local Authority if appropriate
- Offer Mental Health support if appropriate
- Optimise Blood Pressure treatment based on target (hypertension guideline)
- Optimise Lipid treatment based on target (lipid guideline)
- Consider individualised HbA1c target based on patient specific factors, as per NICE Guidance https://www.nice.org.uk/guidance/ng28

GLP-1 mimetic indicated (NICE NG28/ NICE TA924)

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/m^2 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/m^2 **and:**
  - for whom insulin therapy would have significant occupational implications **or**
  - weight loss would benefit other significant obesity-related comorbidities.

New patients currently on oral triple therapy considering escalation

- Consider semaglutide tablets (Rybelsus) (6m trial) first
- Tirzepatide (Mounjaro) can be considered if Rybelsus not tolerated or not effective

During GLP1 shortage

For patients previously on GLP-1 as per NICE NG28 criteria and **achieving target** HbA1c/ weight but unable to obtain GLP1

- Consider semaglutide tablets (Rybelsus) (6m trial) first
- Tirzepatide (Mounjaro) can be considered if Rybelsus not tolerated or not effective
- Make clear from the start that this is to cover GLP1 shortages and patient expected to be switch back when stock returns

For patients previously on GLP-1 as per NICE NG28 criteria, **NOT achieving target** HbA1c/ weight

- Tirzepatide (Mounjaro) can be considered as an option (insulin is another option) if all the following fulfilled
  - i. lifestyle/ holistic interventions; diabetes structured education utilised
  - ii. other pharmacological treatments optimised (note is should only be used as triple therapy as per NICE NG28)

Initiate Tirzepatide (Mounjaro) with 2.5mg ONCE WEEKLY

Ensure existing GLP1 is discontinued

- After 4 weeks escalate to 5mg ONCE WEEKLY
- Review and adjust other therapies (e.g., stop DPP4-inhibitors, consider dose reduction of sulphonylurea or insulin due to hypoglycaemia burden)
- Prescribe ONE KwikPen per prescription. Each pen contains 4 doses (1-month supply).
- Prescribe formulary 4mm insulin pen needles/ 1L sharp bin.
  Beneficial metabolic response to the 5mg dose as per NICE NG28 - **reduction of HbA1c of at least 11 mmol/mol and weight loss of at least 3% in 6 months.**

Beneficial metabolic response and target HbA1c met continue at 5mg once weekly dose.

Beneficial metabolic response and HbA1c target NOT met **Higher doses than 5mg/week* must be discussed with specialist team**

No beneficial metabolic response – **STOP TIRZEPATIDE (MOUNJARO)** and review holistic treatment

Tirzepatide (Mounjaro®) – Key Information (see ABCD guidance)

Mode of Action	Dual Glucagon-like peptide-1 **and** Gastric Inhibitory Polypeptide receptor agonist (**GLP-1/ GIP RA**). Lower glucose levels by reducing appetite (cerebral effect and by delaying gastric emptying) and stimulate the release of insulin while also reducing glucagon levels.
NICE guidance	NICE TA924 Tirzepatide for treating type 2 diabetes https://www.nice.org.uk/guidance/ta924
Product	Pre-filled KwikPens (4-dose pen) 2.5mg, 5mg, 7.5mg, 10mg, 12.5mg, 15mg
Regimen	Initiate 2.5mg ONCE WEEKLY; After 4 weeks escalate to 5mg ONCE WEEKLY
Serious Side Effects	Cases of pancreatitis have been reported in people using tirzepatide. People with type 2 diabetes should be advised to seek medical advice immediately if they experience severe and persistent abdominal pain, nausea, or vomiting. Tirzepatide is a black triangle drug
Caution	Consider avoid in those with a personal or family history of medullary thyroid carcinoma and in those with multiple endocrine neoplasia syndrome type 2 (MEN 2). Preparation contains Benzyl Alcohol.
Hepatic function	No dose adjustment is required for patients with hepatic impairment. Experience with the use of tirzepatide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with tirzepatide
Renal function	No dose adjustment required for patients with renal impairment including end stage renal disease (ESRD). Experience with the use of tirzepatide in patients with severe renal impairment and ESRD is limited. Caution should be exercised when treating these patients with tirzepatide
Notable Drug Interactions	Tirzepatide delays gastric emptying and has the potential to impact the rate of absorption of oral medicines administered at the same time. No dose adjustments are expected to be required for most concomitantly administered oral medicinal products. However, it is recommended to monitor persons on: • Narrow Therapeutic Index Medicines: oral medicinal products with a narrow therapeutic index (e.g. digoxin), especially at initiation of tirzepatide and following dose increases. • Warfarin — may possibly enhance the anticoagulant effect of warfarin. Manufacturer advice is to monitor INR at initiation. • Rapid Onset Effect: The risk of delayed effect should also be considered for oral medicinal products for which a rapid onset of effect is of importance. • Other antidiabetic drugs — due to the increased risk of hypoglycaemia, dose of concomitant sulfonylurea and/or insulin may need to be reduced. For those on sulfonylureas or insulin, a recent HbA1c should be available along with glucose levels to support dose adjustment / sulfonylurea cessation and safe initiation or tirzepatide. • Oral Contraceptives: No dose adjustment of oral contraceptives is required in women with normal BMI. There is limited information about the effect of tirzepatide on oral contraceptives in women with obesity or who are overweight. Since reduced efficacy of oral contraceptives cannot be excluded, it is advised switching to a non-oral contraceptive method or add a barrier method of contraception upon initiating tirzepatide therapy (for 4 weeks), or after each dose escalation (for 4 weeks).
Retinopathy	Tirzepatide has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular oedema, and should be used with caution in these patients with appropriate monitoring. See ABCD guideline for further information.