### Choosing treatments
Base the choice of medicine 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)

### 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
- how to optimise their current treatment regimen before thinking about changing treatments, taking into account 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

### High risk of cardiovascular disease
Adults with type 2 diabetes who have:
- QRISK2 more than 10% in adults aged 40 and over or
- an elevated lifetime risk of cardiovascular disease (defined as the presence of 1 or more cardiovascular risk factors in someone under 40).

Cardiovascular disease risk factors: hypertension, dyslipidaemia, smoking, obesity, and family history (in a first-degree relative) of premature cardiovascular disease.
How to choose first-line medicines

Rescue therapy
For symptomatic hyperglycaemia, consider insulin or a sulfonylurea and review when blood glucose control has been achieved.

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

Not at high CVD risk
Offer
- Metformin
- Or if GI disturbance
  - Metformin MR

Chronic heart failure or established atherosclerotic CVD
Offer
- Metformin
  - or if GI disturbance
  - Metformin MR
  - and as soon as metformin tolerability is confirmed, offer
  - SGLT2 inhibitor ('flozin')
    - with proven cardiovascular benefit

High risk of CVD
QRISK2 of 10% or higher or elevated lifetime risk
Offer
- Metformin
  - or if GI disturbance
  - Metformin MR
  - and as soon as metformin tolerability is confirmed, offer
  - SGLT2 inhibitor ('flozin')
    - with proven cardiovascular benefit

Consider
- DPP-4 inhibitor ('gliptin')
- Pioglitazone
- Sulfonylurea

An SGLT2 inhibitor ('flozin') for some people:
- Canagliflozin TA 390
- Dapagliflozin TA 390
- Empagliflozin TA 390
- Ertugliflozin TA 572

NICE technology appraisals recommend SGLT2 inhibitors as monotherapy options in people:
- who cannot have metformin
- for whom diet and exercise alone do not provide adequate glycaemic control.

The SGLT2 inhibitors are recommended only if a dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate.

In February 2022, using ertugliflozin to reduce cardiovascular risk when blood glucose is well controlled was off label. See NICE's information on prescribing medicines.

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Rescue therapy
For symptomatic hyperglycaemia, consider insulin or a sulfonylurea and review when blood glucose control has been achieved.

Treatment options if further interventions are needed

At any point
HbA1c not controlled below individually agreed threshold
Switching or adding treatments
Consider:
- DPP-4 inhibitor
- SGLT2 inhibitors
- Pioglitazone
- Sulfonylurea

SGLT2 inhibitors may also be an option in dual therapy:
- Canagliflozin (TA 315)
- Empagliflozin (TA 336)
Or in triple therapy:
- Canagliflozin (TA 315)
- Empagliflozin (TA 336)
- Dapagliflozin (TA 288)
- Ertugliflozin

At any point
Cardiovascular risk or status change
If the person has or develops chronic heart failure or established atherosclerotic CVD
Switching or adding treatments
Offer
An SGLT2 inhibitor (if not already prescribed)

If the person has or develops a high risk of CVD (QRISK2 of 10% or higher, or elevated lifetime risk)
Switching or adding treatments
Consider
An SGLT2 inhibitor (if not already prescribed)

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 body mass index (BMI) of 35 kg/m² or higher (adjust accordingly for people from Black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity or
- have a BMI lower than 35 kg/m² and:
  - for whom insulin therapy would have significant occupational implications or
  - weight loss would benefit other significant obesity related comorbidities.
When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

This information is a summary of the recommendations, please consult the guideline for the full recommendations. All supplementary information is taken from the BNF or the SPCs.

In February 2022, using ertugliflozin to reduce cardiovascular risk when blood glucose is well controlled was off label. See NICE’s information on prescribing medicines.

See summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) for up-to-date information.
## Summary of medicines for further treatment

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Options and BNF link</th>
<th>Form</th>
<th>Contraindications or special warnings (see SPCs)</th>
<th>Effect on weight</th>
<th>Hypoglycaemia risk</th>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DPP-4 inhibitor</strong> (‘gliptins’)</td>
<td>Alogliptin Linagliptin Saxagliptin Sitagliptin Vildagliptin</td>
<td>Tablet</td>
<td>Ketoacidosis</td>
<td>None</td>
<td>Low</td>
<td>Dose reduction or caution (not for linagliptin)</td>
<td>Caution or avoid (not for linagliptin and sitagliptin)</td>
</tr>
<tr>
<td><strong>GLP-1</strong></td>
<td>Dulaglutide Exenatide Liraglutide Lixisenatide Semaglutide</td>
<td>Tablet or injection</td>
<td>Ketoacidosis Severe gastro-intestinal disease (not for liraglutide and semaglutide) Liraglutide: diabetic gastroparesis, inflammatory bowel disease</td>
<td>Loss</td>
<td>Low</td>
<td>Dose reduction or caution or avoid Check the BNF monographs for eGFR thresholds</td>
<td>Caution or avoid (not for dulaglutide, exenatide, and lixisenatide) Check the BNF monographs for severity</td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td>Insulin treatment summary See BNF monographs</td>
<td>Injection</td>
<td>See individual SPCs</td>
<td>Gain</td>
<td>High</td>
<td>Dose reduction</td>
<td>Dose reduction</td>
</tr>
<tr>
<td><strong>Pioglitazone</strong></td>
<td>Pioglitazone</td>
<td>Tablet</td>
<td>History of heart failure, previous or active bladder cancer, uninvestigated macroscopic haematuria</td>
<td>Gain</td>
<td>Low</td>
<td>No warnings</td>
<td>Avoid</td>
</tr>
<tr>
<td><strong>SGLT2 inhibitor</strong> (‘flozins’)</td>
<td>Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin</td>
<td>Tablet</td>
<td>Ketoacidosis</td>
<td>Loss</td>
<td>Low</td>
<td>Dose reduction or caution or avoid Check the BNF monographs for eGFR thresholds</td>
<td>Caution or avoid Check the BNF monographs for severity</td>
</tr>
<tr>
<td><strong>Sulfonylurea</strong></td>
<td>Gliclazide Glimepiride Glipizide Tolbutamide</td>
<td>Tablet</td>
<td>All sulfonylureas: ketoacidosis Gliclazide and tolbutamide: avoid where possible in acute porphyrias</td>
<td>Gain</td>
<td>Moderate High in older people</td>
<td>Dose reduction or caution or avoid Check the BNF monographs for eGFR thresholds</td>
<td>Caution or avoid Check the BNF monographs for severity</td>
</tr>
</tbody>
</table>

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