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The authors and NCL JFC accept no liability for use of this information from this beyond its intended use. While we have tried to compile accurate information in this guideline, and to keep it updated in a timely manner, we cannot guarantee that it is fully complete and correct at all times. If you identify information within this guideline that is inaccurate, please report this to the admin.ncl-mon@nhs.net. If a patient is harmed as a consequence of following this guideline, please complete a local incident report and inform admin.ncl-mon@nhs.net.

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Document control

<table>
<thead>
<tr>
<th>Date</th>
<th>Version</th>
<th>Amendments</th>
</tr>
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<tbody>
<tr>
<td>June 2016</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>August 2016</td>
<td>1.1</td>
<td>Typo corrected (canagliflozin 10mg → canagliflozin 100mg)</td>
</tr>
<tr>
<td>August 2019</td>
<td>1.2</td>
<td>Updated pioglitazone cautions and adverse effects. Correction to sitagliptin ‘disadvantages’. Addition of semaglutide (first choice GLP-1 receptor agonist). Restrictions applied to dulaglutide and liraglutide. Addition of ertugliflozin (NICE TA572 &amp; TA583).</td>
</tr>
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</table>

Document management

| Groups / Individuals who have overseen the development of this guidance: | Camden IPU, RFL Diabetologists, Haringey and Camden Medicines Management Team, JFC Support Pharmacists |
| Groups which were consulted and have given approval:                  | All NCL Diabetologists, Diabetes Consultant and Specialist Nurses, GPs, Commissioners               |
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| Disseminated to:                                                    | NCL Diabetologists, Diabetes Consultant and Specialist Nurses, GPs, practice nurses                  |
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Personalised HbA1c targets

Involve adults with type 2 diabetes in decisions about their individual HbA1c target, the patient decision aid on page 14 may facilitate these discussions.

Encourage them to achieve the target and maintain it unless any resulting adverse effects (including hypoglycaemia), or their efforts to achieve their target, impair their quality of life.

Offer dietary advice (see NICE NG28, section 1.3) and drug treatment to support adults with type 2 diabetes to achieve and maintain their HbA1c target.

In adults with type 2 diabetes, measure HbA1c 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

<table>
<thead>
<tr>
<th>Patients group</th>
<th>Target HbA1c presumption (this must be individualised)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients managed by lifestyle and diet</td>
<td>&lt; 48 mmol/mol (6.5%)</td>
</tr>
<tr>
<td><strong>If all the following apply:</strong></td>
<td></td>
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<tr>
<td>• Younger patients &lt; 60 years within 10 years of diagnosis</td>
<td>48 mmol/mol (6.5%)</td>
</tr>
<tr>
<td>• Without established macrovascular disease (IHD, CVA, PVD)</td>
<td></td>
</tr>
<tr>
<td>• Taking a single oral agent which is not associated with risk of hypoglycaemia (metformin, gliptin, SGLT2-i, pioglitazone)</td>
<td></td>
</tr>
<tr>
<td><strong>If all the following apply:</strong></td>
<td>53 mmol/mol (7.0%)</td>
</tr>
<tr>
<td>• Younger patients &lt; 60 years within 10 years of diagnosis</td>
<td></td>
</tr>
<tr>
<td>• Without established macrovascular disease (IHD, CVA, PVD)</td>
<td></td>
</tr>
<tr>
<td>• Without CKD on dialysis</td>
<td></td>
</tr>
<tr>
<td>• Low risk for serious consequences of hypoglycaemia</td>
<td></td>
</tr>
<tr>
<td>• Taking SU/repaglinide/insulin/GLP-1RA OR on more than one oral agent</td>
<td></td>
</tr>
<tr>
<td>• Without significant comorbidities</td>
<td></td>
</tr>
<tr>
<td><strong>If life-expectancy &gt; 10 years and any of the following apply:</strong></td>
<td>58 mmol/mol (7.5%)</td>
</tr>
<tr>
<td>• Age &gt; 60 years or duration diabetes &gt; 10 years</td>
<td></td>
</tr>
<tr>
<td>• Established macrovascular disease (IHD, CVA, PVD)</td>
<td></td>
</tr>
<tr>
<td>• CKD on dialysis</td>
<td></td>
</tr>
<tr>
<td>• Tight control poses a high risk of the consequences of hypoglycaemia (e.g. risk of falling, impaired awareness of hypoglycaemia, people who drive or operate machinery as part of their job)</td>
<td></td>
</tr>
<tr>
<td>• Experiences recurrent hypoglycaemia on SU/insulin</td>
<td></td>
</tr>
<tr>
<td>• Significant comorbidities</td>
<td></td>
</tr>
<tr>
<td>Patients who are frail and elderly (&gt;80 years), dementia and/or life-expectancy &lt; 10 years</td>
<td>69 mmol/mol (8.5%)</td>
</tr>
</tbody>
</table>
Advantages and disadvantages of treatment combinations in adults with type 2 diabetes eligible for METFORMIN

**FIRST INTENSIFICATION** if uncontrolled on monotherapy. Aim for HbA1c of 53mmol/mol (7.0%) or individually agreed target.
Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

- **Metformin + gliclazide**
  - Impact on HbA1c: High
  - Other advantages: ↓microvascular risk, no cardiovascular risk
  - Hypo risk: Moderate
  - Weight: +1.5 to +2Kg
  - Disadvantage: Acute pancreatitis
  - Cost (£): Low

- **Metformin + sitagliptin**
  - Impact on HbA1c: Moderate
  - Other advantages: Nil
  - Hypo risk: Low
  - Weight: Nil
  - Disadvantage: Acute pancreatitis
  - Cost (£): High

- **Metformin + SGLT2-i ‘flozin’**
  - Impact on HbA1c: Moderate
  - Other advantages: ↓BP, ↓CVD events
  - Hypo risk: Low
  - Weight: -3 to -4Kg
  - Disadvantage: GU infections, polyuria, volume depletion, ↑risk of AKI, DKA, bone fractures, ↓lower limb amputation
  - Cost (£): High

- **Metformin + pioglitazone**
  - Impact on HbA1c: High
  - Other advantages: ↓microvascular risk, near universal response, no cardiovascular risk
  - Hypo risk: Low
  - Weight: +4 to +5Kg
  - Disadvantages: Injection, need for titration
  - Cost (£): Variable

**SECOND INTENSIFICATION** if uncontrolled on dual therapy. Aim for HbA1c of 53mmol/mol (7.0%) or individually agreed target.
Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

- **Metformin + gliclazide**
  + sitagliptin or
  + SGLT2-i or
  + insulin or
  + pioglitazone or
  + GLP-1RA (in line with Fact Sheet)

- **Metformin + sitagliptin**
  + gliclazide or
  + SGLT2-i or
  + insulin or
  + pioglitazone

- **Metformin + SGLT2-i**
  + gliclazide or
  + sitagliptin or
  + pioglitazone
  + SGLT2-i (not with dapagliflozin) or
  + insulin or
  + GLP-1RA (in line with Fact Sheet)

- **Metformin + pioglitazone**
  + gliclazide or
  + sitagliptin or
  + SGLT2-i or
  + pioglitazone or
  + GLP-1RA (in line with Fact Sheet)

- **Metformin + insulin**
  + gliclazide or
  + sitagliptin or
  + SGLT2-i or
  + pioglitazone or
  + GLP-1RA (in line with Fact Sheet)

Combination not included in NICE NG28 but is recommended in TA583. RCT evidence to support this combination is very limited therefore only consider if other combinations are cautioned or contraindicated.

North Central London Joint Formulary Committee
Antihyperglycaemic agents for Type 2 diabetes
Version 1.2
Approval date: August 2019
Expiry date: August 2022
Algorithm 1: Blood glucose lowering therapy in adults with type 2 diabetes eligible for METFORMIN

If the person is symptomatically hyperglycaemic, exclude a diagnosis of T1DM and initiate metformin + gliclazide. Consider withdrawing gliclazide when glycaemic control is achieved.

Up to 12 weeks trial of lifestyle changes including healthy eating, weight loss, smoking cessation, blood pressure control, alcohol consumption and increased physical activity.

Aim for HbA1c of 48mmol/mol (6.5%) or individually agreed target for as long as possible after diagnosis.

Refer for Structured Diabetes Education programme.

**INITIATE THERAPY** if HbA1c is above 48mmol/mol (6.5%) or individually agreed target.

- **Metformin** if eGFR>30mL/min (titrate dose using regimen on page 8).
  - Consider metformin MR if standard metformin causes gastrointestinal side effects

**FIRST INTENSIFICATION** if uncontrolled on monotherapy. Aim for HbA1c of 53mmol/mol (7.0%) or individually agreed target.

- Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

**SECOND INTENSIFICATION** if uncontrolled on dual therapy. Aim for HbA1c of 53mmol/mol (7.0%) or individually agreed target.

- Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

**THIRD INTENSIFICATION** Aim for HbA1c of 58mmol/mol (7.5%) or individually agreed target.

- Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

### Definitions:
- **High risk of hypos:** elderly, dementia, CKD 3+, significant drug or alcohol use, erratic lifestyle, low body weight, significant liver disease
- **Significant obesity-related comorbidities:**
  - Sleep apnoea
  - CKD due to obesity
  - Non-alcoholic fatty liver disease
  - Musculoskeletal issues relating to obesity

### NICE continuation criteria
- **DPP-4i (gliptins), SGLT2-i, pioglitazone:** reduction of 5.5mmol/mol (0.5%) or more within 6 months
- **GLP-1 RA: reduction of >11 mmol/mol (1%) AND 3% weight loss within 6 months of initiation (see GLP-1 RA GP Fact Sheet)**

If continuation criteria is not met, withdraw treatment and recheck HbA1c at 2 months.

### Consider earlier referral for ‘Third intensification’ if morbidly obese with significant obesity-related comorbidities
Algorithm 2: Blood glucose lowering therapy in adults with type 2 diabetes IF METFORMIN IS CONTRAINDICATED OR NOT TOLERATED

If the person is symptomatically hyperglycaemic, exclude a diagnosis of T1DM and initiate gliclazide. Review treatment when blood glucose control has been achieved. Up to 12 weeks trial of lifestyle changes including healthy eating, weight loss, smoking cessation, blood pressure control, alcohol consumption and increased physical activity. Aim for HbA1c of 48mmol/mol (6.5%) or individually agreed target for as long as possible after diagnosis. Refer for Structured Diabetes Education programme.

<table>
<thead>
<tr>
<th>INITIATE THERAPY if HbA1c is above 48mmol/mol (6.5%) or individually agreed target.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm that metformin (immediate release and modified release) is contraindicated or not tolerated.</td>
</tr>
<tr>
<td><em>High risk or occupational impact of hypoglycaemia, frail, or medical issues related with obesity</em></td>
</tr>
<tr>
<td><strong>Gliclazide or Repaglinide</strong> if irregular meals or fasting</td>
</tr>
</tbody>
</table>

**FIRST INTENSIFICATION** if uncontrolled on monotherapy. Aim for HbA1c of 53mmol/mol (7.0%) or individually agreed target.

Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

**SECOND INTENSIFICATION** if uncontrolled on dual therapy. Aim for HbA1c of 53mmol/mol (7.0%) or individually agreed target.

Reinforce lifestyle measures, confirm medication adherence, optimise dose and refer to structured education programme if patient has not already attended.

**Definitions:**
- **High risk of hypos:** elderly, dementia, CKD 3+, significant drug or alcohol use, erratic lifestyle, low body weight, significant liver disease
- **Significant obesity-related comorbidities:**
  - Sleep apnoea
  - CKD due to obesity
  - Non-alcoholic fatty liver disease
  - Musculoskeletal issues relating to obesity
- **NICE continuation criteria**
  - DPP-4i (gliptin), SGLT2-i, pioglitazone: reduction of 5.5mmol/mol (0.5%) or more within 6 months
  - GLP-1 RA: reduction of >11 mmol/mol (1%) AND 3% weight loss within 6 months of initiation (see GLP-1 RA GP Fact Sheet)
  - If continuation criteria is not met, withdraw treatment and recheck HbA1c at 2 months.

**Algorithm 2:**

- **IF METFORMIN IS CONTRAINDICATED OR NOT TOLERATED**
  - **If metformin indicated and tolerated, go to Algorithm 1.**
  - **Weight gain would be detrimental to obesity-related comorbidities**
    - **Low hypo risk:** add insulin (usually NPH) or glargine
    - **Hypo risk:** add pioglitazone (check cautions)
    - **Add sitagliptin (not included in NICE NG28)**
  - **Weight loss would be beneficial and SGLT2-i is suitable (check cautions)**
    - **Add gliclazide or pioglitazone (check cautions)**
    - **Add SGLT2-I**
  - **High risk or occupational risk of hypoglycaemia**
    - **Add insulin (usually NPH) or gliclazide**
    - **Add SGLT2-I if suitable (check cautions, not included in NICE NG28)**
    - **Add sitagliptin or pioglitazone (check cautions)**
  - **Add insulin (usually NPH) or gliclazide**
  - **Add SGLT2-I**
  - **Add sitagliptin (check cautions)**
  - **Add SGLT2-I**
  - **Add gliclazide (not included in NICE NG28)**
  - **Add pioglitazone (check cautions)**

**On insulin-based treatment?**

- **History of problematic hypoglycaemia or BMI >35kg/m² (or >30kg/m² if South Asian) and psychological or medical issues related with obesity-related comorbidities**
  - **Insulin + GLP-1RA (specialist initiation)**
  - **Insulin + GLP-1RA**
  - **Start insulin (usually NPH)**
  - **SU + GLP-1RA**
  - **Intensify insulin based treatment**

North Central London Joint Formulary Committee

Antihyperglycaemic agents for Type 2 diabetes

Approval date: August 2019

Version 1.2

Expiry date: August 2022
<table>
<thead>
<tr>
<th>Drug summary table</th>
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</table>

<table>
<thead>
<tr>
<th>Month</th>
<th>Instructions for use</th>
<th>Side effect</th>
<th>Cautions and contraindications</th>
<th>Monitoring &amp; stopping criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Low</td>
<td><strong>Start 500mg OD (immediate release) with or after food</strong> ♦ <strong>↑ by 500mg as tolerated (usually weekly)</strong>  ♦ <strong>Usual MAX = 1000mg BD (or 850mg TDS if patient has three large starchy meals per day)</strong>  ♦ <strong>Consider trial of modified release metformin ONLY if GI tolerability prevents the person continuing with metformin despite gradual titration. Discontinue if not tolerated. A switch back to standard release should be considered once titration complete and patient on stable dose.</strong>  ♦ <strong>Do not use metformin MR in an attempt to improve compliance as there is no evidence</strong></td>
<td>Gastro-intestinal side effects such as wind, diarrhoea and nausea initially ♦ <strong>Rarely lactic acidosis (withdraw treatment) and decreased vitamin B$_{12}$ absorption</strong></td>
<td><strong>Contraindicated in ketoacidosis, renal failure (eGFR &lt;30 ml/min/1.73m$^2$)</strong>  ♦ <strong>If the person has mild to moderate liver dysfunction or cardiac impairment, discuss benefits of metformin so due consideration can be given to its cardiovascular-protective effects before any decision is made to reduce the dose</strong>  ♦ <strong>Advertise patient to discontinue temporarily if acutely unwell and at risk for severe dehydration</strong></td>
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<tr>
<td>Gliclazide</td>
<td>Low</td>
<td><strong>Start 40-80mg OD with food</strong> ♦ <strong>↑ by 80mg according to response</strong>  ♦ <strong>Usual MAX = 160mg BD</strong></td>
<td>Increased appetite &amp; weight gain therefore caution if patient overweight ♦ <strong>Hypoglycaemia, provide ‘Safe driving tips’ from Diabetes.org.uk website</strong>  ♦ <strong>Gastro-intestinal disturbances</strong></td>
<td><strong>Contraindicated in ketoacidosis</strong>  ♦ <strong>Avoid where possible in severe hepatic impairment</strong>  ♦ <strong>Use with care in those with mild to moderate renal impairment, avoid where possible in severe renal impairment due to increased risk of hypoglycaemia.</strong>  ♦ <strong>Avoid where possible in acute porphyria</strong></td>
</tr>
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</tr>
<tr>
<td>Repaglinide</td>
<td>Low</td>
<td><strong>500mcg TDS immediately before or up to 30 minutes before each main meal</strong> ♦ <strong>↑ by 1mg according to response every 1-2 weeks</strong>  ♦ <strong>MAX = 4mg TDS</strong></td>
<td>Gastro-intestinal side effects such as abdominal pain, diarrhoea, constipation, nausea, vomiting ♦ <strong>Hypoglycaemia (rarely), provide ‘Safe driving tips’ from Diabetes.org.uk website</strong></td>
<td><strong>Contraindicated in ketoacidosis</strong>  ♦ <strong>Avoid where possible in severe hepatic impairment</strong>  ♦ <strong>Use with caution in renal impairment</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Sitagliptin</td>
<td>High</td>
<td><strong>100mg OD</strong> ♦ <strong>Reduce dose to 50mg once daily if eGFR 30–50 mL/min/1.73m$^2$; reduce dose to 25 mg once daily if eGFR less than 30mL/min/1.73 m$^2$</strong></td>
<td>Gastro-intestinal side effects such as constipation and nausea ♦ <strong>Peripheral oedema</strong>  ♦ <strong>Upper respiratory tract infection</strong>  ♦ <strong>Nasopharyngitis</strong>  ♦ <strong>Musculoskeletal pain</strong>  ♦ <strong>Less commonly dry mouth, anorexia, headache, drowsiness, dizziness, hypoglycaemia, osteoarthritis</strong></td>
<td><strong>Contraindicated in ketoacidosis</strong>  ♦ <strong>Inform patients about the symptoms of acute pancreatitis – persistent, severe abdominal pain (sometimes radiating to the back) – and to tell their doctor if they have such symptoms. Discontinue if acute pancreatitis is suspected.</strong>  ♦ <strong>Dose of concomitant sulfonylurea or insulin may need to be reduced to prevent hypoglycaemia</strong>  ♦ <strong>Assessment of renal function is recommended prior to initiation and periodically thereafter.</strong></td>
</tr>
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North Central London Joint Formulary Committee

Antihyperglycaemic agents for Type 2 diabetes

Approval date: August 2019
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<table>
<thead>
<tr>
<th>Month cost</th>
<th>Instructions for use</th>
<th>Side effect</th>
<th>Cautions and contraindications</th>
<th>Monitoring &amp; stopping criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone</td>
<td>Low</td>
<td>Start 15mg OD ↑ to 30-45mg OD according to response; higher doses are at a greater risk of side effects (including fluid retention). Elderly start at 15mg OD &amp; ↑ gradually</td>
<td>Oedema; warn patients to look out for oedema, breathlessness or fatigue (see ‘Cautions and Contraindications’ and ‘Monitoring and stopping criteria’) Bone fracture (see ‘Cautions and Contraindications’ and ‘Monitoring and stopping criteria’) Bladder cancer (see ‘Cautions and Contraindications’ and ‘Monitoring and stopping criteria’) Weight gain (see ‘Monitoring and stopping criteria’) Upper respiratory tract infection Musculoskeletal pain Headache Erectile dysfunction Hypoaesthesia Visual disturbances Anaemia</td>
<td>Contraindicated in cardiac failure or history of cardiac failure. Avoid in patients with known LV systolic or diastolic dysfunction. Caution in those with increased risk of heart failure including the elderly (use lower doses and specialist use only with insulin due to higher risk of cardiac failure (see MHRA alert)) Contraindicated with hepatic impairment Contraindicated in ketoacidosis Contraindicated in uninvestigated macroscopic haematuria, previous or active bladder cancer Cautioned in post-menopausal women due to increased risk of fracture. Use lowest effective dose.</td>
</tr>
<tr>
<td>Month cost</td>
<td>Instructions for use</td>
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<td>Cautions and contraindications</td>
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</tbody>
</table>
| All SGLT2-i ('flozin') | High | **Advice for treating patients with SGLT2-i:**  
- Advise increased fluid intake (at least 500 mL/day) to compensate for increased urinary fluid losses, to avoid dehydration and acute kidney injury (AKI)  
- If HbA1c <64 mmol/mol reduce dose of SU by 50% and insulin by 20% to reduce risk of hypoglycaemia on commencing SGLT2-i  
- Advise patient of symptoms of genital candida infection and to commence topical clotrimazole 1% if these develop  
- Advise patient of the risk of dehydration and possible AKI if not able to drink or diarrhoea / vomiting  
- Inform them of the very small and uncertain risk of lower limb amputation (primarily of the toe). Advice patients to:  
  - stay well hydrated  
  - carry out routine preventive foot care  
  - seek medical advice promptly if they develop skin ulceration, discoloration, or new pain or tenderness  
- Inform them of the very small risk of diabetic ketoacidosis (DKA) and of the signs and symptoms of DKA. Advise them to seek immediate medical advice if they develop any of these:  
  - rapid weight loss  
  - feeling sick or being sick  
  - stomach pain  
  - fast and deep breathing  
  - sleepiness  
  - a sweet smell to the breath  
  - a sweet or metallic taste in the mouth  
  - a different odour to urine or sweat  
- Discuss the risk factors for DKA with patients  
  - a low beta cell function reserve (e.g. patients with T2DM who have low C-peptide levels, latent autoimmune diabetes in adults [LADA], or a history of pancreatitis)  
  - conditions leading to restricted food intake or severe dehydration  
  - sudden reduction in insulin  
  - increased insulin requirements due to acute illness  
  - surgery  
  - alcohol abuse  
- Inform them of the small risk of Fournier’s gangrene (necrotising fasciitis of the genitalia or perineum). Advise them to seek immediate medical advice if they develop severe pain, tenderness, erythema, or swelling in the genital or perineal area accompanied by fever or malaise | Gastro-intestinal side effects such as constipation, nausea and thirst  
Urinary Tract infection  
Vulvovaginal infection  
Dizziness postural, syncope  
Dyslipidaemia  
Polyuria  
Rare but serious and potentially life-threatening cases of diabetic ketoacidosis (DKA) have been reported. Many cases occurred during the first 2 months of treatment. Most were associated with off-label use in T1DM. Patients should be told to report signs of DKA including nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, fatigue or sleepiness. Treatment should be discontinued immediately if DKA is suspected or diagnosed. Bone fractures (particularly in older patients with a prior history/risk of cardiovascular disease)  
Lower limb amputation (primarily of the toe) in high cardiovascular risk patients  
Rare but serious and potentially life-threatening cases of Fournier’s Gangrene have been reported – avoid in patients with incontinence or poor genital hygiene [see MHRA alert]. Treatment should be discontinued immediately if Fournier’s Gangrene is suspected or diagnosed. | Patients already prescribed insulin should have the SGLT2-i initiated by the Diabetes Specialist Team due to the higher risk of DKA (patients on insulin will require Ketostix or capillary ketone testing blood strips)  
Do not use in patients in which type 1 DM is possible (e.g. younger slim patients) or in patients with a history of pancreatitis (which may lead to insulin-deficiency)  
Do not use in patients with urine ketones (> +) or in ketoacidosis  
In patients with significant symptoms of decompensated diabetes (weight loss, polyuria, polydipsia, nocturia) consider the possibility of an insulin deficient state (e.g. Early type 1 diabetes, latent autoimmune diabetes, ketosis-prone type 2 diabetes/Flatbush diabetes/type 1.5 diabetes). Avoid SGLT2-i in such patients as may worsen risk of dehydration and, in rare cases, precipitate DKA  
See MHRA alert on DKA. Renal impairment: see individual monographs below  
Liver impairment: see individual monographs  
Heart failure: see individual monographs  
Avoid in women with recurrent vulvovaginal candidiasis  
Caution in patients with conditions that may predispose to acute kidney injury (AKI), including hypovolaemia, CKD, CHF, concurrent diuretics, ACEI, ARB and NSAID. See FDA alert on AKI.  
Caution in patients who have risk factors for amputation (e.g. previous amputations, existing peripheral vascular disease, or neuropathy). In such patients, monitor more closely. See MHRA alert on amputations.  
Follow ‘Advise for treating patients with SGLT2-i’  
Contact Diabetes Specialist Team for advice if required | Only continue if the patient has had a reduction of at least 5.5 mmol/mol (0.5 %) in HbA1c within 6 months  
Determine renal function before treatment, 3 months after starting treatment and at least annually (due to volume depletion, small mean q-EGFR may be observed within the first 6 weeks of treatment).  
Withhold therapy in patients who are hospitalised for major surgery or acute serious illness, acutely volume depleted (e.g. poor oral intake, diarrhoea or vomiting) or prolonged periods of fasting.  
If patient experiences symptoms of severe illness suggestive of DKA (see italics under ‘Advise for treating patients with SGLT2-i’):  
- discontinue treatment with the SGLT2-i immediately if DKA is suspected or diagnosed. Check capillary blood glucose, advise increased carbohydrate intake if normal or low.  
- refer to AE & be screened for DKA (capillary ketones and venous blood gas) do not restart treatment with any SGLT2-i in patients who experienced DKA during use, unless another cause for DKA was identified and resolved  
If patient experiences significant lower limb complication (skin ulcer, osteomyelitis, or gangrene):  
- discontinue SGLT2-i at least until the condition has resolved, and continue to monitor the patient closely  
If Fournier’s gangrene is suspected:  
- discontinue SGLT2-i and urgently start treatment (including antibiotics and surgical debridement as required) |
<table>
<thead>
<tr>
<th>Antihyperglycaemic agents for Type 2 diabetes</th>
<th>Approval date: August 2019</th>
<th>Expiry date: August 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Month</strong></td>
<td><strong>Instructions for use</strong></td>
<td><strong>Side effect</strong></td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>High</td>
<td>Start 100mg OD if GFR &gt;60 mL/min/1.73m². If required may increase to 300 mg after 3 months if GFR still &gt;60 mL/min/1.73m²; higher dose is at a greater risk of adverse reactions related to volume depletion in the first 3 months. See ‘Advice for treating patients with SGLT2-i’ on row ‘All SGLT2-i’ above.</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>High</td>
<td>10mg OD if GFR &gt;60 mL/min/1.73m². Severe hepatic impairment: Start 5mg OD and increase to 10mg OD if tolerated. Not licensed in combination with pioglitazone. See ‘Advice for treating patients with SGLT2-i’ on row ‘All SGLT2-i’ above.</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>High</td>
<td>10mg OD if GFR &gt;60 mL/min/1.73m². Do not routinely increase to 25mg dose as is not associated with a meaningful improvement in HbA1c, BP or cardiovascular outcomes. See ‘Advice for treating patients with SGLT2-i’ on row ‘All SGLT2-i’ above.</td>
</tr>
<tr>
<td>Ertugliflozin</td>
<td>High</td>
<td>5-15mg OD if GFR &gt;60 mL/min/1.73m². See ‘Advice for treating patients with SGLT2-i’ on row ‘All SGLT2-i’ above.</td>
</tr>
<tr>
<td>Semaglutide</td>
<td>High</td>
<td>0.5-1.0mg once weekly (subcutaneous injection). This is the preferred GLP-1 receptor agonist. See ‘Advice for treating patients with SGLT2-i’ on row ‘All SGLT2-i’ above.</td>
</tr>
<tr>
<td>Drug</td>
<td>Cost</td>
<td>Instructions for use</td>
</tr>
<tr>
<td>-------------</td>
<td>------</td>
<td>--------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>High</td>
<td>1.5mg once weekly (subcutaneous injection)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Restricted for patients:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- who are needle-phobic and cannot use the semaglutide pen device.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- with impaired manual dexterity (e.g. due to severe arthritis) and cannot use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>the semaglutide pen device.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- with learning difficulty or mental health issues and require GLP-1 receptor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>agonist administration by a third-party as the dulaglutide device minimises</td>
</tr>
<tr>
<td></td>
<td></td>
<td>the risk of needle-stick injury.</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>High</td>
<td>1.2mg once daily (subcutaneous injection)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Restricted for patients with concurrent gastrointestinal conditions (e.g.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>inflammatory bowel disease)</td>
</tr>
</tbody>
</table>
### Renal/hepatic impairment – initiating treatment

<table>
<thead>
<tr>
<th>Renal function</th>
<th>Hepatic function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD stage 1 &gt;90mL/min</td>
<td>CKD stage 2 60-90mL/min</td>
</tr>
<tr>
<td>Metformin</td>
<td>✓</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>✓</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>✓</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>100mg</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>✓</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>✓</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>✓</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>✓</td>
</tr>
<tr>
<td>Ertugliflozin</td>
<td>✓</td>
</tr>
<tr>
<td>Semaglutide</td>
<td>✓</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>✓</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>✓</td>
</tr>
<tr>
<td>Insulin</td>
<td>✓</td>
</tr>
</tbody>
</table>

- **CKD stage 1** >90mL/min
  - **CKD stage 2** 60-90mL/min
  - **CKD stage 3a** 45-59mL/min
  - **CKD stage 3b** 30-44mL/min
  - **CKD stage 4** 15-29mL/min
  - **CKD stage 5** <15mL/min

- **Specialist initiation only**
- **(clinical experience is lacking)**
- **(limited evidence)**
- **(requirement may be reduced)**
- **(use lowest effective dose)**
- **(monitor carefully with dialysis)**
- **(start at 5mg, increase to 10mg if tolerated)**
- **(requirement may be reduced)**
Patient decision aid for HbA1c target

Make a mark on the lines to show how you feel about these statements. The more you agree with the statement on the left, the further to the left you should put the mark. The more you agree with the statement on the right, the further to the right you should put the mark. You and your healthcare professional can use this to help decide the best target HbA1c level for you.

Thinking about things like driving, having severe hypos would not be a problem for me* | Thinking about things like driving, having severe hypos would be a big problem for me*
---|---
I’m not bothered about the possibility of getting other side effects | Getting other side effects would be a big problem for me
I’m happy to take more medicines if I need to | I don’t want to take any more medicines
I don’t have any health problems apart from my diabetes | I have lots of health problems
Thinking about my age and my health overall, I’m hoping to see longer-term benefits | Thinking about my age and my health overall, shorter-term benefits are more important to me

*Hypos might also be a problem for you for other reasons, such as if you operate machinery, if you are at risk of falling, or if you find it difficult to recognise the warning symptoms of a hypo.

Full NICE decision aid is available at [https://www.nice.org.uk/guidance/ng28/resources/patient-decision-aid-2187281197](https://www.nice.org.uk/guidance/ng28/resources/patient-decision-aid-2187281197)
## Patient decision aid for choice of therapy

<table>
<thead>
<tr>
<th>Issue</th>
<th>How important is this to me?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Getting to a lower target blood glucose (HbA1c) level</td>
<td>Very important</td>
</tr>
<tr>
<td></td>
<td>Important</td>
</tr>
<tr>
<td></td>
<td>Unimportant</td>
</tr>
<tr>
<td></td>
<td>Very unimportant</td>
</tr>
<tr>
<td>How many tablets I would have to take and how often</td>
<td></td>
</tr>
<tr>
<td>The possibility of getting hypos</td>
<td></td>
</tr>
<tr>
<td>The possibility of gaining weight</td>
<td></td>
</tr>
<tr>
<td>The possibility of other side effects</td>
<td></td>
</tr>
<tr>
<td>Other concerns or questions I want to discuss with my health care professional:</td>
<td></td>
</tr>
</tbody>
</table>

Full NICE decision aid is available at [https://www.nice.org.uk/guidance/ng28/resources/patient-decision-aid-2187281197](https://www.nice.org.uk/guidance/ng28/resources/patient-decision-aid-2187281197)