BNF Chapter 6.3 Diabetes mellitus and hypoglycaemia

Formulary prepared and based on BNF, Summary of Product Characteristics and information provided below unless otherwise stated. For full information on treatment side effects, cautions and contraindications, see electronic British National Formulary (www.bnf.org) or the relevant summary of product characteristics (www.medicines.org.uk).

**NICE Clinical Guidelines**

- Type 1 diabetes in adults: diagnosis and management
  - NICE guidelines NG17
- Diabetes (type 1 and type 2) in children and young people: diagnosis and management
  - NICE guideline NG18
- Type 2 diabetes in adults: Management
  - NICE guideline NG28

**NICE Technology Appraisals**

- NICE TA288 Dapagliflozin in combination therapy for treating type 2 diabetes
- NICE TA315 Canagliflozin in combination therapy for treating type 2 diabetes
- NICE TA336 Empagliflozin in combination therapy for treating type 2 diabetes
- NICE TA 390 Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes

**Local Prescribing Information**

Norfolk Diabetes Management Guidelines 2013 From the Norfolk Clinical Diabetes Networks

**Drug Safety Update**

- Pioglitazone: risk of bladder cancer
- Insulin combined with pioglitazone: risk of cardiac failure
- Exenatide (Byetta ▼): risk of severe pancreatitis and renal failure
- Dipeptidylpeptidase-4 inhibitors (‘gliptins’): risk of acute pancreatitis
- SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin): risk of diabetic ketoacidosis
- SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis

**NEL CSU Key Message Guidance available for further information**


- Bulletin 22: Blood Glucose Test Strips
- Blood Glucose Meters and Test Strip cost comparison
- Bulletin 23: Lancets
  - Lancets cost comparison
- Bulletin 24: Pen Needles
  - Needles for pre-filled and reusable Pen Injectors cost comparison
\begin{table}
\centering
\begin{tabular}{|l|c|c|c|}
\hline
\textbf{Formulary Key} & \textbf{1st line formulary choice} & \textbf{Encouraged} & \textbf{2nd line formulary choice} & \textbf{Shared Care (TAG Amber)} & \textbf{Shared Care Agreement} \\
\hline
\textbf{Short acting Insulins} & & & & & \\
\hline
\textbf{Soluble Insulin} & & & & & \\
First line for adults with Type-1 Diabetes on multiple insulin injection regimens with meal-time insulin & & & & & \\
Actrapid® 100 units/mL & 10mL vial & & & & \\
Insuman® Rapid 100 units/mL & 3mL cartridge* & *Compatible pens for 3mL cartridges = ClikSTAR®, Autopen® 24 & & & \\
Humulin S® 100 units/mL & 10mL vial & 3mL cartridge* & *Compatible pens for 3mL cartridges = HumaPen®, Autopen® Classic & & \\
\hline
\textbf{Rapid-Acting Insulin Analogues} & & & & & \\
Second line for adults with Type-1 Diabetes on multiple insulin injection regimens with meal-time insulin when: & & & & & \\
• Nocturnal or late inter-prandial hypoglycaemia is a problem & & & & & \\
• Wish to avoid need to snack, while maintaining equivalent blood glucose control & & & & & \\
• Individual lifestyle factors such as irregular eating patterns makes a rapid-acting insulin analogue desirable & & & & & \\
Apïdïr® (Insulin Glulisine) 100 units/mL & 10mL vial & 3mL cartridge* & 3mL Solostar® (prefilled device) & & NICE does not advise routine use of rapid-acting insulin analogues after meals for adults with type 1 diabetes\textsuperscript{1}. \\
Insulin Lispro Sanofi® 100 units/mL & 10mL vial & 3mL cartridge* & 3mL Solostar® (prefilled device) & & *Compatible pens for 3mL cartridges = AllStar Pro® and JuniorSTAR® \\
NovoRapid (Insulin Aspart) 100 units/mL & 10mL vial & 3 mL Penfill® cartridge* & 3mL Flexpen® (prefilled device) & & *Compatible pens for 3mL Penfill® - Novopen® devices \\
Humalog® (Insulin Lispro) 200 units/mL & 3mL KwikPen (prefilled device) & & & & TAG Green: Prescribable on request of Diabetes Specialist for adults who require greater than 20 units of fast acting insulin and more than 200 units of insulin per day, with poor glycaemic control i.e. HbA1c of greater than 75mmol/mol. \textsuperscript{1} \\
\hline
\textbf{Intermediate and Long Acting Insulins} & & & & & \\
See local insulin pathway for patients with Type 2 diabetes & & & & & \\
Isophane Insulin (NPH) & & & & & \\
First-line for adults with type-2 diabetes requiring insulin. & & & & & \\
Insumam Basal (100 units/mL) & 5mL vial & 3mL cartridge* & 3mL Solostar® (prefilled device) & & *Compatible pens for 3mL cartridges = ClikSTAR®, Autopen® 24 \\
Humulin I (100 units/mL) & 10mL vial & 3mL cartridge* & 3mL Kwikpen® (prefilled device) & & *Compatible pens for 3mL cartridges = HumaPen®, Autopen® Classic \\
Insulatard & 10mL vial & 3mL cartridge* & 3mL Innolet (prefilled device) & & *Compatible pens for 3mL cartridges =NovoPen® 5 or NovoPen® Echo InnoLet® devices are useful for persons with visual acuity and/or dexterity problems \\
\hline
\textbf{Long Acting Insulin Analogues} & & & & & \\
First line for adults with type-1 diabetes & & & & & \\
Multiple daily injection basal–bolus insulin regimens should be offered to people with Type 1 Diabetes rather than twice–daily mixed insulin regimens\textsuperscript{2}. & & & & & \\
Levemir® (Insulin Detemir) 100 units/mL & 3 mL Penfill® cartridge* & 3mL Flexpen® (prefilled device) & 3mL Innolet® (prefilled device) & & *Compatible pens for 3mL Penfill® - Novopen® 5 or NovoPen® Echo \textsuperscript{1}. InnoLet® devices are useful for persons with visual acuity and/or dexterity problems \\
\hline
\textbf{Second-Line for adults with Type-2 Diabetes requiring insulin.} & & & & & \\
Second-line for adults with Type-1 Diabetes if twice daily Levemir not acceptable or not tolerated. & & & & & \\
Abasaglar® (Insulin Glargine) 100 units/mL & 3mL cartridge* & 3mL KwikPen (prefilled device) & & *Compatible pens for 3mL cartridges = Autopen® Classic or HumaPen ranges \\
\hline
\end{tabular}
\end{table}

\begin{itemize}
\item Diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar) \textsuperscript{1}
\item NICE advice [ESNM64]
\end{itemize}
### Tresiba (Insulin Degludec)

- **100 units/ml**
- **3mL Penfill® cartridges**
- **3mL FlexTouch® (prefilled device)**

**TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

### Toujeo® (Insulin Glargine)

- **300 units/ml**
- **1.5mL SoloStar® pen (prefilled device)**

**TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

#### High-strength insulin glargine

**Toujeo®** is not bioequivalent to Lantus: they are not interchangeable without dose adjustment.

### Insulin analogues

#### Biphasic (Pre-mixed insulin)

**Biphasic (Pre-mixed insulin)**

**Restricted use in Type 1 and Type 2 Diabetes for:**

- **Patients with significant nocturnal hypoglycaemia, despite optimal adjustments of lifestyle**
- **"Chaotic patients" who may be at significant risk of diabetic ketoacidosis (DKA) or hyperosmolar hyperglycaemic state (HHS) (previously known as hyperosmolar non-ketotic diabetic state or hyper HONK) if daily basal insulin is missed, despite optimal adjustments of lifestyle, and diet optimising basal insulin/multiple daily injections.**
- **Patients with psychological problems (e.g. eating disorders or patients with intermittent compliance issues with insulin injections), who are not supervised by a daily carer and do not qualify to receive district nurse injections of daily insulin glargine, and who may be at significant risk of DKA or HHS if daily basal insulin is missed.**
- **Patients with a diagnosed allergy to either insulin detemir or insulin degludec**

Initiation should be by a Diabetes consultant / specialist only and all patients should be managed by the initiating specialist team for a minimum of three months or until stable. Patients should be returned to previous treatment if no improvement in overall disease control from baseline is demonstrated.

**Tresiba (Insulin Degludec)**

| 100 units/ml | 3mL Penfill® cartridges* | 3mL FlexTouch® (prefilled device) | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Toujeo® (Insulin Glargine)**

- **300 units/ml**
- **1.5mL SoloStar® pen (prefilled device)**

**TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High-strength insulin glargine**

**Toujeo®** is not bioequivalent to Lantus: they are not interchangeable without dose adjustment.

#### Isophane (NPH) + Soluble Insulin

**Isophane (NPH) + Soluble Insulin**

- **First-line – Type-2 diabetes (where pre-mixed insulin indicated)**
- **First-line – Type-1 diabetes in adults where twice daily insulin regimens are indicated, including:**
  - those who find adherence to lunch-time insulin injections difficult
  - those who have difficulties optimising basal insulin/multiple daily injections.

**Insuman® Comb 15**

| 15% soluble, 85% isophane | 100 units/mL | 3mL Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Insuman® Comb 25**

| 25% soluble, 75% isophane | 100 units/mL | 3mL Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Insuman® Comb 50**

| 50% soluble, 50% isophane | 100 units/mL | 3mL Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Humulin M3® (30% soluble, 70% isophane)**

| 100 units/mL | 3mL Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Humalog® Mix25**

| 25% insulin lispro, 75% insulin lispro protamine | 10mL vial | 3mL Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Humalog® Mix50**

| 50% insulin lispro, 50% insulin lispro protamine | 3mL Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

**Novomix® 30**

| 30% insulin aspart, 70% insulin aspart protamine | 100 units/mL | 3mL Penfill® Cartridge* | **TAG Green** (prescribable on request of consultant / specialist) for restricted use in Type 1 and Type 2 Diabetes as above.

**High strength insulin degludec 200units/ml is not recommended for routine use:** It may be considered for patients with severe insulin resistance requiring large daily doses of insulin (≥3 units/kg/day), where treatment is initiated by a specialist Consultant Diabetologist.

#### Second line choice

- **Novomix® 30** (30% insulin aspart, 70% insulin aspart protamine) 100 units/mL
- **Humalog® Mix25** (25% insulin lispro, 75% insulin lispro protamine) 100 units/mL
- **Humalog® Mix50** (50% insulin lispro, 50% insulin lispro protamine) 100 units/mL
- **Novomix® 30** (30% insulin aspart, 70% insulin aspart protamine) 100 units/mL

**Insulin analogues**

#### Second line – Type 2 diabetes (where pre-mixed insulin indicated)

- Immediate injection before a meal is preferred, or
- Hypoglycaemia is a problem, or
- Blood glucose levels rise markedly after meals

**Second line – Type 1 diabetes in adults** where twice daily insulin regimens indicated and hypoglycaemia affects quality of life.

**Preferred choice**

**Humalog® Mix25** (25% insulin lispro, 75% insulin lispro protamine) 100 units/mL

**Humalog® Mix50** (50% insulin lispro, 50% insulin lispro protamine) 100 units/mL

**Second line choice**

**Novomix® 30** (30% insulin aspart, 70% insulin aspart protamine) 100 units/mL
Antidiabetic drugs

### Metformin

**First-line for all persons with type 2 diabetes requiring blood glucose lowering treatment (unless contraindicated)**

<table>
<thead>
<tr>
<th>Metformin tablets</th>
<th>Step up dose over several weeks to minimise GI side-effects. Dose: 500mg OD for one week (tea-time), then 500mg BD for one week (breakfast and tea-time), then increase by 500mg increments as required (usual max 2g daily).</th>
<th>Review metformin dose if serum creatinine &gt; 130 micromol/l or eGFR &lt; 45ml/min/1.73m2 Stop metformin if serum creatinine &gt; 150 micromol/l or eGFR &lt; 30ml/min/1.73m2</th>
</tr>
</thead>
<tbody>
<tr>
<td>500mg, 850mg</td>
<td>First Line</td>
<td></td>
</tr>
</tbody>
</table>

**Second line choice**

| Metformin MR tablets 500mg, 750mg, 1g | Consider if GI side effects prevent person from continuing with normal release metformin rather than prescribing an alternative drug. | Review metformin dose if serum creatinine > 130 micromol/l or eGFR < 45ml/min/1.73m2 Stop metformin if serum creatinine > 150 micromol/l or eGFR < 30ml/min/1.73m2 |

### Sulphonylureas

**First-line add-on therapy where HbA1c remains above target despite optimal dosing with metformin.**

**Option for Second-line monotherapy for persons with type 2 diabetes where metformin is contraindicated or not tolerated.**

| Gliclazide tablets 80mg | Tablets are half-scored to enable 40mg dosing. 40mg tablets - expensive choice |                                                                                                                                                           |

### Thiazolidinediones

**Option for Second-line add-on therapy**

- Consider adding to metformin if there is a significant risk of hypoglycaemia (or its consequences e.g. those who rely on driving for their income).
- Consider addition to sulphonylurea where metformin is contraindicated or not tolerated.
- Option for triple therapy (with metformin and sulphonylurea) where the use of insulin is unacceptable.

| Pioglitazone tablets 15mg, 30mg, 45mg | Continue pioglitazone therapy only if there is a reduction of ≥ 0.5 percentage points (5.5mmol/L) in HbA1c in 6 months. LFT monitoring required. | DO NOT start or continue therapy in persons with heart failure. Incidence of heart failure increased when glitazones combined with insulin – careful monitoring required. Use with caution in those with increased risk of fractures (especially post menopausal women). Contra-indicated in active or previous bladder cancer. AVOID in hepatic impairment. |

### DPP-4 Inhibitors (Gliptins)

**Option for Second-line add-on therapy**

- Consider adding to metformin if there is a significant risk of hypoglycaemia (or its consequences e.g. those who rely on driving for their income).
- Consider addition to sulphonylurea where metformin is contraindicated or not tolerated.

**Option for triple therapy with metformin and sulphonylurea where the use of insulin is unacceptable.**

**Option for use with insulin with or without metformin when stable dose of insulin has not provided adequate glycaemic control.**

| Alogliptin tablets 25mg, 12.5mg, 6.25mg (Vipidia) | Once daily | Dose reduction required for renal impairment: 12.5mg for moderate renal impairment, 6.25mg for severe or end stage renal impairment. Stop glitin therapy if a reduction of ≥ 0.5 percentage points (5.5mmol/L) in HbA1c is not acheived after 6 months. A glitin may be preferable to pioglitazone if: Further weight gain would cause significant problems, or Pioglitazone is contraindicated, or The person had a poor response to or did not tolerate pioglitazone in the past. |
| Linagliptin tablets 5mg (Trajenta) | Once daily | No dose reduction required for renal or hepatic impairment. |

Combination gliptin products: Suitable for patients on stable regimes with separate tablets where the reduction in number of tablets is beneficial for compliance.

### SGLT-2 Inhibitors

**Option for use in**

- Dual therapy regimens in combination with metformin only if a sulfonylurea is contraindicated or not tolerated, or there is significant risk of hypoglycaemia.
- Combination with insulin with or without other antidiabetic drugs.
- Triple therapy regimens in combination with metformin and a sulfonylurea. Canagliflozin and empagliflozin may be also be used in triple therapy with metformin and a thiazolidinedione.

May be used as **monotherapy** where metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if:

- a dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed and
- a sulfonylurea or pioglitazone is not appropriate.

**NICE TA 398**

Serious, life-threatening, and fatal cases of DKA have been reported in patients taking an SGLT2 inhibitor. In several cases, presentation of DKA was atypical with only moderately elevated blood glucose levels (eg <14mmol/L). This could delay diagnosis and treatment. Patients should be informed of the signs and symptoms of DKA (eg 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, or a different odour to urine or sweat). Patients presenting with these signs and symptoms should be tested for raised ketones.

**MHRA Drug Safety Update: SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis**
### Injectable non-Insulin Antidiabetic Drugs (GLP-1 Agonist)

**TAG Green**: prescribable on request of specialist

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and Administration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lixisenatide 50micrograms/ml (Lixumia)</strong></td>
<td>10micrograms dose pre-filled pen (14 doses) for SC injection</td>
<td><strong>ONCE DAILY administration</strong> 10 micrograms once daily for 14 days, then increased to 20 micrograms once daily, dose to be taken within 1 hour before the first meal of the day or the evening meal. Use with caution if eGFR &lt;30-50ml/min/1.73m². Avoid if eGFR &lt;30ml/min/1.73m². Treatment with a GLP-1 Agonist should only be continued if a beneficial response occurs and is maintained: NICE recommend continuing only if a reduction in HbA1c of at least 1 percentage point [11 mmol/mol] and a weight loss of at least 3% of initial body weight is achieved at 6 months. If this is achieved, patients should be reviewed at 12 months and a weight loss of 5% compared with baseline should be achieved. If these targets are not reached the use of GLP-1 agonist should be reconsidered.</td>
</tr>
<tr>
<td><strong>Canagliflozin 100mg, 300mg Tablets (Invokana)</strong></td>
<td>100 mg once daily preferably before breakfast, if necessary and if tolerated, increase to 300 mg once daily</td>
<td><strong>Avoid</strong> if eGFR less than 60 ml/min/1.73m² as ineffective. Reduce dose to 100 mg once daily if eGFR falls persistently below 60 ml/min/1.73m² and existing canagliflozin treatment tolerated; stop if eGFR less than 45 ml/min/1.73m². Increased risk of urinary tract and genital infections. Possible increased risk of breast and bladder cancer. Do not use in combination with pioglitazone.</td>
</tr>
<tr>
<td><strong>Empagliflozin 10mg, 25mg Tablets (Jardiance)</strong></td>
<td>10 mg once daily, increasing to 25mg max. dose if necessary and tolerated.</td>
<td><strong>Avoid</strong> initiation if eGFR less than 60 ml/min/1.73 m2 as ineffective. In patients whose eGFR falls below 60 ml/min/1.73 m², adjust or maintain dose at 10 mg once daily. stop if eGFR less than 45 ml/min/1.73m².</td>
</tr>
<tr>
<td><strong>Liraglutide 1.8 mg daily</strong></td>
<td>1.5mg by sc inj (pre-filled pen) once weekly</td>
<td><strong>Only used in combination with a sulfonylurea or metformin.</strong> Avoid if eGFR &lt;30ml/min/1.73m². May be used in combination with insulin. Combination therapy, consider lower dose of sulfonylurea/insulin. Avoid if eGFR &lt;15ml/min/1.73m². Use with caution if eGFR &lt;30-50ml/min/1.73m². No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Avoid in patients with end-stage renal disease.</td>
</tr>
<tr>
<td><strong>Semaglutide 1.34mg/ml (Ozempic)</strong></td>
<td>0.25 mg/dose, 0.5 mg/dose, 1 mg/dose solution for SC injection</td>
<td><strong>ONCE WEEKLY administration</strong> 0.25 mg once weekly for 4 weeks, increased to 0.5 mg once weekly for at least 4 weeks, then increased if necessary to 1 mg once weekly. No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Avoid in patients with end-stage renal disease.</td>
</tr>
<tr>
<td><strong>Liraglutide 6mg/mL (Victoza)</strong></td>
<td>3mL pre-filled pen</td>
<td><strong>ONCE DAILY administration</strong> 0.6mg once daily, increased after at least 1 week to 1.2 mg once daily. <strong>Liraglutide 1.8 mg daily is not recommended.</strong> Avoid if eGFR &lt;60ml/min/1.73m².</td>
</tr>
<tr>
<td><strong>Dulaglutide (Trulicity®)</strong></td>
<td>750 microgram/0.5ml, 1.5mg/0.5ml prefilled pen for SC injection</td>
<td><strong>ONCE WEEKLY administration</strong> Monotherapy: 750 microgram by sc inj (pre-filled pen) once weekly. Add on therapy: 1.5mg by sc inj (pre-filled pen) once weekly. Combination therapy, consider lower dose of sulfonylurea/insulin. Avoid if eGFR &lt;15ml/min/1.73m².</td>
</tr>
<tr>
<td><strong>Exenatide MR (Bydureon)</strong></td>
<td>2 mg powder and solvent in pre-filled pen</td>
<td><strong>ONCE WEEKLY administration</strong> Avoid if eGFR &lt;50ml/min/1.73m².</td>
</tr>
<tr>
<td><strong>Exenatide 250micrograms/mL (Byetta)</strong></td>
<td>5micrograms/dose, 10micrograms dose pre-filled pen (60 doses) for SC injection</td>
<td><strong>TWICE DAILY administration</strong> 5 micrograms twice daily for at least 1 month, then increased if necessary up to 10 micrograms twice daily, dose to be taken within 1 hour before 2 main meals (at least 6 hours apart). Use with caution if eGFR &lt;30-50ml/min/1.73m². Avoid if eGFR &lt;30ml/min/1.73m². May be used in combination with insulin.</td>
</tr>
</tbody>
</table>

Co - use of GLP-1 agonists with insulin (SPECIALIST INITIATION ONLY)
### Blood Glucose Testing Strips

Monitoring should be available to the following groups of patients:

- to those on insulin treatment
- to those on oral glucose lowering medications (i.e. sulphonylureas) to provide information on hypoglycaemia
- to assess changes in glucose control resulting from medications and lifestyle changes
- to monitor changes during inter-current illness
- to ensure safety during activities, including driving

Patients should understand the benefits of monitoring and understand how to interpret the results.

| Use low cost choice blood glucose and ketone test strips < £10.00/50. Refer to: | Specific meters may be required for some patients e.g.
| --- | --- |
| Cost comparison & Key message Bulletin available on Knowledge Anglia | Type 1 Diabetes: may test for ketones or use carbohydrate counting meters.
- Children: need to consider safety/convenience/continued engagement with testing.
- Pregnant: may need to test for ketones
- Dexterity problems: some meters / lancing devices etc may be more appropriate
- Visual impairment: care needed but appropriate cost effective choices are available.

### Hypodermic Equipment

#### Needles for Pre-filled and Re-usable Pen Injectors

For adults there is no clinical reason for recommending needles longer than 8mm. 4, 5 and 6mm needles are suitable for all people regardless of BMI; they may not require a lifted skin fold and can be given at 90 degrees to the skin.

<table>
<thead>
<tr>
<th>Use low cost choice of Insulin Pen Needles &lt; £6.00/100. Refer to:</th>
<th>Key Message Bulletin and cost comparison document available on Knowledge Anglia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Message Bulletin and cost comparison document available on Knowledge Anglia</td>
<td></td>
</tr>
</tbody>
</table>

#### Lancets

<table>
<thead>
<tr>
<th>Use low cost choice of Lancets &lt; £3.00/100. Refer to:</th>
<th>Key Message Bulletin and cost comparison document available on Knowledge Anglia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Message Bulletin and cost comparison document available on Knowledge Anglia</td>
<td></td>
</tr>
</tbody>
</table>

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1. NICE CG17 2015

[https://www.nice.org.uk/guidance/ng17](https://www.nice.org.uk/guidance/ng17)
### Insulin Preparations

#### Neutral Insulin Injection

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Manufacturer</th>
<th>Species</th>
<th>Form</th>
<th>Onset (approx)</th>
<th>Peak Activity (approx)</th>
<th>Duration of Action (approx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actrapid</td>
<td>Novo Nordisk</td>
<td>V</td>
<td></td>
<td>&lt;30min</td>
<td>1.5-3.5hr</td>
<td>7-8hr</td>
</tr>
<tr>
<td>Apidra (insulin glulisine*)</td>
<td>Sanofi</td>
<td>V, P, C₄, C₅</td>
<td>10-20 min</td>
<td>55 min</td>
<td>1.5-4hr</td>
<td></td>
</tr>
<tr>
<td>Fiasp (insulin aspart*)</td>
<td>Novo Nordisk</td>
<td>V, P, C₁</td>
<td>4min</td>
<td>1-3hr</td>
<td>3-5hr</td>
<td></td>
</tr>
<tr>
<td>Humalog (insulin lispro*)</td>
<td>Lilly</td>
<td>V, P, C₃</td>
<td>15min</td>
<td>1.5hr</td>
<td>2-5hr</td>
<td></td>
</tr>
<tr>
<td>Humulin S</td>
<td>Lilly</td>
<td>V, C₃</td>
<td>30min-1hr</td>
<td>1-6hr</td>
<td>6-12hr</td>
<td></td>
</tr>
<tr>
<td>Hypurin Bovine Neutral</td>
<td>Wockhardt</td>
<td>V, C₂</td>
<td>30min-1hr</td>
<td>1.5-4.5hr</td>
<td>6-8hr</td>
<td></td>
</tr>
<tr>
<td>Hypurin Porcine Neutral</td>
<td>Wockhardt</td>
<td>V, C₂</td>
<td>30min-1hr</td>
<td>1.5-4.5hr</td>
<td>6-8hr</td>
<td></td>
</tr>
<tr>
<td>Insulin Lispro Sanofi</td>
<td>Sanofi</td>
<td>V, P, C₃</td>
<td>15min</td>
<td>1.5hr</td>
<td>2-5hr</td>
<td></td>
</tr>
<tr>
<td>Insuman Rapid</td>
<td>Sanofi</td>
<td>P, C₄, C₅</td>
<td>&lt;30min</td>
<td>1-4hr</td>
<td>7-9h</td>
<td></td>
</tr>
<tr>
<td>NovoRapid (insulin aspart*)</td>
<td>Novo Nordisk</td>
<td>V, P, C₁</td>
<td>10-20min</td>
<td>1-3hr</td>
<td>3-5hr</td>
<td></td>
</tr>
<tr>
<td>Preparation</td>
<td>Manufacturer</td>
<td>Species</td>
<td>Form</td>
<td>Onset (approx)</td>
<td>Peak activity (approx)</td>
<td>Duration of action (approx)</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------</td>
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</tr>
<tr>
<td>Humalog Mix25</td>
<td>Lilly</td>
<td>V, P, C₃</td>
<td>15min</td>
<td>2hr</td>
<td>22hr</td>
<td></td>
</tr>
<tr>
<td>Humalog Mix50</td>
<td>Lilly</td>
<td>P, C₃</td>
<td>15min</td>
<td>2hr</td>
<td>22hr</td>
<td></td>
</tr>
<tr>
<td>Humulin M3</td>
<td>Lilly</td>
<td>V, P, C₃</td>
<td>30min-1hr</td>
<td>1-12hr</td>
<td>22hr</td>
<td></td>
</tr>
<tr>
<td>Hypurin Porcine 30/70</td>
<td>Wockhardt</td>
<td>V, C₂</td>
<td>&lt;2hr</td>
<td>4-12hr</td>
<td>24hr</td>
<td></td>
</tr>
<tr>
<td>Insuman Comb 15</td>
<td>Sanofi</td>
<td>C₄, C₅</td>
<td>30min-1hr</td>
<td>2-4hr</td>
<td>11-20hr</td>
<td></td>
</tr>
<tr>
<td>Insuman Comb 25</td>
<td>Sanofi</td>
<td>V, P, C₄, C₅</td>
<td>30min-1hr</td>
<td>2-4hr</td>
<td>12-19hr</td>
<td></td>
</tr>
<tr>
<td>Insuman Comb 50</td>
<td>Sanofi</td>
<td>C₄, C₅</td>
<td>&lt;30min</td>
<td>1.5-4hr</td>
<td>12-16hr</td>
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</tr>
<tr>
<td>NovoMix 30</td>
<td>Novo Nordisk</td>
<td>P, C₁</td>
<td>10-20 min</td>
<td>1-4hr</td>
<td>24hr</td>
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</tbody>
</table>
## Isophane Insulin Injection

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Manufacturer</th>
<th>Species</th>
<th>Form</th>
<th>Onset (approx)</th>
<th>Peak activity (approx)</th>
<th>Duration of action (approx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humulin I</td>
<td>Lilly</td>
<td>V, P, C₃</td>
<td>30min-1hr</td>
<td>1-8hr</td>
<td>22hr</td>
<td></td>
</tr>
<tr>
<td>Hypurin Porcine Isophane</td>
<td>Wockhardt</td>
<td>V, C₂</td>
<td>&lt;2hr</td>
<td>6-12hr</td>
<td>18-24hr</td>
<td></td>
</tr>
<tr>
<td>Insulatard</td>
<td>Novo Nordisk</td>
<td>V, C₁, D</td>
<td>&lt;1.5hr</td>
<td>4-12hr</td>
<td>24hr</td>
<td></td>
</tr>
<tr>
<td>Insuman Basal</td>
<td>Sanofi</td>
<td>V, P, C₄, C₅</td>
<td>&lt;1hr</td>
<td>3-4hr</td>
<td>11-20hr</td>
<td></td>
</tr>
</tbody>
</table>

## Insulin Zinc Suspension (Mixed)

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Manufacturer</th>
<th>Species</th>
<th>Form</th>
<th>Onset (approx)</th>
<th>Peak activity (approx)</th>
<th>Duration of action (approx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypurin Bovine Lente</td>
<td>Wockhardt</td>
<td>V</td>
<td>2hr</td>
<td>8-12hr</td>
<td>30hr</td>
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## Protamine Zinc Insulin Injection

<table>
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<th>Species</th>
<th>Form</th>
<th>Onset (approx)</th>
<th>Peak activity (approx)</th>
<th>Duration of action (approx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypurin Bovine PZI</td>
<td>Wockhardt</td>
<td>V</td>
<td>4-6hr</td>
<td>10-20hr</td>
<td>24-36hr</td>
<td></td>
</tr>
<tr>
<td>Preparation</td>
<td>Manufacturer</td>
<td>Species</td>
<td>Form</td>
<td>Onset (approx)</td>
<td>Peak activity (approx)</td>
<td>Duration of action (approx)</td>
</tr>
<tr>
<td>-------------------------------------------</td>
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<td>------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Abasaglar (insulin glargine)</td>
<td>Lilly</td>
<td>P, C₃</td>
<td></td>
<td>30min-1hr</td>
<td></td>
<td>24hr</td>
</tr>
<tr>
<td>Lantus (insulin glargine)</td>
<td>Sanofi</td>
<td>V, P, C₄, C₅</td>
<td></td>
<td>30min-1hr</td>
<td></td>
<td>24hr</td>
</tr>
<tr>
<td>Levemir (insulin detemir)</td>
<td>Novo Nordisk</td>
<td>P, C₁, D</td>
<td></td>
<td>30min-1hr</td>
<td></td>
<td>24hr</td>
</tr>
<tr>
<td>Toujeo (insulin glargine 300 units/ml)</td>
<td>Sanofi</td>
<td>P</td>
<td></td>
<td>30min-1hr</td>
<td></td>
<td>24-36hr</td>
</tr>
<tr>
<td>Tresiba (insulin degludec)</td>
<td>Novo Nordisk</td>
<td>P, C₁, L</td>
<td></td>
<td>30min-1.5hr</td>
<td></td>
<td>&gt;42hr</td>
</tr>
</tbody>
</table>
Non Specialist Insulin Pathway for Type 2 Diabetes

When starting insulin, use a structured programme and continue metformin for people without contraindications or intolerance. Review the continued need for other blood glucose lowering therapies NG28.

Consider other non-insulin therapies if not tried previously.
Do not delay initiation of insulin therapy where indicated.

Offer NPH basal insulin first line once daily:
- **Insulan Basal**
- **Humulin l**
- **Insulatard**

If HbA1c is 75mmol/mol or higher consider starting both NPH and short-acting insulin either separately or as pre-mixed (biphasic) human insulin:

**Biphasic (isophane + soluble insulin)**
- **Insuman Comb 15, 25, 50**
- **Humulin M3**

- Do blood glucose levels rise markedly after meals?
- Does lifestyle affects timing of injections
- Does hypoglycaemia is affect quality of life?

Is patient at risk of hypoglycaemia i.e. frail, elderly, lives alone or needs assistance to administer?

No
Yes

Consider **Abasaglar** (biosimilar insulin glargine) once daily TAG Green ESNM64

Consider changing to pre-mixed (biphasic) preparations that include short-acting insulin analogues:
- **Humalog Mix 25, 50**
- **Novomix 30**

Or if lifestyle / occupation affects insulin regime – refer to specialist diabetes team for consideration of basal bolus insulin regime.

Refer to specialist diabetes team:
Maybe considered for **Tresiba** (Insulin Degludec) 100 units/ml TAG Green ESNM65

Initiation by consultant/specialist only and managed by specialist team for 3 months or until stable. Specialist to provide first prescription.

Patients should be returned to their previous treatment if no improvement in overall disease control from baseline

Refer to specialist diabetes team:
If severe insulin resistance, maybe considered for **Toujeo** (insulin glargine) 300units/ml TAG Green ESNM25

Initiation by consultant/specialist only and managed by specialist team for 3 months or until stable. Specialist to provide first prescription.

Patients should be returned to their previous treatment if no improvement in overall disease control from baseline

Does patient have:
- Significant hypoglycaemia despite optimal adjustments of lifestyle?
- Chaotic lifestyle with risk of DKA if daily insulin is missed?
- Psychological problems (i.e. eating disorders or compliance issues)?
- Allergy to insulin glargine or detemir

Is patient on large daily doses of insulin (≥2units/kg/day)?

No
Yes

Continue with NPH Insulin, review HbA1c in line with individualised targets, lifestyle, co-morbidities and risk of hypoglycaemia.

Refer to specialist diabetes team if continued poor control

AGEM CSU Anglia
Diabetes Formulary
Version 1.9

See AGEM CSU Diabetes Formulary for more information

V1.0 Oct 2018

NHS
Arden and Greater East Midlands Commissioning Support Unit

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