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

Diagnosis and management of type 1 diabetes in children, young people and adults  
NICE guidelines CG15

Type 2 diabetes in adults: Management  
NICE guideline NG28

**NICE Technology Appraisals**

NICE TA203 Liraglutide for the treatment of type 2 diabetes mellitus  
NICE TA203

NICE TA248 Exenatide prolonged-release suspension for injection in combination with oral antidiabetic therapy for the treatment of type 2 diabetes  
NICE TA248

NICE TA268 Dapagliflozin in combination therapy for treating type 2 diabetes  
NICE TA268

NICE TA315 Canagliflozin in combination therapy for treating type 2 diabetes  
NICE TA315

NICE TA336 Empagliflozin in combination therapy for treating type 2 diabetes  
NICE TA336

NICE TA390 Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes  
NICE TA390

**Local Prescribing Information**

GP Prescribing Information - GLP-1 Agonists for Type 2 Diabetes  
http://www.knowledgeanglia.nhs.uk/tag/glp1_agonists.pdf

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  

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

Bulletin 22: Blood Glucose Test Strips  
Bulletin 22

Blood Glucose Meters and Test Strip cost comparison  
Bulletin 23

Bulletin 23: Lancets  
Bulletin 23

Lancets cost comparison  
Bulletin 24

Bulletin 24: Pen Needles  
Bulletin 24

Needles for pre-filled and reusable Pen Injectors cost comparison  
Bulletin 24
### Short acting Insulins

**Adults with Type-1 Diabetes on multiple insulin injection regimens with meal-time insulin**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>10mL vial</th>
<th>Cartridge</th>
<th>Compatible pens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actrapid® 100 units/mL</td>
<td>3mL cartridge</td>
<td>ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Insuman® Rapid 100 units/mL</td>
<td>3mL cartridge</td>
<td>ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Humulin® S 100 units/mL</td>
<td>3mL cartridge</td>
<td>HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
</tbody>
</table>

**Rapid-Acting Insulin Analogues**

**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

<table>
<thead>
<tr>
<th>Insulin</th>
<th>10mL vial</th>
<th>Cartridge</th>
<th>Compatible pens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apidra® (Insulin Glulisine) 100 units/mL</td>
<td>3mL cartridge</td>
<td>ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Humalog® (Insulin Lispro) 100 units/mL</td>
<td>3mL cartridge</td>
<td>HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
<tr>
<td>NovoRapid (Insulin Aspart) 100 units/mL</td>
<td>3mL cartridge</td>
<td>HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
<tr>
<td>Humalog® (Insulin Lispro) 200 units/mL</td>
<td>3mL cartridge</td>
<td>HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
</tbody>
</table>

**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.**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>10mL vial</th>
<th>Cartridge</th>
<th>Compatible pens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insuman Basal (100 units/mL)</td>
<td>3mL cartridge</td>
<td>ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Humulin I (100 units/mL)</td>
<td>3mL cartridge</td>
<td>HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
</tbody>
</table>

**Type 2 diabetes consider only If:**

- the person needs help with injecting insulin (e.g. from a district nurse) and a long-acting insulin analogue would reduce injections from twice to once daily, or
- the person suffers from recurrent hypoglycaemic episodes.

**Type 1 diabetes (adults) consider if:**

- nocturnal hypoglycaemia is a problem on isophane (NPH) insulin
- morning hyperglycaemia on isophane (NPH) insulin results in difficult day-time blood glucose control
- rapid-acting insulin analogues are used for meal-time blood glucose control.

**Long Acting Insulin Analogues**

**Second-Line for adults with Type-2 Diabetes requiring insulin.**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>3mL cartridge</th>
<th>Compatible pens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abasaglar® (Insulin Glargine) 100 units/mL</td>
<td>3mL KwikPen® (prefilled device)</td>
<td>Autopen® Classic</td>
</tr>
<tr>
<td>Levemir® (Insulin Detemir) 100 units/mL</td>
<td>3mL FlexPen® (prefilled device)</td>
<td>InnoLet® devices</td>
</tr>
</tbody>
</table>

**Type 2 diabetes consider only If:**

- the person needs help with injecting insulin (e.g. from a district nurse) and a long-acting insulin analogue would reduce injections from twice to once daily, or
- the person suffers from recurrent hypoglycaemic episodes.

**Type 1 diabetes (adults) consider if:**

- the person is unable to achieve good glycaemic control with established insulins.
Toujeo® (Insulin Glargine)
High-strength insulin glargine 300 units/ml
NICE Advice [ESNMM62]
NICE Advice [ESNMM65]

1.5mL SoloStar® pen (prefilled device)

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

TAG Green: Prescribable on request of Diabetes Specialist for adults who require greater than 200 units of insulin per day, with poor glycaemic control i.e. HbA1c of greater than 75mmol/mol.

**Biphasic (Pre-mixed 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 with learning difficulties and may require assistance

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Strength</th>
<th>Soluble</th>
<th>NPH</th>
<th>Compatibility</th>
<th>Compatibility Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insuman® Comb 15</td>
<td>15% soluble, 85% isophane</td>
<td>100 units/mL</td>
<td>3mL cartridge*</td>
<td>Compatible pens for 3mL cartridges – ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Insuman® Comb 25</td>
<td>25% soluble, 75% isophane</td>
<td>100 units/mL</td>
<td>3mL cartridge*</td>
<td>Compatible pens for 3mL cartridges – ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Insuman® Comb 50</td>
<td>50% soluble, 50% isophane</td>
<td>100 units/mL</td>
<td>3mL cartridge*</td>
<td>Compatible pens for 3mL cartridges – ClikSTAR®, Autopen® 24</td>
<td></td>
</tr>
<tr>
<td>Humulin M3® (30% soluble, 70% isophane)</td>
<td>100 units/mL</td>
<td>3mL cartridge*</td>
<td>Compatible pens for 3mL cartridges – HumaPen®, Autopen® Classic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Second line choice**

Novomix® 30 (30% insulin lispro, 70% insulin aspart protamine) 100 units/mL

3 mL Penfill® cartridge* 3mL Flexpen® (prefilled device)

**Insulin analogues**

Second-line – **Type 2 diabetes** (where pre-mixed insulin indicated). Consider when:
- 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 nocturnal hypoglycaemia is a problem.

**Preferred choice**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Strength</th>
<th>Soluble</th>
<th>Compatibility</th>
<th>Compatibility Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humalog® Mix25 (25% insulin lispro, 75% insulin aspart protamine)</td>
<td>100 units/mL</td>
<td>10mL vial 3mL cartridge*</td>
<td>Compatible pens for 3mL cartridges – HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
<tr>
<td>Humalog® Mix50 (50% insulin lispro, 50% insulin aspart protamine)</td>
<td>100 units/mL</td>
<td>3mL cartridge*</td>
<td>Compatible pens for 3mL cartridges – HumaPen®, Autopen® Classic</td>
<td></td>
</tr>
</tbody>
</table>

**Second line choice**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Strength</th>
<th>Soluble</th>
<th>Compatibility</th>
<th>Compatibility Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliclazide tablets</td>
<td>80mg</td>
<td>40mg dosing</td>
<td>Consider if GI side effects prevent person from continuing with normal release metformin rather than prescribing an alternative drug.</td>
<td></td>
</tr>
</tbody>
</table>

**Antidiabetic drugs**

**Metformin**

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

Metformin tablets

500mg, 850mg
First Line

Step up dose over several weeks to minimise GI side-effects. Review metformin dose if serum creatinine > 130 micromol/l or eGFR < 45ml/min/1.73m2

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).

**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

**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.

**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.

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

SGLT2 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

Canagliflozin and Empagliflozin may be used in triple therapy regimens in combination with metformin and a sulfonylurea or metformin and a thiazolidinedione.

A 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 elevated ketones.

MHRA Drug Safety Update: SGLT2 Inhibitors: updated advice on the risk of diabetic ketoacidosis

Dapagliflozin 5mg, 10mg Tablets (Forxiga)
NICE TA288
10 mg once daily. Initial dose 5mg in severe hepatic impairment. Elderly over 75 years - initiation not recommended

Avoid if eGFR less than 60mL/min/1.73m² as ineffective.

TAG Green - GP prescribable at the request of a Specialist or Consultant.

Increased risk of urinary tract and genital infections. Possible increased risk of breast and bladder cancer.
Do not use in combination with pioglitazone.

Canagliflozin 100mg, 300mg Tablets (Invokana) ▼
NICE TA315
100 mg once daily preferably before breakfast; if necessary and if tolerated, increase to 300 mg once daily

Avoid initiation if eGFR less than 60 mL/minute/1.73 m² as ineffective. Reduce dose to 100 mg once daily if eGFR falls persistently below 60 mL/minute/1.73 m² and existing canagliflozin treatment tolerated: stop if eGFR less than 45 mL/minute/1.73 m²

The TAG committee recommended a Prescriber’s Rating of 6 for Empagliflozin (May 2015): Nothing New - The product may be a new substance but is superfluous because it does not add to the clinical possibilities offered by previous products available. (In most cases these are “me-too” products).
Clinical recommendations from the Therapeutics Advisory Group (TAG) and Commissioners’ Decisions

Empagliflozin 10mg, 25mg Tablets (Jardiance) ▼
NICE TA336
10 mg once daily, increasing to 25mg max. dose if necessary and tolerated.

Avoid initiation if eGFR less than 60 mL/minute/1.73 m² as ineffective. In patients whose eGFR falls below 60 mL/minute/1.73 m², adjust or maintain dose at 10 mg once daily. stop if eGFR less than 45 mL/minute/1.73 m²

Increase of urinary tract and genital infections. Possible increased risk of breast and bladder cancer. Do not use in combination with pioglitazone.

A person should be advised to avoid alcohol before bedtime.

Injectable non-insulin Antidiabetic Drugs (GLP-1 Agonist)

See local guidance on prescribing GLP-Agonists

Option for Third-line add-on therapy in addition to metformin and a sulphonylurea or metformin and a thiazolidinedione or earlier as dual therapy if contraindications to these drugs or not tolerated in patients with:

• a BMI > 35 kg/m² in those of European family origin (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight or
• a BMI < 35 kg/m², and therapy with insulin would have significant occupational implications
• or weight loss would benefit other significant obesity-related comorbidities.

Lixisenatide
50micromgrams/mL
(Lyxumia) ▼

10micrograms dose pre-filled pen (14 doses)
ONCE DAILY administration

Use with caution if eGFR <30-
50ml/min/1.73m²
Avoid if eGFR <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 achieved⁷. If these targets are not reached the use of GLP-1 agonist should be reconsidered.

Exenatide injection
250micrograms/mL
(Byetta) ▼

5micrograms/dose,
10micrograms/dose pre-filled pen (60 doses)
TWICE DAILY administration

Use with caution if eGFR <30-
50ml/min/1.73m²
Avoid if eGFR <30ml/min/1.73m²
May be used in combination with insulin as per shared care agreement.

Exenatide MR
(Bydureon) ▼

NICE TA248

2 mg powder and solvent in pre-filled pen
ONCE WEEKLY administration

Avoid if eGFR <50ml/min/1.73m²

Liraglutide 6mg/mL
(Victoza) ▼

NICE TA203

3mL pre-filled pen 0.6mg once daily,
increased after at least 1 week to 1.2 mg once daily, max. 1.8 mg once daily
ONCE DAILY administration

Avoid if eGFR <60ml/min/1.73m²

Liraglutide 1.8 mg daily is not recommended.

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:

Cost comparison available on Knowledge Anglia

Key message Bulletin document

SPECIFIC METERS MAY BE REQUIRED FOR SOME PATIENTS e.g.

• 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

Use low cost choice of Insulin Pen Needles < £6.00/100. Refer to:

Key Message Bulletin and cost comparison document available on Knowledge Anglia

Lancets

Use low cost choice of Lancets < £3.00/100. Refer to:

Key Message Bulletin and cost comparison document available on Knowledge Anglia

1. NICE CG87 May 2009
http://publications.nice.org.uk/type-2-diabetes-cg87/guidance#glucose-control-insulin-therapy

2. SMC Advice published 7 April 2008
http://www.scottishmedicines.org.uk/SMC_Advice/Advice/456_08_insulin_glargine/insulin_glargine__Lantus_Solostar

3. NICE CG15 November 2005
http://publications.nice.org.uk/type-1-diabetes-cg15/guidance#blood-glucose-control-and-insulin-therapy

4. SMC advice published 14 May 2012
http://www.scottishmedicines.org.uk/SMC_Advice/Advice/780_12_insulin_detemir_Levemir_ABBREVIATED/insulin_detemir_Levemir_ABBREVIATED

5. NICE TA288 Dapagliflozin in combination therapy for treating type 2 diabetes http://www.nice.org.uk/guidance/TA288/chapter/1-guidance

6. NICE TA315 Canagliflozin in combination therapy for treating type 2 diabetes http://www.nice.org.uk/guidance/TA315/chapter/1-guidance

7. GP Prescribing Information - GLP-1 Agonists for Type 2 Diabetes http://www.knowledgeanglia.nhs.uk/tag/glpanalogues

8. NICE TA203 Liraglutide for the treatment of type 2 diabetes mellitus


9. NICE TA248 Exenatide prolonged-release suspension for injection in combination with oral antidiabetic therapy for the treatment of type 2 diabetes
