BNF Chapter: 6.1
Factsheet 1

Local* agreed guidance for anti-diabetic agents for **Type 2** Diabetes

Oral antidiabetic drugs / GLP-1 mimetics

Lifestyle interventions – Monitor after for 3 months

STEP ONE: **HbA1c remains ≥ 48 mmol/mol (6.5%) - ORAL THERAPY**
AIM: HbA1c 48mmol/mol (6.5%) or individualised target

Offer First Line MONOTHERAPY:

1. **Metformin standard release**[2]- (Slow titration over several weeks to minimise GI side effects)
2. **Metformin Modified release (MR)** – consider a trial only if evidence of intolerable GI side-effects with standard release

Consider First Line MONOTHERAPY
If Metformin contraindicated or not tolerated:

1. Sitagliptin /Linagliptin or Pioglitazone[3] or Gliclazide (immediate release tablets)
2. Empagliflozin or Canagliflozin, Dapagliflozin[4]* (if pioglitazone or gliclazide is not appropriate)

STEP TWO: 1st INTENSIFICATION: If HbA1c ≥ 58mmol/mol (7.5%), after at least 3 months of max tolerated dose Consider DUAL THERAPY
AIM: HbA1c of 53mmol/mol (7%) or individualised target

Consider the following combinations below:

Metformin[2] + Sitagliptin/ Linagliptin	Metformin[2] + Pioglitazone[3]	Metformin[2] + Gliclazide	Metformin[2] + Empagliflozin/ Canagliflozin/ Dapagliflozin[4]

Consider the following combinations below if Metformin contraindicated or not tolerated:

Sitagliptin/ Linagliptin + Pioglitazone[3]	Sitagliptin/ Linagliptin + Gliclazide	Pioglitazone[3] + Gliclazide

STEP THREE: 2nd INTENSIFICATION: If HbA1c > 58 mmol/mol (7.5%), or individualised target not met, Consider ORAL TRIPLE THERAPY or INSULIN Based Treatment
AIM: HbA1c of 53mmol/mol (7%) or individualised target

Consider the following combinations below or Insulin based treatment

Metformin[2] + Sitagliptin/ Linagliptin + Gliclazide/ Pioglitazone[3]	Metformin[2] + Pioglitazone[3] + Gliclazide	Metformin[2] + Empagliflozin/ Canagliflozin/ Dapagliflozin[4]* + Pioglitazone[3] OR Gliclazide	**Insulin based treatment –** as per NICE NG28 **Refer to Insulin guidance**

Consider the following if Metformin contraindicated or not tolerated

Insulin based treatment- Refer to Insulin guidance

If triple therapy above is NOT effective, not tolerated or contraindicated,
Consider **Metformin, gliclazide + GLP-1 mimetic**[5]

PRESCRIBING CONSIDERATIONS:

1. Introduce drugs in a stepwise manner, checking for tolerability and effectiveness of each drug. NG28 type 2 diabetes agreed that change in HbA1c would be the main outcome measure to reflect glycaemic control and that a difference of 5 mmol/mol (0.5%) was clinically important.
2. **Metformin:** Review dose if eGFR <45 mL/minute/1.73m^2.
   - Stop metformin if eGFR < 30 mL/minute/1.73m^2.
   - Prescribe metformin with caution for those at risk of sudden deterioration in kidney function and those at risk of eGFR falling < 45 mL/minute/1.73m^2.
3. **Pioglitazone:** Do not offer or continue if patient has: heart failure/history or heart failure, hepatic impairment/diabetic ketoacidosis/ current or history of bladder cancer, uninvestigated microscopic haematuria.
   - **MHRA 2011**: Review safety and efficacy every 3 - 6 months to ensure that only patients that are deriving benefit from pioglitazone continue to be treated.
   - *Prescribing pioglitazone/metformin as separate components is more cost effective.
4. **SGLT2 (canagliflozin, dapagliflozin or empagliflozin):**
   - Dapagliflozin/Canagliflozin/Empagliflozin **ONLY INITIATED** in patients with eGFR > 60 mL/min/1.73m^2
   - ***Dapagliflozin is not recommended in combination with pioglitazone due to theoretical increased risk of bladder cancer.**
   - **MHRA June 2015**: Do not offer an SGLT2, if the patient has a history of diabetic ketoacidosis, as SGLT2i may lead to DKA. Monitor for signs and symptoms include nausea, vomiting, abdominal pain, excessive thirst etc.
   - **MHRA June 2016** Monitor patients receiving canagliflozin who have risk factors for amputation (eg, previous amputations, existing peripheral vascular disease, or neuropathy).
5. **GLP-1 mimetic** considered in adults who have:
   - a BMI ≥ 35 kg/m^2 in those of European descent (adjust accordingly for people from black, asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity OR
   - BMI < 35 kg/m^2 and for whom insulin therapy would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.
   - ONLY continue GLP-1 mimetic therapy if demonstrate beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months).
   - Only offer a GLP-1 mimetic + insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team
   - **Formulary choice GLP mimetics:**
     i. 1st line – EXENATIDE (Byetta ® BD - £82 or Bydureon ®, £74/month)
     ii. 2nd line – LIRAGLUTIDE (Victoza ®, £79-£118/month Prescribing TWO pens per month is cost effective based on 1.2mg daily dose.
6. **Monitoring and Efficacy**:
   Measure HbA1c levels every:
   - 3 to 6 months until individualised HbA1c target met and then 6 monthly once HbA1c level and blood glucose lowering therapy are stable.
   - Review response to therapy 3-6 monthly when individualised targets are not met and 6 monthly thereafter once stable.
   - Review and consider stopping medication having little/no impact on HbA1c in line with NICE guidance. Most of the non-insulin newer agents will only reduce HbA1c by 0.5-1% (5-11mmol/mol) on average.

Based on NICE NG28, Type 2 Diabetes, December 2015.www.nice.org.uk. See guideline for full evidence base and more detail. Prices as per Drug Tariff November 2017, DM+D, BNF November 2017.

Kingston Hospital NHS Foundation Trust, Kingston CCG & Richmond CCG
Developed by: The Medicines Optimisation Team, Kingston CCG with Dr M Spring and Dr M Oldfield, Consultants in Diabetes, and Claire Neely, Diabetes Specialist Nurse, Kingston Hospital.
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BNF Chapter: 6.1
Factsheet 2

Local* agreed guidance for anti-diabetic agents for **Type 2** Diabetes

Insulin Initiation

If other measures do not keep HbA1c < 58 mmol/mol (7.5%), or individualised target not met on SECOND INTENSIFICATION & on ORAL TRIPLE THERAPY
Discuss benefits and risks of INSULIN treatment
AIM: HbA1c of 53mmol/mol (7%) or individualised target not met

STEP ONE: Initiate NPH INSULIN

✓ Continue with METFORMIN (if no contraindication or intolerance)
✓ Review continued need for other blood glucose lowering therapies.

First Line: 1. NPH insulin Once or Twice daily	OR	If HbA1c ≥ 75 mmol/mol [9.0%] or INTENSIFICATION
• **Humulin I®** • **Insulatard®**		• **Humulin I® OR Insulatard** OR • **Humulin M3®** (premixed biphasic human insulin).

STEP TWO: Alternative to NPH either:

Refer to prescribing notes for defined criteria

Long acting analogue insulin If patient meet defined NICE criteria[2]:	**Pre mixed Biphasic insulins[3]:**

• **Glargine (Lantus®**
• **Detemir (Levemir®)**
	• Biphasic (lispro):
	  • **Humalog® Mix 25 or Humalog Mix 50 or**
	• Biphasic (aspart)
	  • **Novomix 30®**

STEP THREE: Specialist Initiation only:

Recommended by consultant endocrinologist/diabetic specialist nurse/GPwSIs -Refer to prescribing notes for defined criteria

GLP-1 mimetic + insulin[4]	
• Exenatide – (Byetta® and Bydureon® once weekly) • Liraglutide – (Victoza®) - maximum of TWO pens per month based on 1.2mg daily dose)	• **High strength** Insulin glargine (Toujeo®) 300 units/ml[5]

PRESCRIBING CONSIDERATIONS:

1. Use a structured programme employing active insulin dose titration that encompasses: injection technique, including rotating injection sites and avoiding repeated injections; at the same point within sites; continuing telephone support; self-monitoring; dose titration to target levels; dietary understanding; DVLA guidance; management of hypoglycaemia; management of acute changes in plasma glucose control; support from an appropriately trained and experienced healthcare professional.
2. **Long acting analogue- Insulin detemir or insulin glargine insulin if patient meet defined NICE criteria refer to:**
   - ✓ Cannot use the delivery device for NPH insulin but could administer a long-acting insulin analogue, or
   - ✓ Needs help to inject insulin & could reduce the number of injections with a long-acting analogue.
   - ✓ Does not reach target HbA1c because of hypoglycaemia, or has significant hypoglycaemia with NPH insulin.
3. **Consider pre-mixed (BIPHASIC) preparations that include short-acting insulin analogues, rather than short-acting human insulin preparations, if:**
   - ✓ a person prefers injecting insulin immediately before a meal, **OR**
   - ✓ hypoglycaemia is a problem, **OR**
   - ✓ blood glucose levels rise markedly after meals.
4. **Offer insulin and GLP-1 agonist only with specialist advice and consultant led multidisciplinary support-** refer to GLP 1 mimetic prescribing criteria overleaf.
5. **Toujeo**: Restricted to those patients with uncontrolled HbA1c (>7.5%/ 58 mmol/mol) who require basal insulin and have:-
   - ✓ high insulin dose with significant insulin resistance (>1unit insulin/kg) and/or
   - ✓ Experiencing recurrent episodes of hypoglycaemia.
   - ✓ Or require assistance with their insulin injection administration and in whom using an analogue would reduce injections from BD to ONCE daily, with frequent A&E attendances/hospital admissions for hyperglycaemia & DKA and cannot use their device to inject NPH insulin.
   - ✓ **Specialist initiation only, transferred to the GP only after 3 months when patients have proven benefit in HbA1c and stable with prescribing support.** HbA1c measured by Specialist prior to transfer.
   - ✓ Prescribe by **BRAND** only

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