

## Type 2 Diabetes Blood Glucose Management in Adults – Primary Care Guideline

### Initiating blood glucose lowering medication in Type 2 Diabetes

- Reinforce advice on diet and lifestyle at all stages of management.
- Clinicians should focus on shared decision making as this seeks to ensure that they are responsive to individual patient preferences, needs, and values. Patient's priorities should be a focus and the clinician should present treatment options and information so that patients can participate more actively in their care.
- Individualisation of treatment is important e.g. in an older patient sulphonylureas may be less appropriate due to the increased risk of hypoglycaemia potentially leading to falls and fractures.
- The final drug choice should be based on effectiveness, safety, tolerability, the patient's clinical and personal needs, licensed indications and cost. Use the [Summary of Product Characteristics](#) and the [BNF](#) when making decisions. The table below summarises the different options.
- Agree an individualised HbA1c target based on the patient's needs and circumstances and encourage them to maintain it. Measure in 3 to 6 monthly intervals as appropriate.
- Refer to a specialist when there is a lack of efficacy of treatment, patient has complex medical needs, considering pregnancy or suffering from advanced diabetes complications.
- **Metformin** is typically the first treatment choice. Proper titration is essential:
  - Begin with low-dose metformin (500 mg) taken once per day with meals (breakfast or dinner). Advise patient that they may experience some gastrointestinal (GI) side effect to start with and that it is important to take the medication with food to reduce this risk.
  - After 7 days, if GI side effects have settled, advance dose to 500 mg twice per day (medication to be taken before breakfast and dinner).
  - Increase by 500 mg each week until the maximum effective dose is reached. This is usually 2g daily in divided doses.
  - GI side effects may appear as dose is increased. If these do not settle, decrease to previous lower dose and try to increase the dose again at a later time.
  - Metformin modified release tablets can be tried in patients who cannot tolerate the standard release tablets.
  - Combination products including metformin can improve compliance, however can limit titration ability.

Summary of drug treatment options (for licensed combinations see appendix 1)

Drug	Long Term Safety Data	Use in Renal Impairment	Advantages	Disadvantages	<a href="#">OCCG Formulary</a>	Cost (1m at max dose)
Metformin	CV benefits	eGFR <45: review dose eGFR<30: stop	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Probably decreases CVD events</li> <li>Weight neutral or weight loss</li> <li>Decreases risk of microvascular complications</li> </ul>	<ul style="list-style-type: none"> <li>GI side effects (consider metformin as cause before investigating lower GI symptoms)</li> <li>Vitamin B12 deficiency</li> <li>Lactic acidosis risk (rare)</li> <li>Contraindications: CKD, acidosis, hypoxia, dehydration</li> </ul>	Green – metformin standard release.	<£2
					Brown – metformin MR only for patients intolerant to standard release. Metformin liquid only for patients with swallowing difficulty.	
Gliclazide (and other sulphonylureas)	No significant concerns	Increases risk of hypoglycaemia.	<ul style="list-style-type: none"> <li>Decreases risk of microvascular complications</li> </ul>	<ul style="list-style-type: none"> <li>Hypoglycaemia</li> <li>Weight gain</li> </ul>	Green – Gliclazide	<£5
					Brown – Glipizide, glimepiride, glibenclamide and tolbutamide (unusual regime to use)	
					Black – Gliclazide MR (lack of evidence)	
Alogliptin, Linagliptin (and other DPP4 inhibitors)		Linagliptin safe (including renal replacement therapy). Others reduce dose (eGFR < 30 or 50 depending on	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Well tolerated</li> <li>Can be used in combination with insulin</li> <li>Moderate HbA1c lowering efficacy</li> </ul>	<ul style="list-style-type: none"> <li>Urticaria/angioedema</li> <li>Unproven association with acute pancreatitis</li> <li>May increase heart failure (alogliptin and saxagliptin)</li> </ul>	Green – Alogliptin (first line)	£31-34
					Brown – Saxagliptin, sitagliptin and vildagliptin (not first choice). Linagliptin (for use in renal impairment)	

		drug)				
Pioglitazone	Concerns about heart failure, fracture, and (possibly) bladder cancer	safe	<ul style="list-style-type: none"> <li>No hypoglycaemia</li> <li>Decreases triglycerides</li> <li>Reduces CV events (secondary endpoint data)</li> <li>Can be used in combination with insulin</li> </ul>	<ul style="list-style-type: none"> <li>Weight gain</li> <li>Oedema/heart failure</li> <li>Bone fractures</li> <li>May increase bladder cancer (controversial)</li> <li>Avoid in macular oedema</li> </ul>	Green	<£2
Empagliflozin dapagliflozin Ertugliflozin and canagliflozin	Limited long term data. Concerns about DKA at only moderately elevated blood sugar concentrations.	Dapagliflozin: eGFR <60 - do not use. Cana and empagliflozin: do not start if eGFR < 60. If already on drug continue unless eGFR falls below 45.	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Weight loss</li> <li>Decreases blood pressure</li> <li>Effective at all type 2 diabetes stages</li> <li>Empagliflozin showed reduction of CV death in high risk patients (EMPA-ReG study 2015)</li> <li>Can be used in combination with insulin</li> </ul>	<ul style="list-style-type: none"> <li>Genitourinary infections (Thrush, UTIs)</li> <li>Polyuria (about 300 ml)</li> <li>Volume depletion/hypotension</li> <li>Increases LDL-C</li> <li>Increases creatinine (temporary)</li> <li>Risk of euglycaemic DKA (rare)</li> </ul>	Green Empagliflozin and dapagliflozin first line. Dapagliflozin has shown CV outcome benefit in primary prevention; empagliflozin, in secondary prevention  See <a href="#">SGLT2i checklist</a> , <a href="#">patient information leaflet on DKA risk</a> and <a href="#">OCCG letter to clinicians</a> .  Stop if not successful after 6 months.	Around £36
Lixisenatide, Semaglutide (and other GLP-1 mimetics)	No significant concerns	Liraglutide, Dulaglutide and Semaglutide: eGFR <15: do not use.	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Weight reduction</li> <li>Decreases PPG excursions</li> </ul>	<ul style="list-style-type: none"> <li>GI side effects</li> <li>Rarely associated with acute pancreatitis</li> <li>Increases heart rate</li> <li>Injectable</li> </ul>	Brown <u>Daily</u> Lixisenatide cheapest and so first choice, but in patients with high CV risk consider Liraglutide in light of reduction in mortality.	£50-70

		<p>Lixisenatide: eGFR &lt;30 do not use.</p> <p>Exenatide: eGFR 30-50: use with caution. eGFR &lt;30 do not use.</p>	<ul style="list-style-type: none"> <li>Decreases some CVD risk factors</li> <li>LEADER trial showed liraglutide 1.8mg gave a statistically significant reduction in cardiovascular risk in patients at high CV risk</li> <li>Sustain 6 trial showed semaglutide gave a statistically significant reduction in cardiovascular risk in patients at high CV risk.</li> <li>REWIND trial showed dulaglutide gave a statistically significant reduction in cardiovascular risk in patients at high CV risk.</li> </ul>	<ul style="list-style-type: none"> <li>Training requirements</li> <li>If combining with insulin, consider referral to cDSN team.</li> </ul>	<p>Liraglutide 1.2mg second line (<a href="#">see guideline</a>). Stop if not successful after 6 months (reduction in weight and HbA1c required).</p> <p><u>Once Weekly</u> (only for patients who would gain significant benefit from once weekly injection)</p> <p>Semaglutide – first choice, if eye disease see guidelines Dulaglutide – first choice for those who are not suitable for treatment with semaglutide Exenatide MR – existing patients only.</p> <p><b>Yellow</b> Liraglutide 1.8mg, only on recommendation of a member of the diabetes specialist team.</p>	
Repaglinide and Nateglinide	No significant concerns	Safe (avoid in liver disease)	<ul style="list-style-type: none"> <li>Flexible dosing</li> <li>Decreases PPG excursions</li> </ul>	<ul style="list-style-type: none"> <li>Hypoglycaemia</li> <li>Weight gain</li> <li>Need for frequent dosing</li> </ul>	Brown– consider conversation with specialist before use.	<£6

	No restrictions
	Appropriate for Continuation in Primary Care following specialist recommendation
	Prescribe in Restricted Circumstances
	Specialist Prescribing Only
	Not recommended for use

### Practical Management Points

- Offer structured education to adults with type 2 diabetes and/or their family or carers at the time of diagnosis with annual reinforcement and review. Refer to diabetes education at [diabetes.education@nhs.net](mailto:diabetes.education@nhs.net) ([Diabetes2gether](#) or [Diabetes 4ward.](#))
- Assess patient's risk of foot problems at time of diagnosis. If patient is low risk check annually, for moderate to high risk refer to foot service – [See the Thames Valley Diabetes Footcare Pathway.](#)
- Arrange [eye screening](#) around the time of diagnosis and repeat annually.
- Add medication if lifestyle advice does not reduce blood pressure below 140/80mmHg (below 130/80mmHg if there is kidney, eye or cerebrovascular damage).
- Offer atorvastatin 20 mg for the primary prevention of CVD to people with type 2 diabetes who have a 10% or greater 10-year risk of developing CVD. Estimate the level of risk using the QRISK2 assessment tool. ([local lipid guidelines](#))
- Advise patients on what to do if they are ill. Discuss [sick day rules](#).
- Advise patients on the [DVLA rules](#) on diabetes and driving
- Do not routinely offer self-monitoring of blood glucose unless; the patient is on insulin, their treatment may increase their risk of hypoglycaemia whilst driving or operating machinery, is pregnant, or there is evidence of hypoglycaemic episodes. See [SMBG guideline](#) and [PIL](#).
- Investigate unexplained discrepancies between HbA1c and other glucose measurements. Seek advice from a team with specialist expertise in diabetes or clinical biochemistry.

#### REMEMBER AT EVERY STAGE:

- Reinforce importance of diet and lifestyle choices
- Check adherence and reinforce the importance of taking medication
- Assess hypoglycaemia risk
- Optimise BP and cholesterol management
- Refer to patient structured education
- Consider referral to Medicines Use Review (MUR) or New Medicines Service (NMS) at a pharmacy

## References

1. [NG28 \(Type 2 diabetes in adults: management\)](#)
2. [NG19 \(diabetes foot care\)](#)
3. [NICE TA 390 \(Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes\)](#)
4. [NICE TA 336 \(Empagliflozin in combination therapy for treating type 2 diabetes\)](#)
5. [NICE TA 315 \(Canagliflozin in combination therapy for treating type 2 diabetes\)](#)
6. [NICE TA 288 \(Dapagliflozin in combination therapy for treating type 2 diabetes\)](#)
7. [BNF 70](#)
8. [Summary of Product Characteristics \(SPC\)](#)
9. [ADA/European Association for the Study of Diabetes \(EASD\), January 2015, Position Statement on Management of Hyperglycemia in Type 2 Diabetes](#)
10. [The Alphabet Strategy for Diabetes Care: a patient-centred approach to multifactorial intervention](#)

**Appendix 1: Licensed combinations of anti-diabetic drugs** (correct as of July 2019, check each [SPC](#) for most up to date information)

Drug	Licensed Combinations
Metformin	Monotherapy or in combination with other oral anti-diabetic agents or insulin.
Gliclazide	Treatment of type 2 diabetes.
Sitagliptin	Monotherapy; Dual therapy with metformin, sulfonylurea or pioglitazone; Triple therapy with metformin & sulfonylurea or pioglitazone; Insulin (with or without metformin).
Alogliptin	Licensed in combination with other glucose lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.
Vildagliptin	Monotherapy; Dual therapy with metformin, sulfonylurea or pioglitazone; Triple therapy with metformin & sulfonylurea; Insulin (with or without metformin)
Linagliptin, Saxagliptin	monotherapy when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment. combination therapy in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control
Pioglitazone	Monotherapy; Dual therapy with metformin or sulfonylurea; Triple therapy with metformin & sulfonylurea; Insulin (if metformin not appropriate)
Dapagliflozin, Empagliflozin, Canagliflozin, Ertugliflozin	Monotherapy if metformin is inappropriate; in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.
Acarbose	Recommended for the treatment of non-insulin dependent (NIDDM) diabetes mellitus in patients inadequately controlled on diet alone, or on diet and oral hypoglycaemic agents.
Lixisenatide	Oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control.
Dulaglutide	Monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications. Add-on therapy in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control,
Liraglutide, semaglutide	Treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise as monotherapy when metformin is considered inappropriate due to intolerance or contraindications, or in addition to other medicinal products for the treatment of diabetes.
Exenatide	Dual therapy with metformin, a sulfonylurea or pioglitazone; Triple therapy with metformin & a sulfonylurea or metformin & pioglitazone.



**Oxfordshire  
Clinical Commissioning Group**