

## **Blood glucose management in type 2 diabetes in adults**

### **Introduction**

The guidance has been developed to support the implementation of National Institute for Health and Care Excellence (NICE) diabetes guidelines (NG28) to deliver high quality care and health outcomes for people (aged 18 and over) with diabetes in primary care, across the WEL (Newham, Tower Hamlets and Waltham Forest) CCGs. This guidance summarises NICE guidelines, NICE Technology Appraisal 390 and local recommendations to implement evidence-based cost effective use of antidiabetic drugs. It should be used in conjunction with Summary of Product Characteristics of the specific medicines being prescribed.

The publication of updated NICE guidelines in December 2015 and a review of local prescribing identified the need to develop local guidelines to support clinicians to manage the treatment of type 2 diabetes especially with the introduction of several new drugs in recent years.

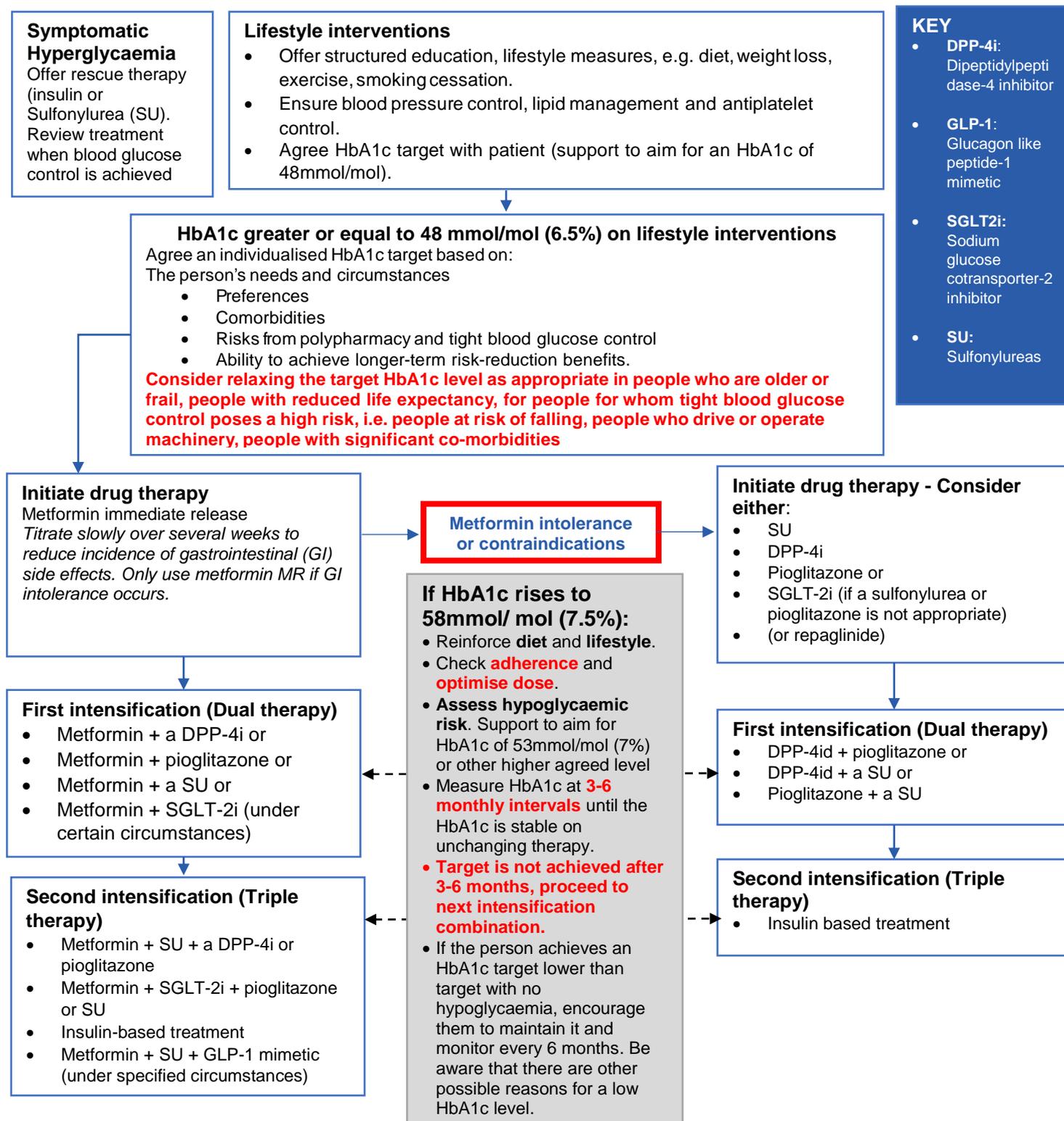
NICE updated the guidance on Type 2 diabetes in December 2015 and further updated in May 2017 based on new safety recommendations, indications for newer oral antidiabetic therapies, licensed combinations for licensed individual medicines and the potential impact of patent expirations on the health-economy<sup>1</sup>. It outlines a simplified approach (algorithm 1) to blood glucose management.

The WEL guidance reinforces NICE recommendation to use metformin where appropriate as the first line, the role of modified release (MR) metformin and its combination products as well as the place in therapy of the newer antidiabetic drugs.

### **Key recommendations**

- Regularly discuss and reinforce lifestyle interventions (e.g. stopping smoking, losing weight, exercising, and healthy eating) and blood pressure control. Refer patients to a structured education programme
- When starting oral hypoglycaemic therapy, agree an individualised HbA1c target tailored to individual needs and circumstances. Consider their personal preferences, comorbidities, risks from polypharmacy and their ability to benefit from long term interventions and quality of life. Such an approach is especially important in the context of multimorbidity.
- Good glucose control in the first 10 years of diagnosis appears to offer some reduction in complications after 10 years of diagnosis resulting in a legacy effect.
- Reassess the person's needs and circumstances at each review and consider stopping any medicines that are not effective.
- Where more than one drug from the same class is appropriate, choose the option with the lowest acquisition cost.
- Support patients to achieve their agreed HbA1c levels. Measure HbA1c levels at 3 - 6 monthly intervals until HbA1c is stable then at six monthly intervals once stable. If HbA1c, lower than target is achieved without hypoglycaemia, encourage them to maintain it if safe to do so.
- If a patient's target HbA1c is not adequately achieved after six months, as per the treatment algorithm (see Figure 1), Clinicians should review and intensify treatment options. Glucose lowering agents which are not tolerated, should be de-prescribed.
- Consider relaxing the target HbA1c level in people who are older or frail, people with reduced life expectancy, for people for whom tight blood glucose control poses a high risk, i.e. people at risk of falling, people who drive or operate machinery and people with significant co-morbidities
- Refer to the Clinical Effectiveness Group (CEG) Summary Guidelines Type 2 diabetes: Reducing Hypoglycaemia January 2017 to support you in managing patients with hypoglycaemia.
- Refer to the current Summary of Product Characteristics (SPC) for further information on the properties of the available glucose lowering agents listed in this guidance. Note that the content of individual SPC's are subject to constant revision. Clinicians are advised to ensure they are accessing the current version of an SPC (available via the Electronic Medicines Compendium (eMC) at [www.medicines.org.uk](http://www.medicines.org.uk))
- **The information contained herein is for guidance purposes only. Clinicians are expected to take guideline recommendations into account when exercising their clinical judgement. However, this guidance does not override the individual responsibility of making decisions appropriate to the circumstances of the individual patient.**

**Figure 1 Treatment algorithm for the blood glucose management in type 2 diabetes in adults** <sup>(1)</sup>



**Table 1: Patient considerations in selecting a class of medication** <sup>(2)</sup>

	Metformin	SU	Pioglitazone	DPP-4-i	SGLT2-i	GLP-1 receptor agonist	Insulin
<b>Efficacy</b>	High	High	High	Intermediate	Intermediate	High	Highest
<b>Hypoglycaemic risk</b>	Low	Moderate	Low	Low	Low	Low	High
<b>Weight</b>	Neutral/loss	Gain	Gain	Neutral	Loss	Loss	Gain
<b>Side effects</b>	GI/ lactic acidosis	Hypoglycaemia	Oedema, heart failure, bladder cancer, bone fracture. <b>Avoid in patients with history of cancer</b>	Rare	GU, dehydration	GI	Hypoglycaemia
<b>Cost</b>	Low	Low	Low	High	High	High	Variable

**Table 2: Summary of properties of available glucose lowering agents [Refer to individual Summaries of Product Characteristics for further details]** <sup>(3) (4) (5)</sup>

Class (or specific treatment in class)	Useful information	Primary action	Advantages	Formulary product	Renal/Hepatic dose adjustment	Shared care/ Transfer of care guidelines
Biguanides	Symptoms of peripheral neuropathy (check Vit B 12 levels) Renal  Can be used in both monotherapy, dual, triple therapies and in combination with insulin.	↓ Hepatic glucose production	<ul style="list-style-type: none"> <li>• Extensive experience of use</li> <li>• No Hypoglycaemia</li> </ul>	<b>FORMULARY FIRST LINE: MEFORMIN</b> (slow introduction of standard metformin formulation)	<b>RENAL</b> Dose adjustment required. Reduce dose if eGFR is less than 45 ml/min/1.73 m <sup>2</sup> and stop if eGFR is less than 30 ml/min/1.73 m <sup>2</sup>	Not required for primary care prescribing
				<b>METFORMIN MODIFIED RELEASE</b> (For patients who have persistent gastro-intestinal (GI) side effects despite the slow introduction of standard metformin formulation)	<b>HEPATIC</b> Discuss benefits of therapy with patients in mild to moderate liver impairment so informed decision can be made on whether to continue or stop Metformin.	
Sulfonylureas	Can be used if a rapid response is required as there is a lower risk of hypoglycaemic symptoms.  Educate patient about the risk of hypoglycaemia.  Avoid in pregnancy/breastfeeding  Should not be used with short, rapid or pre-mixed insulins.	↑ Insulin secretion	<ul style="list-style-type: none"> <li>• Extensive experience of use</li> </ul>	<b>FORMULARY FIRST LINE: GLICLAZIDE</b> (standard release)	<b>RENAL</b> Caution in eGFR between 30-60 ml/min/1.73 m <sup>2</sup> Contraindicated for eGFR less than 30mL/ min.	Not required for primary care prescribing
				<b>GLICLAZIDE MODIFIED RELEASE</b> (If poor concordance but no hypos to gliclazide)	<b>HEPATIC</b> Contra-indicated in severe hepatic insufficiency.	
				<b>GLIMEPRIDE</b> (To reduce pill burden)	<b>RENAL</b> Caution in eGFR between 30-60 ml/min/1.73 m <sup>2</sup> Contraindicated for eGFR less than 30mL/ min.  <b>HEPATIC</b> Contra-indicated in severe hepatic insufficiency.	

Class (or specific treatment in class)	Useful information	Primary action	Advantages	Formulary product	Renal/Hepatic dose adjustment	Shared care/ Transfer of care guidelines
Meglitinides	Do not use repaglinide in combination with sulfonylureas  Avoid in pregnancy/breastfeeding	↑ Insulin secretion	<ul style="list-style-type: none"> <li>Dosing flexibility</li> <li>Reduces post-prandial glucose excursions</li> </ul>	<b>REPAGLINIDE</b>	No adjustment required in renal impairment but no evidence available for dialysis patients, seek specialist input.	Not required for primary care prescribing
Thiazolidinediones	Avoid in pregnancy/breastfeeding and acute porphyrias Do not use in patients with either: <ul style="list-style-type: none"> <li>Heart failure</li> <li>Current or a history of bladder cancer</li> <li>Uninvestigated macroscopic haematuria.</li> </ul>	↑ Insulin sensitivity	No hypoglycaemia  ↑ HDL ↓ Triglycerides	<b>PIOGLITAZONE</b>	No adjustment required in renal or mild to moderate hepatic impairment.  Contraindicated in severe hepatic disorder	Not required for primary care prescribing
Dipeptidyle peptidase-4 (DPP-4) inhibitors	Weight neutral	↕ Insulin secretion Glucagon secretion	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Weight neutral</li> </ul>	<b>FORMULARY CHOICES: SITAGLIPTIN</b>	<p><b>RENAL</b> eGFR 30-50 ml/min/1.73 m<sup>2</sup> Reduce to 50mg eGFR 15-29 ml/min/1.73 m<sup>2</sup> Reduce to 25mg eGFR &lt;15 ml/min/1.73 m<sup>2</sup> or on dialysis reduce to 25mg treatment may be administered</p> <p>Assessment of renal function is recommended prior to initiation and periodically thereafter.</p> <p><b>HEPATIC</b> Has not been studied in patients with severe hepatic impairment. Exercise care</p>	Not required for primary care prescribing
				<b>LINAGLIPTIN</b> (for renal patients)	No dose adjustment or reduction needed for both renal and hepatic impairment. Limited experience of use in hepatic impairment.	

Class (or specific treatment in class)	Useful information	Primary action	Advantages	Formulary product	Renal/Hepatic dose adjustment	Shared care/ Transfer of care guidelines
				<b>ALOGLIPTIN</b>	No dose adjustment or reduction needed for renal impairment and mild to moderate hepatic impairment (Child-Pugh scores of 5 to 9). Limited experience of use in severe hepatic impairment (Child-Pugh scores > 9) therefore not recommended.	
				<b>VILDAGLIPTIN</b>	<p><b><u>RENAL</u></b>            No dose adjustment is required in patients with mild renal impairment (eGFR <math>\geq</math> 50 ml/min). In patients with moderate or severe renal impairment or with end-stage renal disease (ESRD), the recommended dose of Galvus is 50 mg once daily. Assessment of renal function is recommended prior to initiation and periodically thereafter.</p> <p><b><u>HEPATIC</u></b>            Should not be used in patients with hepatic impairment.</p>	

Class (or specific treatment in class)	Useful information	Primary action	Advantages	Formulary product	Renal/Hepatic dose adjustment	Shared care/ Transfer of care guidelines
Sodium-glucose co-transporter 2 inhibitor (SGLT-2i)	<ul style="list-style-type: none"> <li>Risk of diabetic ketoacidosis (DKA-specialist oversight). Cases of life-threatening DKA have been reported. If DKA is suspected or diagnosed, SGLT-2 inhibitors should be discontinued.</li> <li>Use in caution with thiazide or loop diuretics.</li> <li>Monitor renal function prior to initiation and at least yearly thereafter.</li> </ul> <p>Canagliflozin may increase the risk of lower-limb amputation (mainly toes) in patients with type 2 diabetes (4).</p>	By inhibiting SGLT2, reduces reabsorption of filtered glucose and lowers the renal threshold for glucose	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Reduces weight</li> <li>Reduces blood pressure</li> </ul>	<b>FORMULARY FIRST LINE: EMPAGLIFLOZIN</b> (renal outcome/ CVD benefits)- <b>more specialist views needed</b>	<b>RENAL</b> Empagliflozin should be discontinued when eGFR is persistently below 45 ml/min/1.73m <sup>2</sup>  In patients tolerating empagliflozin whose eGFR falls persistently below 60 ml/min /1.73m <sup>2</sup> the dose of empagliflozin should be adjusted to or maintained at 10mg once daily  <b>HEPATIC</b> Not recommended in severe hepatic impairment.	Specialist initiated (including any specialists in primary care with appropriate experience and training) and primary care to continue with either shared care or transfer of care documentation.
				<b>DAPAGLIFLOZIN</b>	<b>RENAL</b> If renal function falls below CrCl < 60 ml/min or eGFR < 60 ml/min/1.73 m <sup>2</sup> , dapagliflozin treatment should be discontinued  <b>HEPATIC</b> Initial dose 5mg in severe impairment, increased according to response to a maximum of 10mg.	
				<b>CANAGLIFLOZIN</b>	<b>RENAL</b> Do not initiate in eGFR < 60 mL/min/1.73 m <sup>2</sup> or CrCl < 60 mL/min. In patients tolerating canagliflozin whose eGFR falls	

Class (or specific treatment in class)	Useful information	Primary action	Advantages	Formulary product	Renal/Hepatic dose adjustment	Shared care/ Transfer of care guidelines
					<p>persistently below 60 mL/min/1.73 m<sup>2</sup> or CrCl 60 mL/min, the dose of canagliflozin should be adjusted to or maintained at 100 mg once daily.</p> <p>Discontinue in eGFR below 45 mL/min/1.73 m<sup>2</sup> or CrCl persistently below 45 mL/min.</p> <p>Canagliflozin should also not be used in patients with end stage renal disease (ESRD) or in patients on dialysis.</p> <p><b>HEPATIC</b> Not recommended in severe hepatic impairment</p>	
GLP-1 mimetics	<p>Add as part of triple therapy ONLY if</p> <ul style="list-style-type: none"> <li>BMI is <math>\geq 35\text{kg/m}^2</math> in people of European descent (adjust for ethnic groups) and there are specific psychological or medical problems associated with high body weight</li> <li>BMI <math>&lt; 35\text{kg/m}^2</math> and insulin is unacceptable because of occupational implications or weight loss would benefit other co-morbidities.</li> </ul> <p>Avoid in pregnancy and breastfeeding.</p>	<p>↑ Insulin secretion</p> <p>↓ Glucagon secretion</p> <p>↓ Slows gastric emptying</p> <p>↑ Satiety</p>	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia</li> <li>Reduces weight</li> </ul>	<p><b>FORMULARY FIRST LINE:</b> <b>LIRAGLUTIDE</b></p> <hr/> <p><b>DULAGLUTIDE</b> (hepatic)</p>	<p><b>RENAL</b> Not recommended for patients with eGFR less than 30 ml/min/1.73m<sup>2</sup></p> <p><b>HEPATIC</b> Not recommended-limited experience</p> <hr/> <p><b>RENAL</b> Not recommended for patients with eGFR less than 30 ml/min/1.73m<sup>2</sup></p> <p><b>HEPATIC</b> No dosage adjustment</p>	<p>Specialist initiated (including any specialists in primary care with appropriate experience and training) and primary care to continue with either shared care or transfer of care documentation.</p>

Class (or specific treatment in class)	Useful information	Primary action	Advantages	Formulary product	Renal/Hepatic dose adjustment	Shared care/ Transfer of care guidelines
	<p>Discontinue if pancreatitis suspected. Discontinue if reduction in HbA1c is less than 1% (11 mmol/mol) and there is less than 3% weight loss after 6 months (only HbA1c reduction required for dual therapy).</p> <p>Only offer a GLP-1 mimetic in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team.</p>			<p><b>EXENATIDE (BYDUREON®) INJECTION</b></p>	<p><b><u>RENAL</u></b> Not recommended for patients with end stage renal disease, moderate renal impairment or severe renal impairment.</p> <p><b><u>HEPATIC</u></b> No dosage adjustment</p>	

## Type 2 Diabetes- Insulin

**Insulins should only be initiated by practitioners who have undertaken the appropriate training.**

Insulin initiation should be considered in line with NICE CG87, for patients with type 2 diabetes, whose individual targets for glycaemic control are not achieved on optimum oral treatments. NICE recommendations are to intensify treatment for patients with an HbA1c concentration greater than 58mmol/mol (7.5%); consider a range of options to achieve this. Prioritise insulin initiation for those patients at highest risk especially of microvascular complications over time, especially for younger patients with the highest HbA1c concentrations. Individual treatment targets should be agreed but ideally aim for HbA1c of 53mmol/mol (7%), avoiding hypoglycaemia.

<b>Key Prescribing Points</b> <sup>(5)</sup>	
<p><b>Do's</b> </p> <ul style="list-style-type: none"> <li>• Prescribe insulins by <b>brand</b></li> <li>• Include the <b>insulin dose</b> in the direction of the prescription</li> <li>• Prescribe via the <b>subcutaneous</b> route</li> </ul>	<p><b>Don'ts</b> </p> <ul style="list-style-type: none"> <li>• Use abbreviations such as 'U' or 'IU'</li> <li>• Use "as directed" or "prn" as directions</li> </ul>

### Summary of NICE Guideline (NG28)- Insulin Therapy <sup>(6)</sup>

**Step 1:** Continue with Metformin and review the need for other HBA<sub>1c</sub> lowering drugs. <sup>(6)</sup>

**Step 2:** Select the most appropriate insulin for initiation <sup>(6)</sup>

Begin with Human NPH insulin taken at bedtime or twice daily according to need:

- Humulin I
- Insulatard
- Insuman basal

**Step 3:** Monitor people on insulin for the need to change the regimen <sup>(6)</sup>

If patients are not controlled on large doses of once daily insulin (i.e. greater than 0.5 units of insulin per kg of body weight or >50 units of once daily insulin) consider the benefits of changing to twice daily pre-mixed insulin.

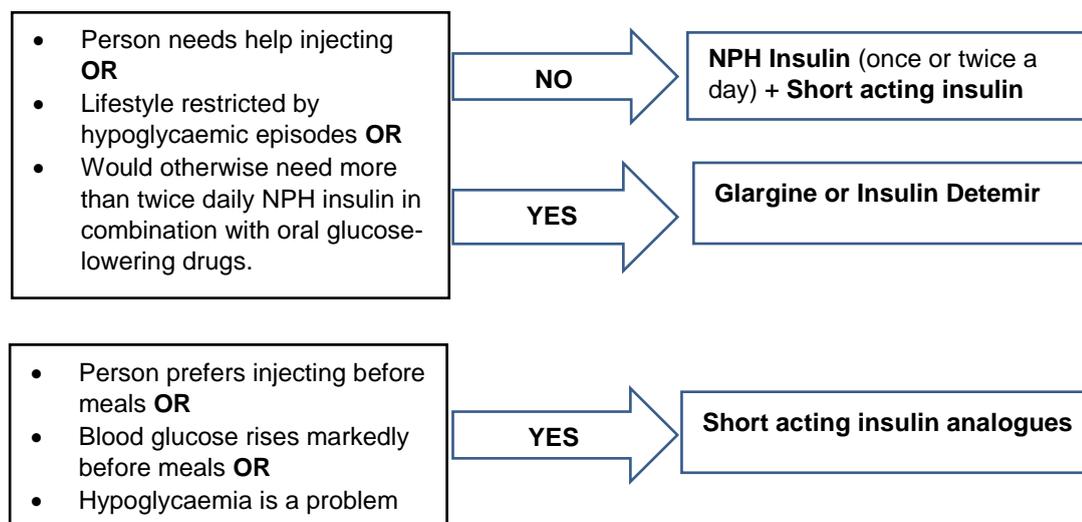
Consider switching to insulin glargine (i.e. Abasaglar ®) or insulin detemir or from NPH insulin in adults with type 2 diabetes:

- who do not reach their target HbA1c because of significant hypoglycaemia **or**
- who experience significant hypoglycaemia on NPH insulin irrespective of the level of HbA1c reached **or**
- who cannot use the device needed to inject NPH insulin but who could administer their own insulin safely and accurately if a switch to one of the long-acting insulin analogues was made **or**
- who need help from a carer or healthcare professional to administer insulin injections and for whom switching to one of the long-acting insulin analogues would reduce the number of daily injections.

Insulin Glargine of choice: Abasaglar ® for new patients being initiated on insulin glargine.

Insulin Degludec is a neutral, soluble, ultra-long acting insulin analogue which is available in 100 units/ml and a higher strength 200 units/ml.

### Continue Metformin + review need for other HbA<sub>1c</sub> lowering drugs



## References

1. **PrescQIPP.** Treatment Algorithm for Type 2 diabetes in adults. *Type 2 diabetes webkit*. [Online] June 2016. [Cited: 18 10 2017.] <https://www.prescqipp.info/resources/send/323-diabetes-oral-hypoglycaemics/2940-attachment-1-treatment-algorithm-for-type-2-diabetes-in-adults>.
2. **NICE.** NG 28, Type 2 diabetes in adults: management. *NICE*. [Online] December 2015. <https://www.nice.org.uk/guidance/ng28>. NG28.
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## Approval and Version Control

<b>Guidelines: Pharmacological management of hyperglycaemia in Type 2 Diabetes</b>		<b>Issue date:</b> 07/04/18 <b>Review Date:</b> 07/03/20	
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<b>Name</b>	<b>Position</b>		<b>Organisation</b>
Maninder Kaur Singh	Lead Prescribing Advisor		Newham CCG
Anisha Sharma	Prescribing Advisor		Waltham Forest CCG
Shena Chauhan	Senior Prescribing Advisor		Tower Hamlets CCG
Roisin Wright	Diabetes specialist Nurse		Barts Health NHS Trust and Tower Hamlets CCG
Bola Sotubo	Assistant Director of Medicines Management		Newham CCG
Dr Munir Ali-Zubair	Clinical Lead for Diabetes		Waltham Forest CCG
Dr. Shazadah Khan	GP Lead for Diabetes,	Newham CCG	
<b>Consultation with:</b> Waltham Forest CCG Diabetes Strategy Board Newham Diabetes Partnership Barts Health Trust Diabetes Network East London Foundation Trust (ELFT) Newham Community Health Services (ELFT) Barts Health Trust Drugs and Therapeutics Committee			
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<b>Version</b>	<b>Date Implemented</b>	<b>Details of significant changes</b>	
0.1	17 <sup>th</sup> November 2014	Draft version	
0.2	June 2017	Changes made after consultation with key stakeholders	
0.3	21 <sup>st</sup> July 2017	Further changes made after to format after Diabetes TAF meeting	
0.4	10 August 2017	Agreed changes and order from PrescQIPP algorithm and tables	
0.5	21 August 2017	Agreed changes as part of August Diabetes Task and Finish Group meeting	
0.6	18 <sup>th</sup> September 2017	Amendments made based on stakeholder comments	
0.7	20 <sup>th</sup> September 2017	Tower Hamlets (TH) comments added	
0.8	16 <sup>th</sup> October 2017	Comments from TH considered and amended as part of the Diabetes Task and Finish Group.	
0.9	7 <sup>th</sup> Nov 2017	Comments from Newham considered and amended for circulation to the Diabetes Task and Finish Group	
1.0	22 <sup>nd</sup> Nov 2017	Final check for accuracy post approval by WEL MOC	
1.1	13 <sup>th</sup> March 2018	Changed Dulaglutide – removed hospital only prescribing	