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NHS Southwark NHS Lambeth

Flowchart for the Management of Blood Glucose in Type 2 Diabetes Mellitus

Aim for target HbA1c 6.5-7.5% (or agreed individualised targets)
Target set based on macrovascular and microvascular complications. Higher target if at risk of hypoglycaemia. Avoid intensive management to HbA1c < 6.5%

Lifestyle changes – diet, alcohol, physical activity, smoking cessation, refer to DESMOND (see box 3)

BOX 1: HbA1c can be monitored 6 monthly once stable.

2-6 monthly HbA1c – target?

N / Y

BMI < 22
or very symptomatic (polyuria, polydipsia)
or significant weight loss
or ketones

Refer to specialist care

BMI >22

Creatinine > 150µmol/l or eGFR < 40ml/min

Y

Sulphonylurea
See point 7 in box 3

2-6 monthly HbA1c – target?
Keep HBA1c above 6.5% but below 7.5% - see point 9, box 3

Y / N

N

Metformin
Nb: Metformin MR may be considered if conventional release metformin not tolerated. See point 2 in box 3 and overleaf.

2-6 monthly HbA1c – target?

Y / N

Add sulphonylurea
See point 7 in box 3

2-6 monthly HbA1c – target?
Keep HBA1c above 6.5% but below 7.5% - see point 9, box 3

Y / N

BOX 2: Metformin and the kidney

- Do not start metformin if eGFR <40ml/min – seek specialist advice.
- Review metformin dose if Cr>130µmol/l or eGFR <45ml/min
- Stop/avoid metformin if Cr>150µmol/l or eGFR <30ml/min
- Patients with advanced cardiac disease may be at risk of sudden deterioration of renal function.

BOX 3: GENERAL COMMENTS

1. Increase medication stepwise to maximum tolerated dose.
2. Educate patient to self-titrate metformin over several weeks to minimise risk of gastro-intestinal (GI) side effects. If metformin not tolerated despite slow titration & taking after meals, consider metformin MR.
3. Monitor for side effects of medication. If at any step patient cannot tolerate drug or drug is contraindicated, move to the next step (see flow chart)
4. Metformin may be considered in obese patients even if HbA1c satisfactory
5. Consider a sulphonylurea first line if not overweight or a rapid therapeutic response is required due to hyperglycaemic symptoms
6. Consider a rapid-acting insulin secretagogue for those with erratic lifestyles.
7. Consider sitagliptin or a glitazone if significant risk of hypoglycaemia with a sulphonylurea.
8. Consider acarbose for patients unable to use other oral hypoglycaemic agents
9. The ACCORD and ADVANCE studies[7] found intensive glucose control (HbA1c <6.5%) did not offer any advantage with regard to major CV events. NICE cautions against the use of highly intensive management strategies to achieve levels of <6.5%.
10. The full version of the NICE guideline[1] notes that as glitazones worked in combination with metformin, fixed-dose combination products would be suitable for use where there were no cost implications or where improved drug adherence issues increase cost effectiveness.
11. DESMOND: **D**iabetes **E**ducation and **S**elf **M**anagement for **O**ngoing and **N**ewly **D**iagnosed - a structured education programme.

CONSIDER ADDING EITHER:

- A glitazone

OR

- Sitagliptin (this is the gliptin on the local formulary)

If needed, seek specialist advice via telephone on initiation of glitazone or sitagliptin.

OR REFER FOR:

- **Insulin therapy**
- **Exenatide**

ORAL HYPOGLYCAEMICS - Refer to product literature for full list of doses, cautions, contraindications, and drug interactions[3].

Agent	Recommended dose range (BNF Sept 2008)	Cost of 4 weeks treatment (£)	Comments
BIGUANIDE *Metformin normal release*	Start at 500mg daily and titrate dose 2-6 weekly Max 3g daily, most physicians limit dose to 2.5g daily Doses are normally taken with meals (breakfast, lunch, dinner)	500mg tds - - - ---------- £2.79 850mg tds----------£2.01	• Contraindicated in renal impairment – caution in patients at risk of sudden deterioration in kidney function • Doses in company literature may differ to BNF doses. • Metformin normal release is **first line** choice • NICE recommend a trial of metformin M/R in patients unable to tolerate & continue metformin due to GI side effects • Not suitable if normal release dose is greater than 2g daily
Metformin modified release (M/R)	Initially 500mg once daily, increased every 10-15 days, max. 2g once daily with evening meal. Patients taking less than 2g daily of normal release can start on same daily dose of M/R	1.5g daily----------£9.21 2g daily----------£12.28	
SULPHONYLUREAS • Avoid sulphonylureas where possible in severe hepatic and renal impairment and in acute porphyria. Educate patient about risks of hypoglycaemia, particularly if he or she has renal impairment			
Gliclazide	Initially 40-80mg daily, titrate according to response. Max. 320 mg daily.	80mg od----------£1.08 160mg daily-----£2.16 160 mg bd --------£4.32	• Up to 160mg daily can be taken as a single dose, with breakfast. • Doses higher than this should be divided
Glipizide	Initially 2.5-5mg daily, Titrate dose according to response. Max. 20mg daily.	2.5mg daily--------£1.48 5mg daily----------£1.26 10mg daily----------£2.52	• Doses are taken just before breakfast or lunch. • Up to 15mg daily can be taken as a single dose. Divide higher doses.
GLITAZONES – initiation on specialist advice only (e.g via telephone) - this may be a GP with a specialist interest or a diabetologist. • Contraindicated in hepatic impairment, patients with heart failure (HF) or a history of HF. Incidence of HF is increased when glitazones are combined with insulin; rosiglitazone is not licensed for use with insulin[4]. Closely monitor patients during treatment with insulin and a glitazone for signs and symptoms of fluid retention, including weight gain or oedema. Rosiglitazone contra-indicated in acute coronary syndrome and is not recommended in patients with ischaemic heart disease and/or peripheral arterial disease[5]. Rosiglitazone might be associated with a small increased risk of cardiac ischaemia, particularly in combination with insulin; rosiglitazone should be used in patients with previous or current ischaemic heart disease **only** after careful evaluation of individual risk. Glitazones should be avoided in patients with **high cardiovascular risk** e.g.: estimated risk of future MI > 20% in 10 years; past history of cardiovascular disease/ankle oedema, suboptimal blood pressure or lipid control, microalbuminuria[6]. • Glitazones should not be started or continued in those at high risk of fracture. • Only consider triple therapy with metformin and sulphonylurea in patients where insulin is inappropriate (limited role due to likely failing insulin release at this stage) • Monitor liver function before treatment, and then periodically thereafter e.g. two months after initiation, then at 6 months, then 6 monthly after that. Do not initiate treatment if ALT >2.5 X upper limit of normal (ULN) or any evidence of liver disease. During therapy, if ALT increases to 3 X ULN, reassess liver enzymes ASAP. If ALT remains >3 X ULN, discontinue therapy. • May be preferable to sitagliptin if there is marked insulin insensitivity, sitagliptin is contra-indicated, or a poor response or intolerance to sitagliptin was observed in the past. • Continue glitazone only if there is a reduction of ≥0.5% in HbA1c in 6 months		
Pioglitazone	15-30mg once daily, increased to a max. of 45mg daily according to response	15mg daily------£14.25 30mg daily------£33.25 45 mg daily------£36.96	In patients administered rosiglitazone in combination with a sulphonylurea, an increase in rosiglitazone to 8 mg/day should be undertaken cautiously following appropriate clinical evaluation to assess the patient's risk of developing adverse reactions relating to fluid retention. This should also be borne in mind for pioglitazone[2].
Rosiglitazone	Initially 4mg daily, when used in combination with metformin, the dose can be increased to 8mg daily (in 1 or 2 divided doses) after 8 weeks according to response.	4mg daily--------£20.00 8mg daily--------£30.00	
GLIPTINS – initiation on specialist advice only (e.g via telephone) - this may be a GP with a specialist interest or a diabetologist. **NOTE:** Sitagliptin is on the local hospital (GSTFT, KCH and UHL) joint formulary • Continue gliptin only if there is a reduction of ≥0.5% in HbA1c in 6 months • Only consider triple therapy with metformin and sulphonylurea in patients where insulin is inappropriate • May be of particular benefit in patients where significant weight gain has occurred/expected with insulin (or insulin refused) and in whom exenatide is contra-indicated or refused • May be preferable to glitazones in patients where weight gain would cause significant problems, or a glitazone is contra-indicated or not tolerated/poor response		
Sitagliptin	100mg daily, with or without food	100mg daily-----£33.26	Avoid in moderate to severe renal impairment (CrCl<50ml/min)

WHEN TO REFER PATIENTS:

1. Acutely unwell patients (these patients may require insulin urgently, refer to specialist service)
   - Severe hypoglycaemia
   - Rapid weight loss
   - Urinary ketones
   - Dehydration
2. Patients with advanced cardiac disease or hepatic impairment
3. Referral for insulin start in those with sub-optimal control on maximal tolerated oral agents.
4. Pregnant women, urgent referral to diabetes antenatal clinic

References:

1. NICE Type 2 Diabetes, May 2009 available via www.nice.org.uk
2. Expert opinions of diabetologists and diabetes nurses from Guy's and St Thomas' foundation Trust and King's College Hospital Foundation Trust
3. Summary of Product Characteristics for metformin and metformin MR, sulphonylureas, glitazones and sitagliptin available via www.medicines.org.uk
4. Personal communication with GlaxoSmithKiine Medical Information Department 30.12.09
5. Prescribing and Clinical Effectiveness Newsletter, Derbyshire PCT. October 2009. available at: http://www.ukmicentral.nhs.uk/therapeu/pace/PACE0807.pdf
6. Southwark PCT Medicines Update: Guidance on the use of glitazones, October 2007
7. NPCi blog on ACCORD and ADVANCE studies, available at: http://www.npci.org.uk/blog/?p=147

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