The management of type 2 diabetes: Newer oral hypoglycaemics and antidiabetic drugs

In this briefing we reinforce the current NICE recommendation to use metformin where appropriate as first line treatment in patients requiring oral medication for type 2 diabetes.

Key recommendations

- Regularly discuss and (where appropriate) manage lifestyle interventions (e.g. stopping smoking, losing weight, taking more exercise), and control blood pressure. Refer patient to a structured education programme if available.[1]
- When starting oral hypoglycaemic therapy, agree an individualised HbA1c target that is tailored to the patients needs and circumstances. Take into account their personal preferences, comorbidities, risks from polypharmacy and their ability to benefit from long term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity. Reassess the person's needs and circumstances at each review and think about whether to stop any medicines that are not effective.[1]
- Prescribe metformin (unless contra-indicated or not tolerated or a rapid response is required) as first line therapy for all new patients requiring medication; titrate the dose adequately to avoid metformin intolerance.[1]
- Only consider a trial of modified release metformin if patients have persistent gastro-intestinal (GI) side effects despite the slow introduction of the standard metformin formulation. A short trial of modified release metformin should be considered before using aternative treatments.[1]
- A sulphonylurea, dipeptidyl peptidase-4 (DPP-4) inhibitor, pioglitazone or an SGLT-2 inhibitor (if a sulfonylurea or pioglitazone is not appropriate) can be considered for monotherapy, if metformin is contra-indicated or not tolerated.[1,2]
- Base choice on effectiveness, safety (including hepatic and renal monitoring), tolerability, person's individual circumstances, preferences, needs, available licensed indications and cost. For first and second intensification options see algorithm 1. If two drugs in the same class are appropriate, choose the option with the lowest acquisition cost.[1]
- Do not offer or continue pioglitazone if the person has heart failure or a history of heart failure, hepatic impairment, diabetic ketoacidosis, current, or a history of bladder cancer, uninvestigated macroscopic haematuria. Review safety and efficacy every 3 - 6 months to ensure that only patients that are deriving benefit continue to be treated.[1]

Background

The updated NICE guidance outlines a simpler three stage approach to the management of blood glucose. There is strong evidence on the use of metformin and to date, research has largely focussed on metformin combinations.[1] Newer agents should be used according to clear guidance and a treatment algorithm and licenced indications after a trial of metformin as monotherapy has been unsuccessful (after proper titration of doses). Detemir and glargine (but not degludec) are advised as alternatives to NPH insulin in specified circumstances. See algorithm 1, attachment 1.

Treatment compliance should be assessed at every opportunity and information on lifestyle measures should regularly be given to patients.[1]

Savings (ePACT February to April 2016)

Across England and Wales, over £98 million is spent annually on metformin. An average of 54 % of all prescriptions for antidiabetic drugs were prescribed as metformin which accounts for 29% of the cost for antidiabetic drugs.

If metformin prescribing met the level that the top 25th centile are achieving then the potential savings would be over **£13.7 million, which equates to £22,632 per 100,000 patients.**

£45.5 million is spent annually across England on modified release metformin. **Over £7.5 million could be saved annually by switching 50% of metformin MR patients to immediate release metformin. This equates to £12,337 per 100,000 patients.**

Table 1: Oral antidiabetic drug (usual or maximum dose), cost and NICE threshold for continuing treatment[1]

Anti-diabetic drug (usual or maximum dose)	Cost/28 days[3,4]	Criteria and threshold for stopping or reviewing treatments
Metformin 500mg tablets (2g daily) Metformin modified release 1g tablets (2g daily)	£3.48 - £8.52	Initiate metformin if eGFR >45ml/min/1.73m^2. Review the dose of metformin if eGFR is below 45 ml/minute/1.73m^2. Stop metformin if eGFR is below 30 ml/minute/1.73m^2.

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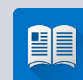
Anti-diabetic drug (usual or maximum dose)	Cost/28 days[3,4]	Criteria and threshold for stopping or reviewing treatments
Sulfonylureas (glimepiride, glipizide, gliclazide, glibenclamide, tolbutamide)	£0.99-£44.48	Risk of hypoglycaemia. Consider if rapid response is required and review treatment when blood glucose control has been achieved.
Pioglitazone 15 - 45mg	£10.12-£30.46	Do not offer or continue pioglitazone if they have any of the following:[4] • Heart failure or history of heart failure. • Hepatic impairment. • Diabetic ketoacidosis. • Current, or a history of, bladder cancer. • Uninvestigated macroscopic haematuria.
DPP-4 inhibitors : Sitagliptin, saxagliptin, linafliptin, alogliptin	£26.60 -£33.26	Review dose in renal impairment or hepatic impairment in line with Summary of Product Characteristics (SPC).
Sodium-glucose co-transporter-2 (SGLT-2) inhibitors: dapagliflozin, canagliflozin, emagliflozin	£36.59	Review dose in renal impairment or hepatic impairment in line with the SPC.
Glucagon-like peptide-1 (GLP-1) mimetics ; exenatide, exenatide pr, liraglutide, lixisenatide, dulaglutide, albiglutide	£54.14 - £109.87	For triple therapy only. Continue only if reduction in HbA1c of ≥1.0% (11mmol/mol) AND 3% weight loss at 6 months. Specialist advice should be sought for the use of the combination of a GLP-1 agonist and insulin.

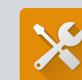
References

1. National Institute for Health and Care Excellence (NICE). NICE Guideline, NG 28. Type 2 Diabetes in adults: management. December 2015. http://guidance.nice.org.uk/ng28
2. National Institute for Health and Care Excellence (NICE). Technology appraisal 390. Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes. May 2016. Available at https://www.nice.org.uk/guidance/ta390/resources/canagliflozin-dapagliflozin-and-empagliflozin-as-monotherapies-for-treating-type-2-diabetes
3. National Institute for Health and Care Excellence (NICE). NICE Advice [KTT12], Type 2 Diabetes mellitus. January 2015. Available at www.nice.org.uk/advice/ktt12 on 20/2/16
4. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press; March 2016. Accessed 12/3/16 via www.medicinescomplete.com/mc/bnf/current/
5. Prescription Pricing Division (PPD). NHS Business Services Authority. Drug Tariff June 2016. Accessed 17/6/16 via www.nhsbsa.nhs.uk

Additional resources available: https://www.prescqipp.info/resources/category/320-management-of-type-2-diabetes

 Bulletin

Data pack

 Audits, algorithm, patient letter

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