Diabetes drugs: when to use and what to avoid

Dr Andrew McGovern and Dr Michael Feher outline the merits of different diabetes drugs

Key
HR highly recommended options
NR not recommended options

Based on the authors' personal opinions, and not advice from an official body

Class	Medication	Indicated	Contraindicated	Watch out for	Additional comments
NICE-recommended first-line drug treatment					
Biguanides	Metformin – standard release **HR**	As initial oral therapy	Patient has severe renal impairment - eGFR <30 Advise to reduce dose with eGFR <60	Gastrointestinal disturbance (bloating, abdominal pain, constipation or diarrhoea) B12 deficiency (although clinical manifestations rare)	Reduces cardiovascular risk No hypoglycaemia No association with lactic acidosis but still caution with any condition that reduces renal function or gives tissue hypoxia (with increased lactate formation) Low cost
	Metformin modified release **HR**	Patient has gastrointestinal effects with standard release metformin	As above	As above	As above
NICE-recommended second drug options*					
Sulfonylureas	Gliclazide **HR** Glimepiride **HR** Glipizide **HR** Glibenclamide **NR** Tolbutamide **NR**	Potent glycaemic reduction needed Early diabetes Not overweight	High risk of hypoglycaemia Severe renal impairment Frail elderly	Hypoglycaemia weight gain	Treatment effect is often lost after about four years Cardiovascular impact uncertain Low cost
Meglitinides ('glinides')	Repaglinide Nateglinide	Other options have poor response or adverse effect Marked postprandial hyperglycaemia Injectable options are not suitable	Severe renal impairment Elderly	Hypoglycaemia, weight gain	Dose required with each meal Cardiovascular impact uncertain NICE only explicitly recommends this is used when metformin contraindicated or not tolerated
Thiazolidinediones (TZDs)	Pioglitazone	Possible role in insulin sparing in those with high insulin resistance Possible role in non-alcoholic fatty liver An option for first or second intensification	Heart failure, osteoporosis, history of bladder cancer, hepatic impairment, maculopathy	Weight gain, fluid retention, heart failure, bone fractures	Increased heart failure risk Small risk of bladder cancer Good glycaemic durability Low cost
DPP4 inhibitors ('gliptins')	Sitagliptin **HR** Linagliptin **HR** Alogliptin Vildagliptin Saxagliptin	May be used when sulphonylureas not suitable, in the elderly, or in those with renal impairment Suitable for first or second intensification		Few adverse effects	No hypoglycaemia Possible increased risk of heart failure with saxagliptin Modest glycaemic efficacy Can be used in end stage renal failure High cost
SGLT2 inhibitors ('flozins')	Dapagliflozin **HR** Empagliflozin **HR** Canagliflozin	Weight loss is beneficial, patient has high cardiovascular risk, or as an insulin sparing agent	Patient has renal impairment, a history of multiple or severe genitourinary tract infections or ketoacidosis	Genitourinary infections, polyuria, volume depletion, ketoacidosis (very rare)	No hypoglycaemia Reduces cardiovascular risk** Lowers blood pressure Weight loss Foot amputation risk with canagliflozin High cost
NICE-recommended injectable options					
GLP-1 receptor agonists	Dulaglutide **HR** Liraglutide **HR** Lixisenatide **HR** Albiglutide Exenatide	Weight loss is beneficial or oral therapies have not been suitable Can be added to metformin if HbA1c still over 58 after second intensification in patients with BMI ≥35 (33 in Asians)	Are not overweight (not considered cost effective), or have renal impairment	Gastrointestinal disturbance, injection site reactions	No hypoglycaemia Reduces some cardiovascular risks*** Weight reduction Possible risk of pancreatitis skin nodules with exenatide High cost
Insulin	Multiple options	Patient requires substantial glycaemic reduction, have long-standing diabetes or oral therapies have not been suitable	Have high risk of hypoglycaemia	Hypoglycaemia Weight gain	Theoretically unlimited efficacy Patient (and physicians) often reluctant to initiate Variable cost
Last resort					
Alpha-glucosidase inhibitors	Acarbose	Other oral options have been exhausted and injectable options are not suitable	Patient has inflammatory bowel disease or severe renal impairment	Gastrointestinal disturbance (flatulence, diarrhoea)	No hypoglycaemia Modest efficacy May reduce cardiovascular risk Divided doses often required

* Can be used as an add-on to metformin or as monotherapy if patient is intolerant
** Trial evidence supports cardiovascular benefit for empagliflozin only with data awaited for dapagliflozin and canagliflozin. Real-world evidence suggestive of benefit with canagliflozin and dapagliflozin.
*** Cardiovascular safety trial evidence so far only for liraglutide (with benefit demonstrated) and lixisenatide (neutral cardiovascular effect)

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