Q6 Classify the oral hypoglycaemic drugs; include their mechanism of action, and their most significant side effects (March 2013)

Drug class	Mechanism	Side effects
Biguanides (eg, metformin)	Stimulates the movement of GLUT-4 receptors to the membrane of skeletal muscle and adipose tissue cells, increasing glucose uptake by those cells. Also inhibits gluconeogenesis and glycogenolysis in the liver, and delays intestinal glucose absorption.	▪ Life threatening lactic acidosis may occur in the presence of renal impairment ▪ Diarrhoea, n/v, abdominal discomfort common ▪ Must be withheld prior to administration of iodinated IV contrast
Sulfonylureas (eg, gliclazide)	Combine with K_{ATP} receptors on pancreatic β cells, closing the ATP-dependent potassium channels to depolarize the cell, resulting in an influx of calcium which stimulates insulin secretion.	▪ Risk of hypoglycaemia ▪ GIT disturbance ▪ Stimulate appetite and may cause weight gain
Meglitinides (eg, repaglinide)	Act by stimulating the same receptor as the sulfonylurea drugs but at a different side.	▪ Risk of hypoglycaemia ▪ Repaglinide is a major substrate of CYP3A4 and caution should be used when administering with clarithromycin or antifungals, as may result in high plasma levels of repaglinide and consequent severe hypoglycaemia
Thiazolidinediones (eg, rosiglitazone)	Act on the PPARγ in fat cells to induce insulin sensitivity	▪ Associated with increased risk of peripheral limb fracture in post menopausal women, and also some cases of diabetic maculopathy. ▪ They are also prone to cause severe fluid retention and precipitate heart failure, and so are contraindicated in CCF ▪ Contraindicated in people with known IHD.
Alpha-glucosidase inhibitors (eg, Acarbose)	Act by inhibit the enzyme the breaks down dietary complex carbs to sugar, reducing the quantity of glucose available for absorption	▪ Abdominal discomfort and distention ▪ Flatulence ▪ Elevates serum transaminases ▪ Should not produce hypoglycaemia itself as does not promote insulin release
DPP-IV inhibitors (eg, sitagliptin)	Inhibit the activity of the enzyme DPP-IV, which normally breaks down the gut hormones GLP-1 (glucagon-like peptide 1) and the protein GIP (gastric inhibitor peptide). GLP-1 and GIP stimulate glucose-mediated insulin release from the pancreas following an oral load of glucose.	▪ Monitor in renal insufficiency ▪ May cause hypoglycaemia