

ORAL AGENTS FOR TREATMENT OF TYPE 2 DIABETES

DRUG	ACTION	EFFICACY	ADVERSE EFFECTS	PRECAUTIONS
<u>SULFONYLUREAS</u> ACETOHEXAMIDE CHLORPROPAMIDE GLIMEPIRIDE GLIPIZIDE GLYBURIDE TOLAZAMIDE TOLBUTAMIDE	Receptors associated with K ⁺ channels in beta cells; facilitation of insulin secretion	HbA1c falls 1-2% in responders. ~50% of new pts. respond; ≤85% response in pts. selected for age >40 y, mod. obesity, FPG <200 mg/dL. Secondary failure 5-10%/y.	Prolonged hypoglycemia (see Table 12) Weight gain (Hyponatremia; flushing after alcohol: chlorpropamide only)	Renal insufficiency Hepatic disease Patient unable to eat Alcoholism
<u>STIMULATORS OF PRANDIAL INSULIN SECRETION</u> NATEGLINIDE REPAGLINIDE	Receptors associated with K ⁺ channels in beta cells; facilitation of insulin secretion	HbA1c falls ≈2% in patients never treated with oral agents; no improvement in patients switched from sulfonylureas	Dizziness in 1-5% of patients Hypoglycemia can occur	Give drug only before meals
<u>BIGUANIDES</u> METFORMIN	Inhibition of hepatic glucose production by unknown mechanism	HbA1c falls 1-2% in responders. When given as monotherapy: no weight gain, no hypoglycemia.	Anorexia, nausea, gas, diarrhea, abdominal pain. To minimize GI symptoms: take with meals; titrate dose upward slowly Lactic acidosis: 0.03 cases/1000 pt.-y.	Contraindications: renal insufficiency (creat. >1.5 for men, >1.4 for women); hepatic disease; alcoholism; metabolic acidosis; severe CHF. Suspend treatment for radiologic contrast studies; surgery.
<u>ALPHA-GLUCOSIDASE INHIBITORS</u> ACARBOSE MIGLITOL	Decreased absorption of dietary CHO, owing to inhibition of hydrolysis of complex CHO in gut	HbA1c falls ~0.5% in responders. When given as monotherapy: no hypoglycemia. Take immediately before meals containing CHO.	Gastrointestinal symptoms: gas, bloating, diarrhea	Inflammatory bowel disease Intestinal obstruction Creat. >2.0 mg/dL
<u>THIAZOLIDINEDIONES</u> PIOGLITAZONE ROSIGLITAZONE	Nuclear receptors alter gene transcription; enhancement of insulin action on fat cells and skeletal muscle.	Slow onset of action (weeks-months). Effective only in insulin-resistant pts. When given as monotherapy: no hypoglycemia. Take with meals.	Volume expansion; dilutional anemia; heart failure Elevated liver enzymes [Hepatic failure was associated with troglitazone, but apparently not with these drugs]	Monitor liver function tests Avoid rosiglitazone together with insulin