MEDICATIONS FOR TYPE 2 DIABETES

AVAILABLE PHARMACOLOGIC OPTIONS AND RECOMMENDATIONS

- The 2009 ADA/EASD consensus statement for the initiation and adjustment of therapy for type 2 diabetes and the 2009 AACE clinical practice guidelines for the management of diabetes provide guidance in selecting antidiabetic medications and their appropriate use to meet glycemic goals.[1,2]

TABLE 1. TYPE 2 DIABETES MEDICATIONS[1,3,4]

Biguanide	Suppresses hepatic glucose production Increases glucose uptake and utilization in skeletal muscle
Sulfonylureas	Enhance pancreatic insulin secretion
TZDs	Increase sensitivity of muscle, fat, and liver cells to insulin Suppress hepatic glucose production Increase glucose uptake in skeletal muscle and adipose cells Stimulate pancreatic insulin secretion
Glucosidase inhibitors	Inhibit carbohydrate breakdown in GI tract
Glinides	Stimulate pancreatic insulin secretion
GLP-1 agonists and DPP-4 inhibitors	Slow gastric motility Suppress hepatic glucagon production Augment glucose-mediated insulin secretion
Amylin agonist	Slows gastric emptying Inhibits glucose-dependent glucagon production
Bile acid sequestrant	Exact mechanism unknown May alter intestinal glucose absorption and/or hepatic glucose production
Insulin	Replaces basal and/or post-prandial endogenous insulin deficiencies

GUIDANCE FOR IMPLEMENTING COMBINATION THERAPY[1,2]

- Type 2 diabetes is a progressive disease, and many patients will require additional antidiabetic medications over time.
- The preferred option of the ADA/EASD algorithm is the addition of a sulfonylurea or basal insulin if therapeutic lifestyle changes and metformin fail to achieve the goal, followed by intensification of insulin therapy with additional pre-prandial injections.
- Consider the synergistic effects of particular combinations and other interactions when implementing combination therapy. Keep in mind that, in general, two agents with different mechanisms of action will have the greatest combined effect.

AACE = American Association of Clinical Endocrinologists; ADA = American Diabetes Association; BID = twice a day; CHF = congestive heart failure; EASD = European Association for the Study of Diabetes; DPP-4 = dipeptidyl peptidase-4; GI = gastrointestinal; GLP-1 = glucagon-like peptide-1; HbA_{1C} = glycosylated hemoglobin; NPH = neutral protamine Hagedorn; PO = orally; QD = once daily; TID = three times a day; TZDs = thiazolidinediones.

TABLE 2. TYPE 2 DIABETES MEDICATIONS: CLINICAL FEATURES[1,2,4]

Antidiabetic Agents	Dosing	HbA_{1c} Reduction (Monotherapy)	Hypoglycemia	Weight Change	Contraindications/ Caveats
Biguanide: Metformin	500-2000 mg QD to 2000 mg daily PO in divided doses with meals	~1%-2%	No	Neutral	Dose adjustment in renal impairment
Sulfonylureas: Chlorpropamide, glimepiride, glipizide, glyburide	0.75-40 mg in single or divided doses	~1%-2%	Yes	Gain	Dose adjustment in renal or liver impairment
α–Glucosidase Inhibitors: Acarbose, miglitol	25-100 mg TID with the first bite of each meal	~0.5%-0.7%	No	Loss	Tolerability issues
Glinides: Nateglinide, repaglinide	60-120 mg TID before meals	0.5%-1.5%	Yes	Gain	None
Thiazolidinediones: Pioglitazone, rosiglitazone	15-45 mg QD (pioglitazone) or 4 mg QD or BID (rosiglitazone)	1.0%-1.5%	No	Gain	Contraindicated in CHF
GLP-1 Agonist: Exenatide	5-10 mcg BID before 2 main meals	~1.0%	No	Loss	Dose adjustment in renal impairment
DPP-4 Inhibitors: Saxagliptin, sitagliptin	100 mg QD with or without food	~0.8%-1.0%	No	Neutral	Dose adjustment in renal impairment
Amylin Agonist: Pramlintide*	60-120 mcg immediately before meals	0.5%-1.0%	No	Loss	Contraindicated in gastroparesis
Bile Acid Sequestrant: Colesevelam	3750 mg QD or 1875 mg BID (tablets) or 3.75 g QD or 1.875 g BID (oral)	~0.5%-0.7%	No	Neutral	Contraindicated in hypertriglyceridemia
Insulin	1-4 injections day	1%-3%+	Yes	Gain	None

*Approved for use in the US only as adjunctive therapy with regular insulin or rapid-acting insulin analogs.

REFERENCES

1. Nathan DM, Buse JB, Davidson MB. A consensus statement of the ADA and the EASD. *Diabetes Care*. 2009;32:193-203.
2. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an AACE/ACE consensus panel. *Endocr Pract*. 2009;15:540-559.
3. DeFronzo RA. *Diabetes*. 2009;58:773-795.
4. Inzucchi SE. *Endocrinol Metab Clin North Am*. 2007;36(Suppl 2):2-17.