

MedVentive Guide to Type 2 Diabetes Mellitus Pharmacotherapy

Drug Class	Formulary Agent	Most Common Dose	Cost / Month (AWP or MAC)
Insulin Secretagogues	glipizide (g)	5 - 10mg QD-BID	\$2 - \$5
	glipizide ER (g) ^{N^{PA}}	5 - 10mg QD	\$8 - \$17
	glyburide (g)	5 - 10mg QD- BID	\$6 - \$24
Biguanide	metformin (g)	500 – 1,000mg BID	\$9 - \$11
	metformin XR (g)	500 – 2,000mg QD	\$7 - \$27
Thiazolidinediones	rosiglitazone (Avandia) ^{F³}	4 – 8mg QD	\$90 - \$168
	pioglitazone (Actos) ^{B^{PA}}	30 – 45mg QD	\$181 - \$196
Combination Product	rosiglitazone / metformin (Avandamet) ^{F^{PA}, M^{PA}}	2mg / 500mg BID	\$105 - \$171
		4mg / 500mg BID	
Alpha-glucosidase Inhibitor	miglitol (Glyset) ^{B³, H³, M^{PA}, N^{PA}, T³}	25 – 50mg TID	\$70 - \$77

Clinical Considerations

Insulin Secretagogues:

- Average decrease in FPG level: 60 – 70 mg/dL, A1C: 1.5% – 2%.
- Hypoglycemia is the most common and potentially severe adverse effect of the sulfonylureas. The incidence and severity of hypoglycemia increase with the duration of action and potency of the sulfonylureas.
- Glipizide, a short-acting agent, is preferred in elderly patients and those with decreased renal or hepatic function to minimize the high risk for hypoglycemia.
- Administer 30 minutes prior to meals. If gastrointestinal intolerance occurs, administer with food.
- A sulfonylurea should not be used in patients with severe hepatic or renal dysfunction.

Biguanide:

- Average decrease in FPG level: 60 – 70 mg/dL, A1C: 1.5% – 2%.
- Metformin is preferred in overweight patients. It produces modest weight loss or negligible weight gain, and decreases plasma triglyceride and low-density lipoprotein (LDL) cholesterol levels.
- Gastrointestinal adverse effects (e.g., diarrhea and abdominal discomfort) may occur and resolve after several weeks. To minimize, administer metformin with food. If symptoms occur during dosage titration, return to the previous metformin dose at which no symptoms occurred and wait at least two weeks before increasing the dose again, or consider switching the patient to metformin XR.
- Lactic acidosis is rare (i.e., 0.03 cases per 1,000 patient-years) in the absence of contraindications (e.g., renal disease or renal dysfunction [serum creatinine \geq 1.4 mg/dL in women, \geq 1.5 mg/dL in men], hepatic dysfunction, hemodynamic instability, heart failure requiring pharmacologic treatment, acute or chronic metabolic acidosis, alcoholism, advanced age [patients \geq 80 years old should have normal creatinine clearance documented prior to initiating therapy]).
- For patients requiring the administration of radiocontrast dye, metformin should be withheld prior to the study and 48 hours subsequent to the procedure until normal renal function has been documented by serum creatinine measurement.

Thiazolidinediones:

- Average decrease in FPG level: 35 – 60 mg/dL, A1C: 0.7% – 1.6%.
- Consider for patients who are obese with signs of insulin resistance and/or those who are not able to achieve treatment goals with appropriate use of other agents.
- Consider increasing the dose every six to eight weeks until treatment goal is achieved (FPG 80 - 120 mg/dL, HbA_{1c} < 7%) or the maximum effective dose is reached.
- Weight gain and increases in LDL and HDL cholesterol levels have been associated with thiazolidinedione use.
- Serum transaminase levels (i.e., ALT, AST) should be obtained at baseline, every two months during the first year of therapy, and periodically thereafter.

Selected Precautions/Contraindications

- **Pioglitazone and rosiglitazone should not be given to patients with active liver disease or who have an ALT > 2.5 x ULN at baseline.**
- Thiazolidinediones have been associated with mild-to-moderate edema and plasma volume expansion. **They should be used with caution in patients with mild to moderate heart failure and avoided in patients with more severe heart failure (i.e., NYHA Class III and IV) unless the expected benefit outweighs the potential risk.**
- Treatment with pioglitazone and rosiglitazone in premenopausal anovulatory patients with insulin resistance may result in resumption of ovulation. Patients should be advised pregnancy can occur if adequate contraception is not used.

Alpha-Glucosidase Inhibitor:

- Average decrease in FPG level: 25 – 30 mg/dL, A1C: 0.5% – 1%.
- Consider miglitol for patients who are taking a sulfonylurea or metformin and require an additional FPG level reduction of approximately 25 – 30 mg/dL or in patients with mild fasting hyperglycemia. Miglitol is also indicated in patients with predominant postprandial hyperglycemia.
- Miglitol must be administered with the first bite of food in order to be effective. In addition, its effectiveness is diminished in patients eating a low carbohydrate diet because it works by interfering with starch digestion and absorption.
- Gastrointestinal adverse effects (i.e., bloating, abdominal discomfort, diarrhea and flatulence) occur in up to 30% of patients. To minimize, initiate with a low dose (e.g., 25 mg QD – BID) with the smallest meals of the day. Consider increasing the dose by 25 mg increments every two to four weeks to minimize gastrointestinal side effects.
- Miglitol is contraindicated in patients with inflammatory bowel disease, a serum creatinine > 2 mg/dL, or cirrhosis.

Insulins:

- Products containing rapid acting insulin should be administered within 15 minutes of a meal/snack, and regular insulin should be administered 30 minutes before a meal/snack.

Insulin Type	Formulary Agent	Onset (hours)	Peak (hours)	Duration (hours)	Cost / Month (per 10ml vial)
Rapid & Short-acting	Lispro (Humalog)	0.25	0.5 – 1.5	6 – 8	\$81
	Insulin aspart (Novolog) ^{F^{PA}}	0.25	1 – 3	3 – 5	\$81
	Regular (Humulin R / Novolin R ^{F³})	0.5 - 1	2 – 4	8 – 12	\$35
Intermediate-Acting	NPH (Humulin N / Novolin N ^{F³})	1 – 2	6 – 14	≥ 24	\$35
Long-Acting	Insulin glargine (Lantus)	---	---	≥ 24	\$67
Pre-Mixed Insulins	NPH / Regular Mixture 70% / 30% (Humulin 70/30, Novolin 70/30 ^{F³})	0.5 – 1	3 – 10	14 – 18	\$35
	NPH / Regular Mixture 50% / 50% (Humulin 50/50)	0.5 – 1	3 – 10	14 – 18	\$35
	Lispro Protamine / Lispro 75% / 25% (Humalog Mix 75/25) ^{F³}	0.25 – 0.5	1 – 6	14 - 18	\$81

OTHER IMPORTANT CONSIDERATIONS

- All treatments may have secondary failure over time; therefore, treatment must be subject to continual monitoring and revision.
- After several years, monotherapy is unlikely to maintain glycemic control. Combination therapy produces additive therapeutic effects. Combining agents is usually more effective than stopping one agent and substituting another, or increasing the dose of an agent already being given at the recommended maximum effective dose.
- Limited data exists regarding three-drug combinations.
- Patients requiring pharmacotherapy should receive a blood glucose monitor.

KEY

FPG – fasting plasma glucose

A1C – glycosylated or glycated hemoglobin

* **Ideal Body Weight** for *females* in kg = 45 kg + 2.3(height in inches > 60)

* **Ideal Body Weight** for *males* in kg = 50 kg + 2.3(height in inches > 60)

ULN – upper limit of normal

(g) – generic equivalent available

Cost/Month is based on average wholesale price (AWP) from RedBook Update July 2005 or generic pricing established using Maximum Allowable Cost (MAC) as established by local third party payors;

B³ – Tier 3 copay for Blue Cross Blue Shield of Massachusetts members

B^{PA} - not covered by Blue Cross Blue Shield of Massachusetts without prior authorization

F³ – Tier 3 copay for Fallon Community Health Plan members

F^{PA} - not covered for Fallon Community Health Plan members without prior authorization

H³ - Tier 3 copay for Harvard Pilgrim Health Care members

M^{PA} – not covered by Mass Health without prior authorization

N^{PA} – not covered by Neighborhood Health Plan without prior failure of 1st line agent or prior authorization

T³ - Tier 3 copay for Tufts Health Plan