Glycemic Control Algorithm For Type 2 Diabetes Mellitus In Adults

Texas Diabetes Council

Revised 7/22/10

Glycemic Goals[1]

Individualize goal based on patient risk factors

	A1c ≤6%	<7%	<8%
FPG	≤110	120	140 mg/dL
2h PP	≤130	180	180 mg/dL

Initial Intervention[2]

1. Diabetes Self-Management Education *and*
2. Self-monitored Blood Glucose[3] *and*
3. Medical Nutrition[3], Weight Control[3], Exercise[3] *and*
4. Monotherapy if A1c <1% above goal otherwise Dual Therapy (optimize therapy as tolerated)

Goals not met after 3 months of optimized therapy

If A1c < 1% above goal:

If on monotherapy → add second agent (oral or GLP-1)

If on dual therapy → add third agent (oral or GLP-1 or insulin[6])

If A1c ≥ 1% above goal:

If on monotherapy → add second agent +/- once-daily insulin[6]
OR add two non-insulin agents (oral or GLP-1)

If on dual therapy → add third agent (oral or GLP-1)
OR add insulin[6]

Goals Achieved

Continue Therapy
A1c every 3-6 months

Goals not met after 3 Months of optimized therapy

Add or intensify insulin[6]
Consider referral to endocrinologist / diabetes specialist

Recommended Options for Dual Therapy[4]

Metformin
+ TZD or DPP-4 or SU[5] or GLP-1 or Meglitinide or colesevelam

Recommended Options for Triple Therapy

Metformin
+ TZD or SU[5]
+ GLP-1 or DPP-4 or AGI or colesevelam

Metformin
+ TZD or DPP-4 or AGI or SU[5] or colesevelam
+ Insulin

Abbreviations

AGI	Alpha-glucosidase inhibitors
DPP-4	Dipeptidyl peptidase-4 Inhibitor
FPG	Fasting plasma glucose
GLP-1	Glucagon-like peptide-1 agonist
PP	Postprandial
SU	Sulfonylurea
TZD	Thiazolidinedione

Footnotes:

1. **Intensify management if:** Absent/stable cardiovascular disease, mild-moderate microvascular complications, intact hypoglycemia awareness, infrequent hypoglycemic episodes, recently diagnosed diabetes. **Less intensive management if**: Evidence of advanced or poorly controlled cardiovascular and/or microvascular complications, hypoglycemia unawareness, vulnerable patient (ie, impaired cognition, dementia, fall history). Refer to TDC "A1c Goal" treatment strategy for further explanation. A1c is referenced to a non-diabetic range of 4-6% using a DCCT-based assay. ADA Clinical Practice Recommendations. *Diabetes Care* 2010;33(suppl 1):S19-20.
2. If initial A1c on presentation is ≥10%, consider the use of insulin, with or without oral agents, as the initial intervention (see Insulin Algorithm). Other agents may be introduced as glycemic control improves. If ketoacidosis or recent rapid weight loss, consider Type 1 diagnosis.
3. These interventions should be maintained life-long; (refer to Medical Nutrition, Weight Loss, and Exercise Algorithms).
4. Refer to the Diabetes Medications Supplement: Working Together to Manage Diabetes found in the Texas Diabetes Council's Diabetes Toolkit.
5. If a SU is selected, low dose glipizide ER or glimepiride are recommended because they have a lower incidence of hypoglycemia than glyburide.
6. Refer to Insulin Algorithm for Type 2 Diabetes Mellitus in Children and Adults / Initial Insulin Therapy for Type 2 Diabetes Mellitus in Children and Adults: A Simplified Approach

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See web site http://www.texasdiabetescouncil.org for latest version and disclaimer.
Bibliography on back.

References

Recent Review Articles

- Inzucchi SE. Oral antihyperglycemic therapy for type 2 diabetes: scientific review. *JAMA.* 2002;287(3):360-72.
- Inzucchi SE, McGuire DK. New drugs for the treatment of diabetes: part II: Incretin-based therapy and beyond. Circulation. 2008 Jan 29;117(4):574-84.
- Riddle, MC. Glycemic management of type 2 diabetes: An emerging strategy with oral agents, insulins and combinations. *Endocrinol Metab Clin N Am.* 2005;34(1):77-98.
- Drucker DJ, Sherman SI, Gorelick FS, Bergenstal RM, Sherwin RS, Buse JB. Incretin-based therapies for the treatment of type 2 diabetes: evaluation of the risks and benefits. Diabetes Care. 2010 Feb;33(2):428-33.

Dual Therapy

Metformin or Sulfonylurea + Acarbose

- Chiasson JL, Josse RG, Hunt JA, et al. The efficacy of acarbose in the treatment of patients with non-insulin-dependent diabetes mellitus. A multicenter controlled clinical trial. *Ann Intern Med.* 1994; 121 (12):928-35.

Metformin + Pioglitazone

- Einhorn D, Rendell M, Rosenzweig J, et al. Pioglitazone hydrochloride in combination with metformin in the treatment of type 2 diabetes mellitus: a randomized, placebo-controlled study. The Pioglitazone 027 Study Group. *Clin Ther.* 2000;22(12):1395-409.

Metformin + Rosiglitazone

- Fonseca V, Rosenstock J, Patwardhan R, et al. Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus: a randomized controlled trial. *JAMA.* 2000;283(13):1695-702. Erratum in: *JAMA* 2000;284(11): 1384.

Sulfonylurea + Pioglitazone

- Kipnes MS, Krosnick A, Rendell MS, et al. Pioglitazone hydrochloride in combination with sulfonylurea therapy improves glycemic control in patients with type 2 diabetes mellitus: a randomized, placebo-controlled study. *Am J Med.* 2001;111(1):10-7.

Sulfonylurea + Rosiglitazone

- Wolffenbuttel BH, Gomis R, Squatrito S, et al. Addition of low-dose rosiglitazone to sulphonylurea therapy improves glycaemic control in Type 2 diabetic patients. *Diabet Med.* 2000; 1 7(1):40-7.

Metformin or Sulfonylurea + Exenatide

- Buse JB, Henry RR, Han J,et.al. Effects of exenatide (exendin-4) on glycemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes. *Diabetes Care.* 2004;27(1 1):2628-35.
- DeFronzo RA, Ratner RE, Han J, et.al. Effects of exenatide (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. *Diabetes Care.* 2005;28(5):1092-100.

Nateglinide or Repaglinide + Metformin

- Raskin P, Klaff L, McGill J, et al Efficacy and safety of combination therapy: repaglinide plus metformin versus nateglinide plus metformin. *Diabetes Care.* 2003;26(7):2063-8. Erratum in: *Diabetes Care.* 2003;26(9):2708.

Repaglinide + Metformin

- Moses R, Slobodniuk R, Boyages S, et al. Effect of repaglinide addition to metformin monotherapy on glycemic control in patients with type 2 diabetes. *Diabetes Care.* 1 999;22(1): 119-24.

Nateglinide + Metformin

- Horton ES, Clinkingbeard C, Gatlin M, et al. Nateglinide alone and in combination with metformin improves glycemic control by reducing mealtime glucose levels in type 2 diabetes. *Diabetes Care.* 2000;23(1 1): 1660-5.

Nateglinide + Thiazolidinedione

- Rosenstock J, Shen SG, Gatlin MR, et al. Combination therapy with nateglinide and a thiazolidinedione improves glycemic control in type 2 diabetes. *Diabetes Care.* 2002;25(9):1 529-33.
- Fonseca V, Grunberger G, Gupta S, et al. Addition of nateglinide to rosiglitazone monotherapy suppresses mealtime hyperglycemia and improves overall glycemic control. *Diabetes Care.* 2003;26(6):1685-90.

Repaglinide + Thiazolidinedione

- Raskin P, Jovanovic L, Berger S, et al. Repaglinide/troglitazone combination therapy: improved glycemic control in type 2 diabetes. *Diabetes Care.* 2000;23(7):979-83.

Liraglutide + metformin:

- Nauck M, Frid A, Hermansen K, Shah NS, Tankova T, Mitha IH, Zdravkovic M, Düring M, Matthews DR; LEAD-2 Study Group.Efficacy and safety comparison of liraglutide, glimepiride, and placebo, all in combination with metformin, in type 2 diabetes: the LEAD (liraglutide effect and action in diabetes)-2 study. Diabetes Care. 2009 Jan;32(1):84-90.

Liraglutide + sulfonylurea:

- Marre M, Shaw J, Brändle M, Bebakar WM, Kamaruddin NA, Strand J, Zdravkovic M, Le Thi TD, Colagiuri S; LEAD-1 SU study group. Liraglutide, a once-daily human GLP-1 analogue, added to a sulphonylurea over 26 weeks produces greater improvements in glycaemic and weight control compared with adding rosiglitazone or placebo in subjects with Type 2 diabetes (LEAD-1 SU). Diabet Med. 2009 Mar;26(3):268-78.

Triple Therapy

Sulfonylurea + Metformin + Alpha glucosidase inhibitors

- Lam KS, Tiu SC, Tsang MW, et al. Acarbose in NIDDM patients with poor control on conventional oral agents. A 24-week placebo-controlled study. *Diabetes Care.* 1998;21(7):1154-8.
- Standl E, Schernthaner G, Rybka J, et al. Improved glycaemic control with miglitol in inadequately-controlled type 2 diabetics. *Diabetes Res Clin Pract.* 2001;51(3):205-13.

Sulfonylurea + Metformin + Thiazolidinedione

- Dailey GE 3rd, Noor MA, Par k JS, et al. Glycemic control with glyburide/ metformin tablets in combination with rosiglitazone in patients w ith type 2 diabetes: a ra ndomized, double-blind trial. *Am J Med.* 2004; 11 6(4):223-9.
- Aljabri K, Ko zak SE, Thompson D M. Addition o f pi oglitazone or bedti me insulin to maximal doses o f sulfonylurea and metformin in type 2 diabetes patients with poor glucose control: a prospective, randomized trial. *Am J Med.* 2004; 11 6(4):230-5.

Sulfonylurea + Metformin + Exenatide

- Kendall DM, Riddle MC, Rosenstock J, et.al. Effects of exenatide (exendin-4) on glycemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. *Diabetes Care.* 2005;28(5): 1083-91.
- Heine RJ, Van Gaal LF, Johns D, et al. Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized study. *Ann Intern Med.* 2005; 143(8):559-69.

Liraglutide + metformin and TZD:

- Zinman B, Gerich J, Buse JB, Lewin A, Schwartz S, Raskin P, Hale PM, Zdravkovic M, Blonde L; LEAD-4 Study Investigators. Efficacy and safety of the human glucagon-like peptide-1 analog liraglutide in combination with metformin and thiazolidinedione in patients with type 2 diabetes (LEAD-4 Met+TZD). Diabetes Care. 2009 Jul;32(7):1224-30.

Liraglutide + metformin and Sulfonylurea:

- Russell-Jones D, Vaag A, Schmitz O, Sethi BK, Lalic N, Antic S, Zdravkovic M, Ravn GM, Simó R; Liraglutide Effect and Action in Diabetes 5 (LEAD-5) met+SU Study Group.Liraglutide vs insulin glargine and placebo in combination with metformin and sulfonylurea therapy in type 2 diabetes mellitus (LEAD-5 met+SU): a randomised controlled trial. Diabetologia. 2009 Oct;52(10):2046-55.

Colesevelam

- W elchol™ Prescribing Information. Daiichi Sankyo, Inc. October 2009.
- Bays HE, Goldberg RB, Truitt KE, Jones MR. Colesevelam hydrochloride therapy in patients with type 2 diabetes mellitus treated with metformin: glucose and lipid effects. Arch Intern Med. 2008 Oct 13;168(18):1975-83.
- Goldberg RB, Fonseca VA, Truitt KE, Jones MR. Efficacy and safety of colesevelam in patients with type 2 diabetes mellitus and inadequate glycemic control receiving insulin-based therapy. Arch Intern Med. 2008 Jul 28;168(14):1531-40.