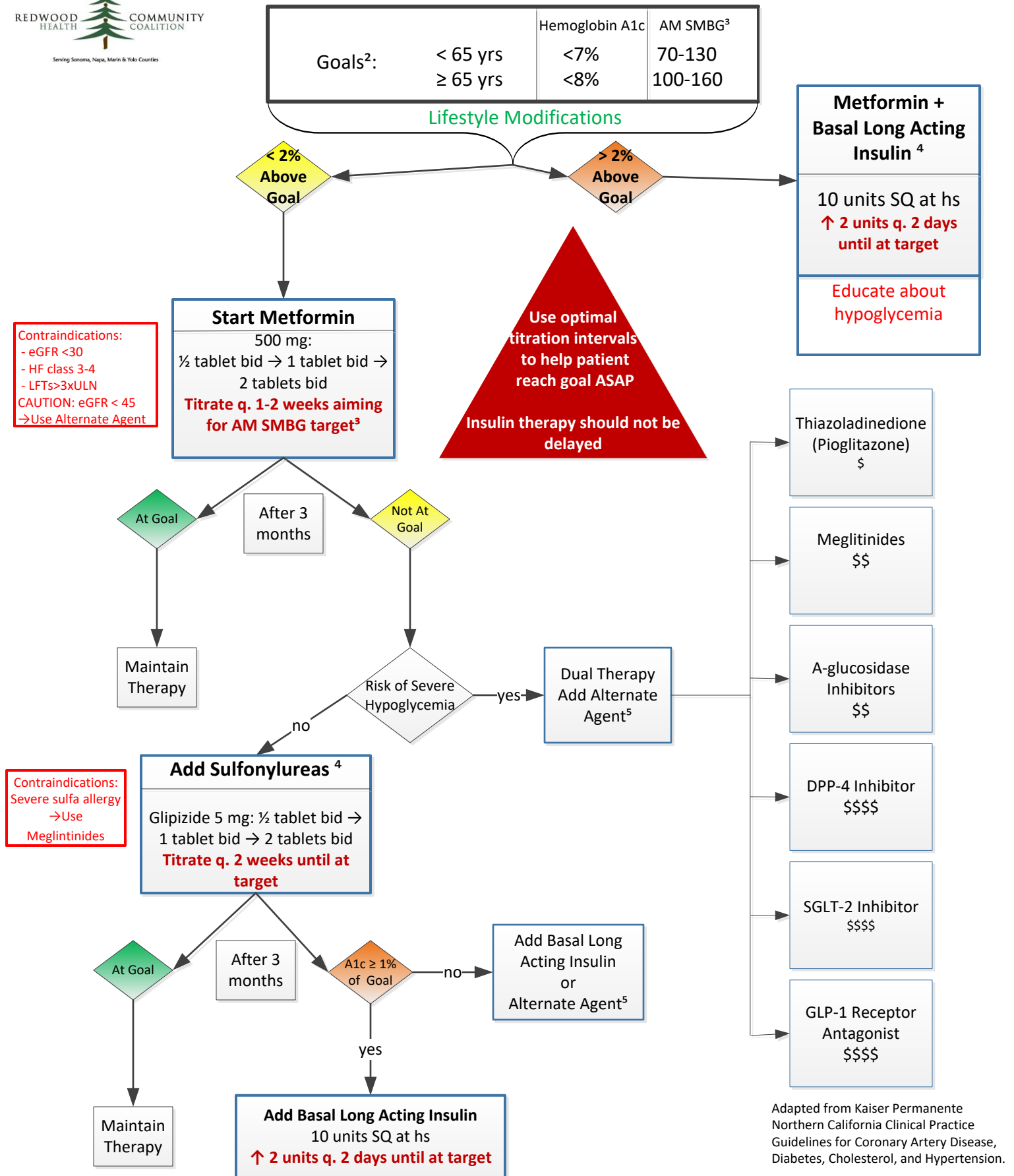




Adapted from Kaiser Permanente Northern California Clinical Practice Guidelines for Coronary Artery Disease, Diabetes, Cholesterol, and Hypertension.

¹ Excluding Pregnancy – for pregnant women and women intending pregnancy, use CDAPP guidelines.

² Individualize A1c goal based on risk of hypoglycemia, duration of DM, life expectancy, comorbidities, vascular complications, patient resources and support system.

³ Self Monitoring Blood Glucose targets: postprandial < 180mg/dL; bedtime 100-150 mg/dL.

⁴ Carries increased risk of Hypoglycemia. **Severe hypoglycemia** = resulting or likely to result in seizures, LOC, or needing help from others. **Mild hypoglycemia** = recognized signs and symptoms or neuro-glycopenia (e.g. hunger or sweating) that the patient can effectively self-treat.

⁵ Choice dependent on patient and disease-specific factors. Each new class of non-insulin agents lowers A1c ~ 1%. If A1c target is still not achieved after 3 months of dual therapy, proceed to three-drug combination.

Medications for Management of Type 2 Diabetes

	Medication	Efficacy / Advantages	Hypo-glycemic risk	Weight	Cost	Maximum Recommended Dose	Optimal Titration Interval	Caution/ side effects
First line mono-oral agent, therapy	<u>Biguanides</u> metformin ² (500, 850, 1000mg) ER ² (500, 750, 1000mg)	High/ ↑risk CV event	Low	Neutral or Loss	‡ ¹	2,000mg daily	1-2 weeks	Serum creatinine; repeat q 12 months Do not use if HF class 3-4; LFTs>3xULN; or eGFR<30. Maximum dose 1000mg if eGFR 30-45 Increased risk GI side effects -> consider extended release Long-term use associated with vitamin B12 deficiency
Dual, second-line oral therapy	<u>Sulfonylureas (SU)</u> glipizide ² (2.5, 5, 10mg) glimepiride ² glyburide ER (2.5, 5, 10mg) <u>Combination Med</u> Glyburide/metformin ^{1,2} (1.5-250mg, 2.5/5mg-500mg)	High/ ↑microvascular risk	High	Gain	‡ ¹	20mg twice daily	2 weeks	Sulfa allergy Hypoglycemia Weight gain D/C SU with initiation of insulin
Dual therapy; alternative agent	<u>Thiazolidinediones (TZD)</u> pioglitazone ² (15, 30, 45mg) <u>Combination Med</u> Pioglitazone/metformin ⁴ (15/500/850mg)	High/ ↑insulin sensitivity	Low	Gain	‡ ¹	45mg daily		Heart failure Edema Increased fractures Bladder cancer concerns
	<u>Meglitinides (Glinide)</u> repaglinide ² (0.5,1, 2mg) nateglinide ² (60,120mg)	↓A1C lowering / ↓pp glucose	High	Gain	‡\$ ¹	16mg daily 360mg daily		
	<u>Alpha-glucosidase inhibitors (AGI)</u> acarbose ² (25,50, 100mg) miglitol ² (25,50, 100mg)				\$	300mg	1-2 months	Often poorly tolerated Modest efficacy (0.4-0.7% reduction A1C) Need to be dosed more than once/day Effective in reducing PPG with high carb intake
Dual therapy; alternative agent	<u>DPP-4 Inhibitors</u> alogliptin ³ (6.25, 12.5, 25mg) sitagliptin ⁴ saxagliptin ⁴ linagliptin ⁴ <u>Combination Med</u> ^{1,3} alogliptin/pioglitazone ² (12.5-15/30/45, 25-15/30/45mg) alogliptin/metformin ² (12.5-500/1,000mg)	Intermediate	Low	Neutral	\$\$\$	25mg daily		Rare

	Medication	Efficacy / Advantages	Hypoglycemic Risk	Weight	Cost	Maximum Recommended Dose	Optimal Titration Interval	Caution/side effects
Insulin	<u>SGLT-2 inhibitors</u> canagliflozin ⁴ dapagliflozin ⁴ empagliflozin ⁴ <u>Combination Med</u> canagliflozin/metformin, <i>Invokamet</i> ⁴ empagliflozin/metformin, <i>Synjardy</i> ⁴ dapagliflozin/metformin, <i>Xigduo</i> ⁴ empagliflozin/linagliptin, <i>Glyxambi</i> ⁴	Intermediate/ may improve CV risk; ↓BP	Low	Loss	\$\$\$\$	5mg daily		Increase genital mycotic infections Dehydration Fracture risk Polyuria ↑ LDL-C ↑ creatinine
	<u>GLP-1 R Agonist</u> (SQ pen injector) liraglutide, <i>Victoza</i> ³ dulaglutide ⁴	High/ ↑CV risk	Low	Loss	\$\$\$\$	1.8mg daily 1.5mg daily		GI side effects Pancreatitis risk ↑ Heart rate
	<u>Long-acting Insulin, basal</u> Insulin glargine, <i>Basalgar</i> ² , <i>Lantus</i> ⁴ insulin detemir, <i>Levemir</i> ⁴	Highest	Highest	Gain	\$-\$\$\$	10U SQ HS or 0.1-0.2U/kg/d	10-15%, or 2-4U 1-2x/wk	Hypoglycemia; duration 18 - 26hrs Training/monitoring requirements
	<u>Intermediate-acting Insulin, NPH</u> insulin isophane, <i>HumulinN</i> ³ , <i>NovolinN</i> ³	Highest	Highest	Gain	\$\$\$			Hypoglycemia; duration 16 - 24hrs
	<u>Short-acting Insulin</u> regular insulin, <i>HumulinR</i> ³ , <i>NovolinR</i> ³ , <i>Afrezza</i> ⁴ (inhalation)	Highest	Highest	Gain	\$-\$\$\$			Hypoglycemia; duration 5 - 8hrs
	<u>Fast-acting Insulin</u> insulin lispro, <i>Humalog</i> ³ insulin aspart, <i>Novolog</i> ³ insulin glulisine, <i>Apidra</i> ³	Highest	Highest	Gain	\$			Hypoglycemia; duration 3 - 4hrs Monitor blood glucose before breakfast and before meals 2-4 times/day

¹Generic available; ²Partnership Healthplan of California formulary; ³PHC formulary restrictions apply: quantity limit or step therapy – previous claims for metformin, a secondary formulary oral antidiabetic agent &/or basal insulin required (see formulary); ⁴PHC non-formulary – TAR required; ⁵PHC not available
<https://client.formularynavigator.com/Search.aspx?siteTestID=1196>