REDWOOD HEALTH COMMUNITY COALITION
Serving Sonoma, Napa, Marin & Yolo Counties

Medication Titration Algorithm for Type 2 Diabetes [1]

V2.1 updated 6/1/2017

Goals[2]:		Hemoglobin A1c	AM SMBG[3]
	< 65 yrs	<7%	70-130
	≥ 65 yrs	<8%	100-160

Lifestyle Modifications

< 2% Above Goal

> 2% Above Goal

Metformin + Basal Long Acting Insulin [4]

10 units SQ at hs
↑ 2 units q. 2 days until at target

Educate about hypoglycemia

Use optimal titration intervals to help patient reach goal ASAP

Insulin therapy should not be delayed

Contraindications:
- eGFR <30
- HF class 3-4
- LFTs>3xULN

CAUTION: eGFR < 45
→Use Alternate Agent

Start Metformin

500 mg:
½ tablet bid → 1 tablet bid → 2 tablets bid
Titrate q. 1-2 weeks aiming for AM SMBG target[3]

At Goal

After 3 months

Not At Goal

Maintain Therapy

Risk of Severe Hypoglycemia

yes

no

Dual Therapy Add Alternate Agent[5]

Thiazoladinedione (Pioglitazone)
$

Meglitinides
$$

A-glucosidase Inhibitors
$$

DPP-4 Inhibitor
$$$$

SGLT-2 Inhibitor
$$$$

GLP-1 Receptor Agonist
$$$$

Contraindications:
Severe sulfa allergy
→Use Meglintinides

Add Sulfonylureas [4]

Glipizide 5 mg: ½ tablet bid → 1 tablet bid → 2 tablets bid
Titrate q. 2 weeks until at target

At Goal

After 3 months

A1c ≥ 1% of Goal

no

Add Basal Long Acting Insulin or Alternate Agent[5]

yes

Maintain Therapy

Add Basal Long Acting Insulin
10 units SQ at hs
↑ 2 units q. 2 days until at target

[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, co-morbidities, 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 oral agent, mono-therapy	Biguanides 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	Sulfonylureas (SU) glipizide[2] (2.5, 5, 10mg) glimepiride[2] glyburide ER (2.5, 5, 10mg) Combination Med 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	Thiazolidinediones (TZD) pioglitazone[2] (15, 30, 45mg) Combination Med Pioglitazone/metformin[4] (15/500/850mg)	High / ↑insulin sensitivity	Low	Gain	$[1]	45mg daily		Heart failure Edema Increased fractures Bladder cancer concerns
	Meglitinides (Glinide) repaglinide[2] (0.5,1, 2mg) nateglinide[2] (60,120mg)	↓A1C lowering / ↓pp glucose	High	Gain	$$[1]	16mg daily 360mg daily		
	Alpha-glucosidase inhibitors (AGI) acarbose[2] (25,50, 100mg) miglitol[2] (25,50, 100mg)				$$	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
	DPP-4 Inhibitors alogliptin[3] (6.25, 12.5, 25mg) sitagliptin[4] saxagliptin[4] linagliptin[4] Combination Med[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
	SGLT-2 inhibitors canagliflozin[4] dapagliflozin[4] empagliflozin[4] Combination Med canagliflozin/metformin, *Invokamet*[4] empagliflozin/metformin, *Synjardy*[4] dapagliflozin/metformin, *Xigduo*[4] empagliflozin/linagliptin, *Glyxambi*[4]	Intermediate/ may improve CV risk; ↓BP	Low	Loss	$$$$	5mg daily		↑ genital mycotic infections Dehydration Fracture risk Polyuria ↑ LDL-C ↑ creatinine Possible ↑ risk of lower-limb amputation with canagliflozin
	GLP-1 R Agonist (SQ pen injector) liraglutide, *Victoza*[3] dulaglutide[4]	High/ ↓CV risk	Low	Loss	$$$$	1.8mg daily 1.5mg daily		GI side effects Pancreatitis risk ↑ Heart rate
Insulin	Long-acting Insulin, basal Insulin glargine, *Basalgar*[2], *Lantus*[4] insulin detemir, *Levemir*[4]	Highest	Highest	Gain	$-$$$	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
	Intermediate-acting Insulin, NPH insulin isophane, *HumulinN*[3], *NovolinN*[3]	Highest	Highest	Gain	$$$			Hypoglycemia; duration 16 - 24hrs
	Short-acting Insulin regular insulin, *HumulinR*[3], *NovolinR*[3], *Afrezza*[4] (inhalation)	Highest	Highest	Gain	$-$$$			Hypoglycemia; duration 5 - 8hrs
	Fast-acting Insulin insulin lispro, *Humalog*[3] insulin aspart, *Novolog*[3] insulin glulisine, *Apidra*[3]	Highest	Highest	Gain	$			Hypoglycemia; duration 3 - 4hrs Monitor blood glucose before breakfast and before meals 2-4 times/day

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