

Diabetes Medication Therapy Management

Quick Start Practical Guide



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Special Thanks to:

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Outline

- Introduction and Objectives
- Diabetes overview
- SMBGs
- Sample Patient Case
- Medication algorithms
- Medications

Objectives

- Understand patient considerations in starting or adjusting medication therapy
- Recommend and evaluate diabetes medication therapy
- Learn with and from our diabetes patient

Diabetes Overview



Glycemic Recommendations for Nonpregnant Adults with Diabetes

A1C	<7%*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (<10.0 mmol/L)

*Goals should be individualized based on these values.

†Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.



Hypoglycemia Classification

Hypoglycemia	Blood Sugar
Glucose Alert Value (Level 1)	≤ 70 mg/dL* (3.9 mmol/L)
Clinically Significant Hypoglycemia (Level 2)	< 54 mg/dL* (3 mmol/L)
Severe Hypoglycemia (Level 3)	No specific level*

*Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

estimated Average Glucose (eAG)

- A1c is hard for patient to understand and relate
- A1c is marker for outcomes in clinical trials

$$\text{eAG (mg/dl)} = 28.7 \times \text{A1c} - 46.7$$

$$1\% \text{ A1c} \approx 30 \text{ mg/dl}$$

- Test A1c **q3mo** if not at goal or changing thx, otherwise **q6mo**

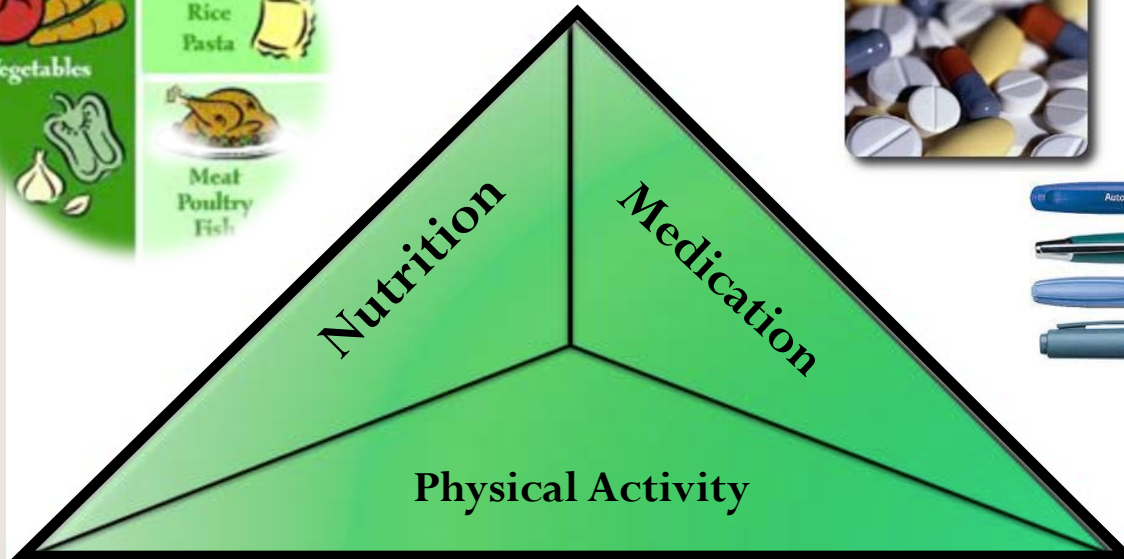
A1c (%)	eAG (mg/dL) (mmol/L)
5	97 (5.4)
6	126 (7.0)
7	154 (8.6)
8	183 (10.2)
9	212 (11.8)
10	240 (13.4)
11	269 (14.9)
12	298 (16.9)

<http://professional.diabetes.org/GlucoseCalculator.aspx>

A1c-derived Average Glucose

(ADAG study; Diabetes Care 2008;31:1473)

Diabetes Management Basics



Examples of SMBG

International Diabetes Federation, 2009



7-point profile

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday							
Tuesday	X	X	X	X	X	X	X
Wednesday	X	X	X	X	X	X	X
Thursday	X	X	X	X	X	X	X
Friday							
Saturday							
Sunday							

Meal-based testing

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday	X	X					
Tuesday							
Wednesday			X	X			
Thursday							
Friday							
Saturday					X	X	
Sunday							



Detection/assessment of fasting hyperglycaemia

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday							X
Tuesday	X						
Wednesday							X
Thursday	X						
Friday							X
Saturday	X						
Sunday							

Bedtime and morning fasting SMBG can be used to identify fasting and assess fasting hyperglycaemia.

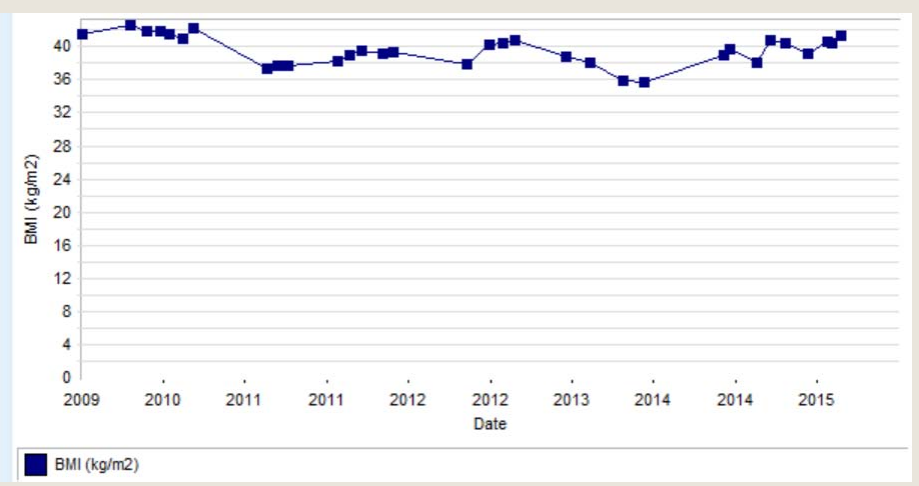
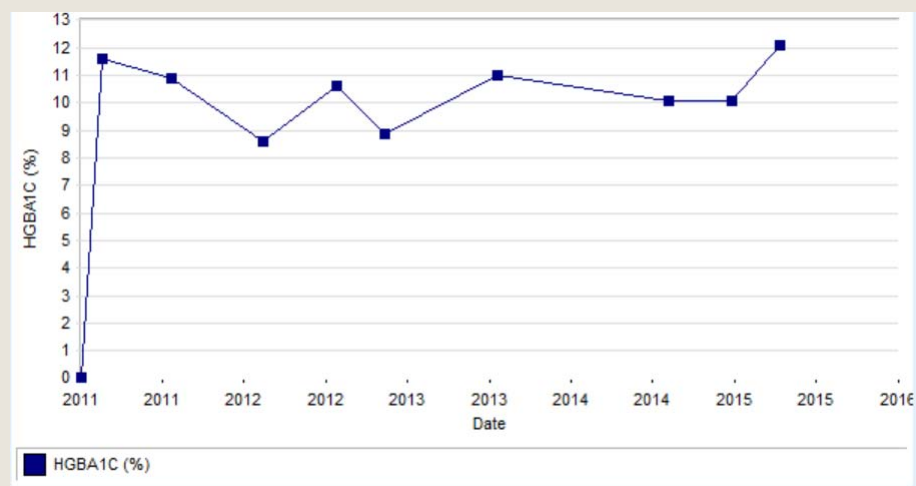
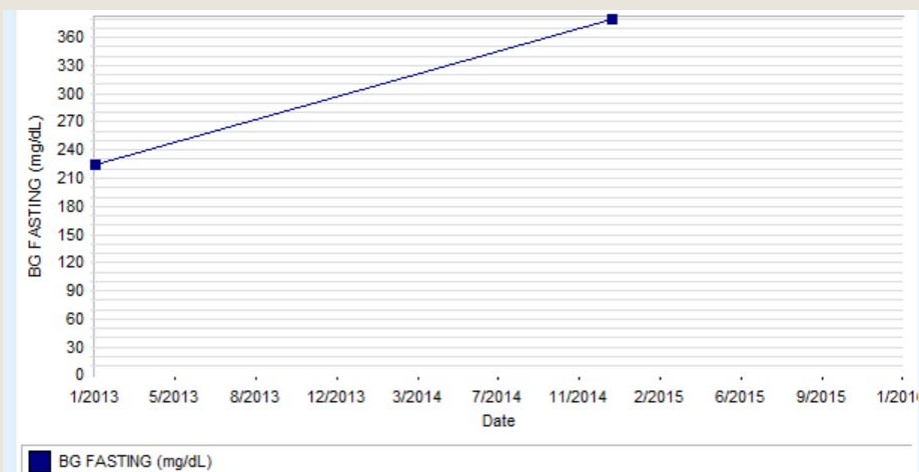
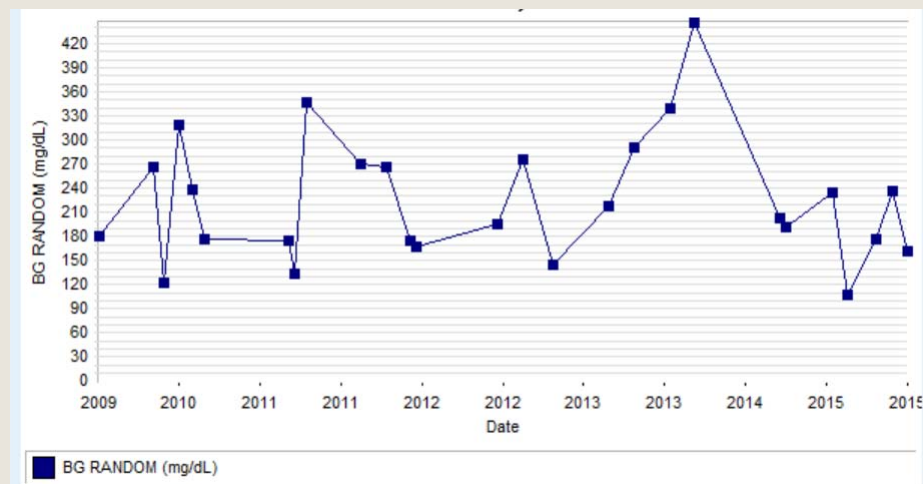
Detection of asymptomatic hypoglycaemia

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday			X		X		
Tuesday							
Wednesday			X		X		
Thursday							
Friday			X		X		
Saturday							
Sunday							

Pre-lunch and pre-supper SMBG can be used to detect asymptomatic hypoglycaemia ⁽⁸⁵⁾.

Patient Case

Patient Case



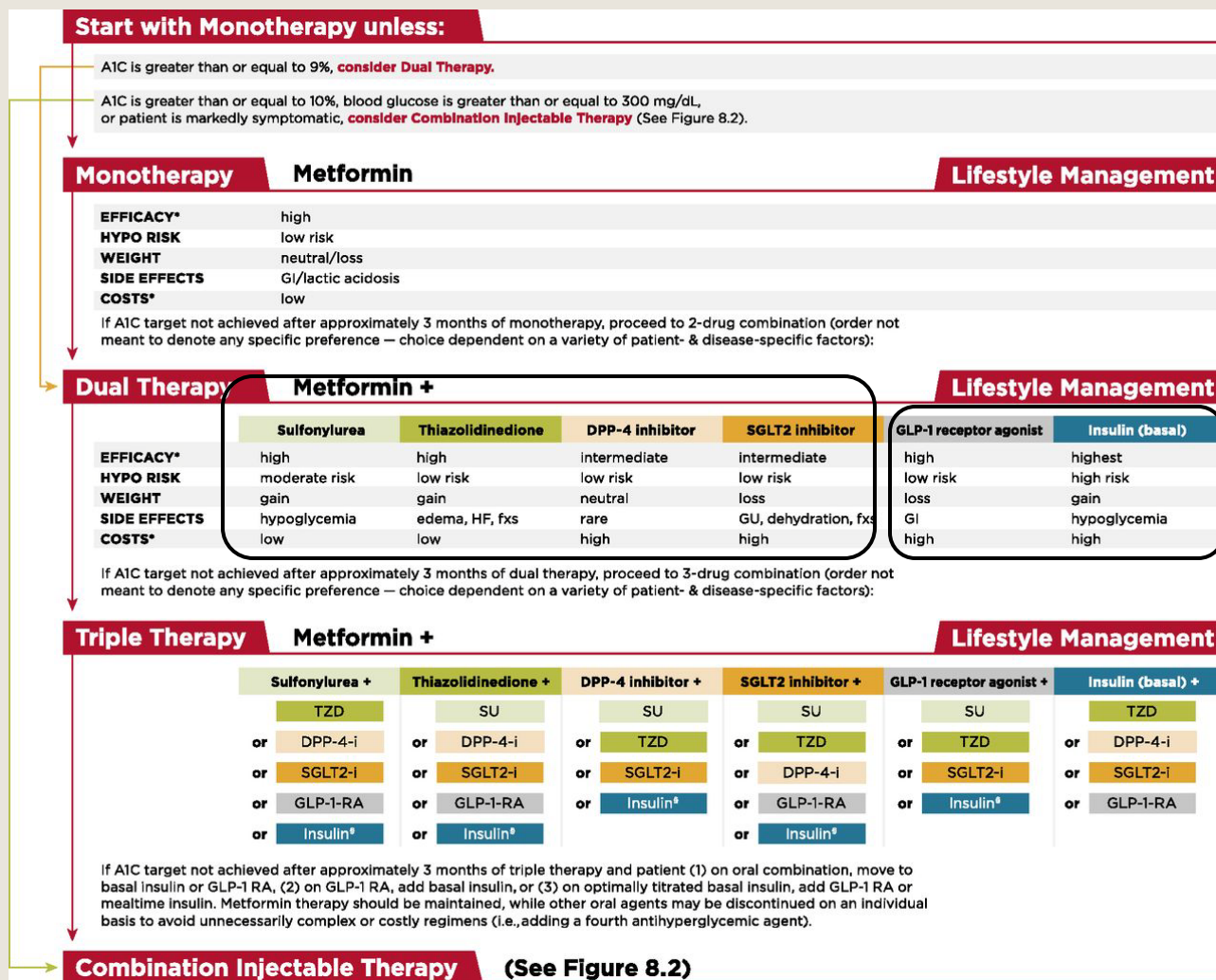
Patient Case

Medications									
+ ✎ ✖ ↺ Interactions: ⚠ Active Only ▼ 📄 📊 🔄 🔍 Drugstore.com ▼									
Description	Instructions	Last Rx	Generic	Start Date	Stop Date	Uncoded BMN	Class		
⊕ CLOTRIMAZOLE ANTI-FUNGAL 1 % CR...	aply to feet daily for foot fungus.	02-Oct-2014 #45g X 3	CLOTRIMAZOLE	02-Oct-2014		N	N	Topical Pi	
⊕ LIPITOR 20 MG TABS	Take one tablet by mouth each night for high cholesterol. No myalgias, spanish label	10-Feb-2014 #90 X 1	ATORVASTATI...	10-Feb-2014		N	N	Cardiovas	
⊕ BENAZEPRIL HCL 40 MG TABS	1 tablet Every 12 hours for high blood pressure.	13-Dec-2013 #180 X 3	BENAZEPRIL...	08-Jul-2013		N	N	Cardiovas	
⊕ METFORMIN HCL 1000 MG TABS	1 tablet Every 12 hours	13-Dec-2013 #180 X 4	METFORMIN...	03-Dec-2012		N	N	Endocrine	
⊕ NOVOLIN R 100 UNIT/ML INJ SOLN	Take 25 units every morning before eating and 49 units before dinner.	10-Sep-2014 #2 X 4	INSULIN REG...	07-Feb-2013		N	N	Endocrine	
⊕ NOVOLIN N 100 UNIT/ML SUSP	use 60 units Every AM use 60 units every evening	10-Sep-2014 #2 X 4	INSULIN ISOP...	07-Feb-2013		N	N	Endocrine	
⊕ ACCU-CHEK SOFTCLIX LANCETS MISC	Use as directed or equivalent lancets on formulary	13-Dec-2013 #100 X 4	LANCETS	03-Dec-2012		N	N	Miscellane	
⊕ ACCU-CHEK AVIVA PLUS STRP	use as directed for glucose testing	10-Sep-2014 #100 X 4	GLUCOSE BLO...	03-Dec-2012		N	N	Miscellane	

Medication algorithms

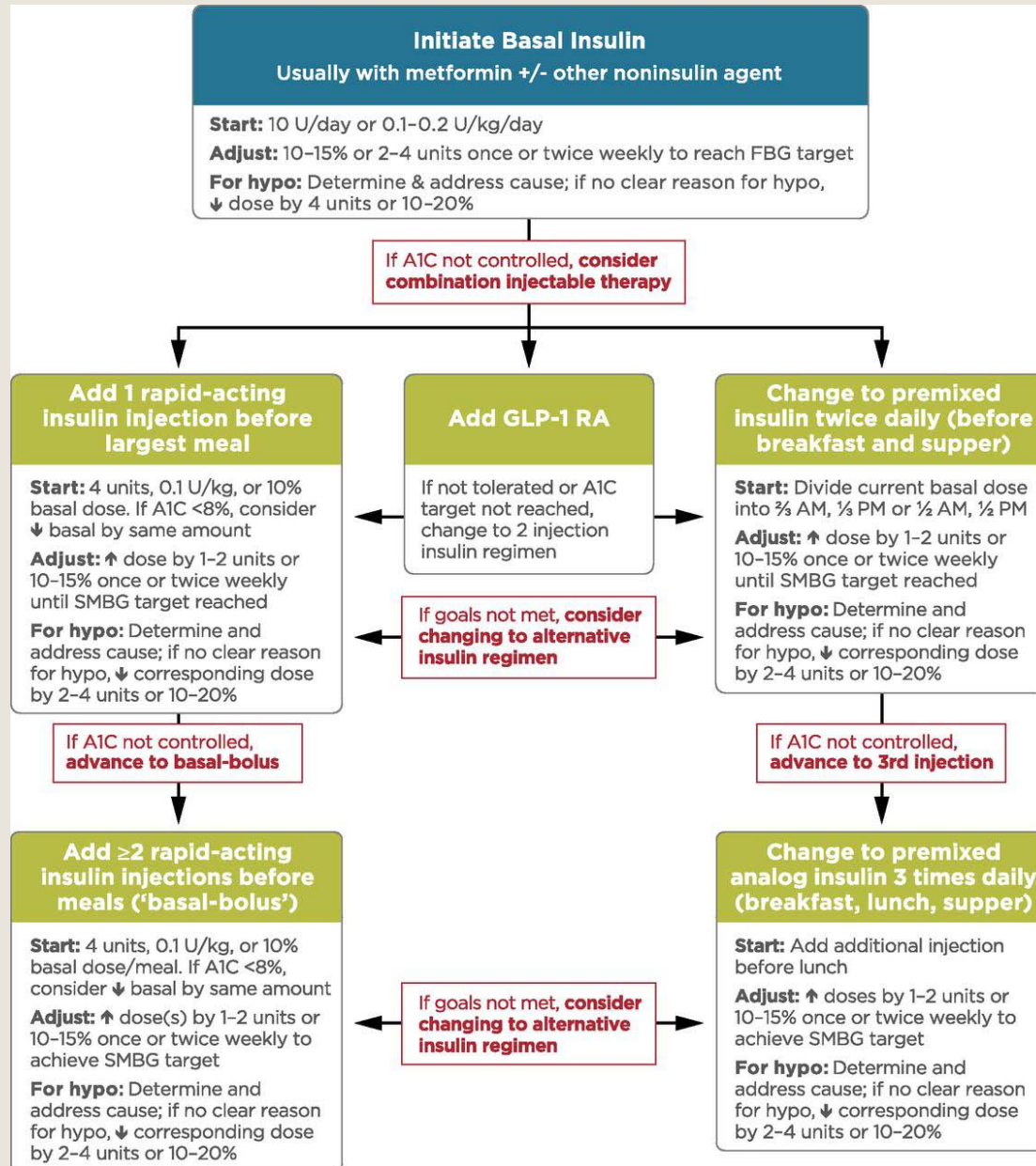
ADA Standards of Care 2017

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

Combination injectable therapy for type 2 diabetes.



Diabetes Medication Therapy



General Recommendations: Therapy for Type 2 Diabetes

- A patient-centered approach should be used to guide choice of pharmacological agents
 - Considerations include
 - patient preferences
 - efficacy
 - cost
 - potential side effects hypoglycemia
 - weight considerations
 - comorbidities
- Due to the progressive nature of type 2 diabetes, insulin therapy is eventually indicated for many patients with type 2 diabetes
- On the flip side, with better glycemic control, medication regimen can be simplified/reduced

Diabetes Medicines

TYPE 2 DIABETES MEDICINES AND HOW THEY WORK:¹

WHEN YOU HAVE DIABETES

YOUR LIVER

... releases too much glucose when your body does not need it.

BIGUANIDES

...keep the liver from releasing too much glucose

YOUR INTESTINE

...breaks down carbohydrates from food into glucose. When glucose is taken up into your blood, your blood glucose level increases.

YOUR MUSCLE/FAT CELLS

... do not use insulin properly. When this happens, glucose stays in the blood and is not converted into energy.

YOUR PANCREAS

... does not produce enough insulin

ORAL MEDICINES CONTROL BLOOD SUGAR BY:

ALPHA-GLUCOSIDASE

INHIBITORS

...slow down the digestion and absorption of carbohydrates and decrease glucose levels after meals.

THIAZOLIDINEDIONES (TZD's)

...make muscle and fat cells more sensitive to insulin. This helps convert more glucose into energy.

SULFONYLUREAS AND GLINIDES

Stimulate the pancreas to produce more insulin

Kidneys

- reabsorbs glucose

SGLT2 inhibitors

- Urinate out glucose

Diabetes Medicines

Other medicines:

INSULIN moves glucose from the blood into your body's cells.

DPP-4 INHIBITORS prevent the breakdown of gut hormones that increase the release of insulin from your pancreas and decrease glucagon release after meals. Glucagon increases your glucose level by causing the liver to release glucose from storage.

INCRETIN MIMETIC & AMYLIN ANALOG are injectable hormones that increase the production of insulin from your pancreas, slow movement of food through your stomach, reduces glucagon release after meals, and decreases appetite.

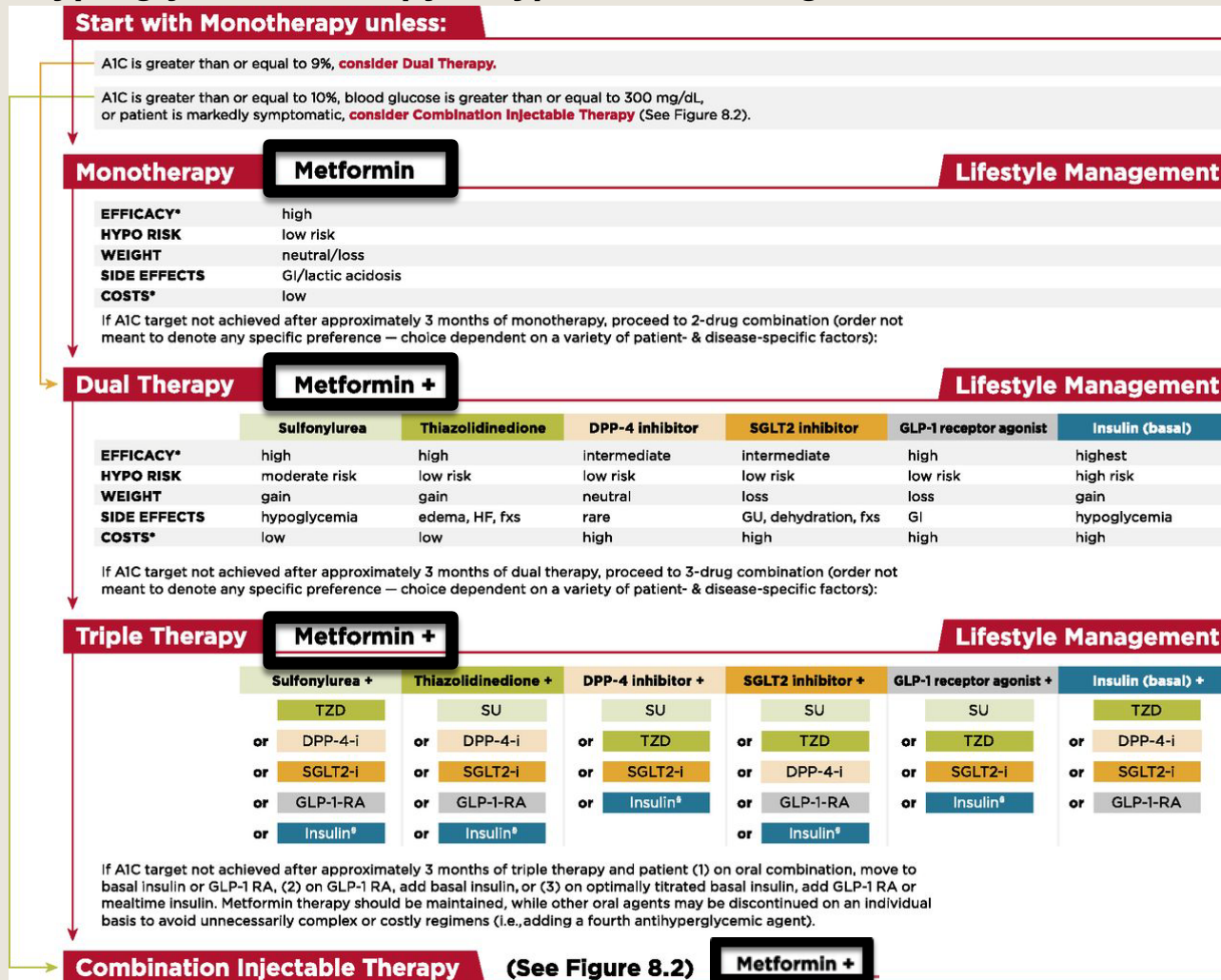
BILE ACID SEQUESTRANTS: colesevelam (Welchol), lowers cholesterol by decreasing the amount of bile acids (which is used to make cholesterol) reabsorbed in the body but also helps lower blood sugars (mechanism of which is uncertain)

DOPAMINE-2 AGONIST: bromocriptine (Cycloset), activates dopaminergic receptors that changes metabolism and increase sensitivity to insulin

Biguanides: Metformin

~AWP \$100/mo

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

Metformin



Monotherapy

Metformin

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Metformin



Preferred initial agent for type 2 diabetes
(except if contraindications for use)

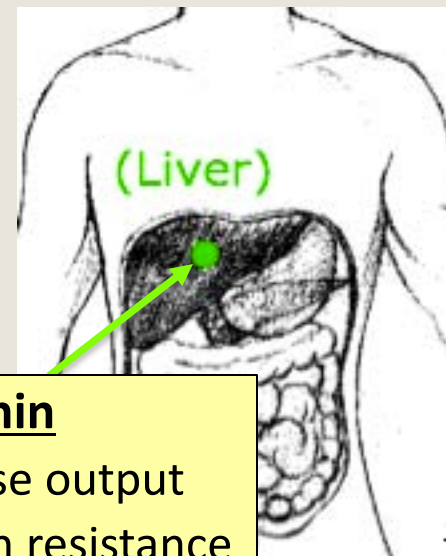
Benefits:



- +CV effects
- Ok in pregnancy

Effect of Metformin

- ↓ Hepatic glucose output
- improves insulin resistance



Negatives:



Check B12 esp in anemia
and periph neuropathy

- fishy odor
- LOW: lactic acidosis (incidence rate of 5-9/100,000)

Metformin: CI/Precautions



- **Renal dysfunction**
 - eGFR ≥ 45 to 60 ml/min/1.73m²: Continue; check renal fxn q3-6 mo
 - eGFR ≥ 30 to 45 ml/min/1.73m²: Reduce dose in half or 50% max dose; check renal fxn q3 mo. Do not initiate if never started.
 - eGFR <30 ml/min/1.73m²: Discontinue
- MDRD equation
 - http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm
 - http://www.nkdep.nih.gov/professionals/gfr_calculators/orig_con.htm
- Other hypoxic states; surgery; radiologic studies using iodinated contrast materials (stop at time of/prior to *and* withhold 48 hr after)

Metformin Initiation & Titration

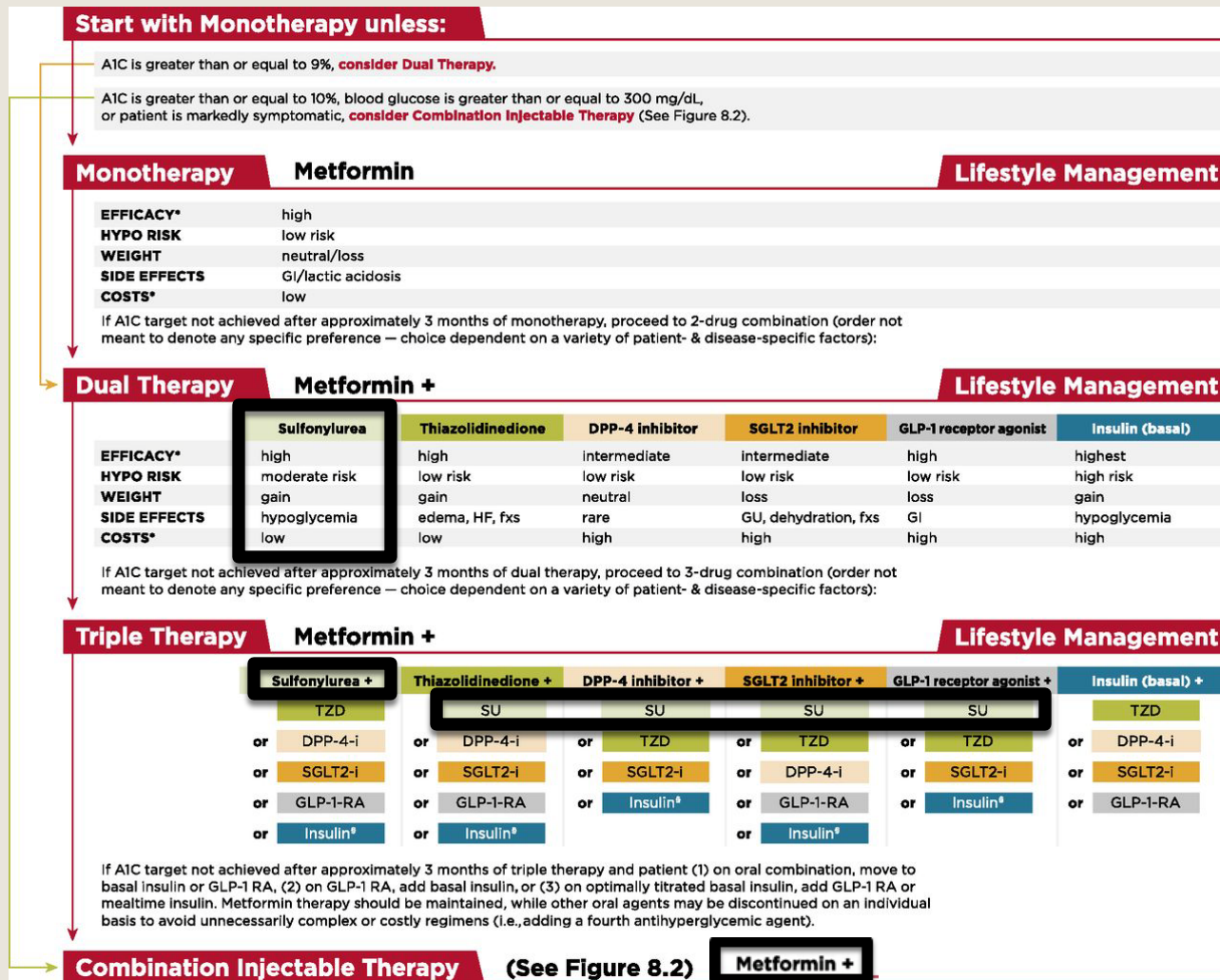
- Assess renal and liver function first
- 1 in 3 patients have GI side effects and may stop using med
- Start with low dose: 500 mg qPM with dinner
- After 7-14 days, and if GI SEs tolerable, titrate dose by 250mg to 500mg to:
 - 500 mg BID
 - 500mg qAM and 1,000 mg qPM
 - 1,000 mg BID (preferred over 850 mg TID)
 - At anytime GI SEs with ↑ dose, reduce to previous dose and titrate later after 2 wks
- Maximum effective dose 1,000 mg BID (FDA-approved max is 2,550 mg daily)
 - 1,000mg po BID better vs 850mg po TID as better adherence with similar efficacy
 - XR, solution (500mg/5ml) formulations available
- Storage: 15 to 30° C (59 to 86° F)



Insulin Secretagogues: Sulfonylureas

~AWP \$100/mo

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

Insulin Secretagogues: Sulfonylureas

- Sulfonylureas (2nd Generation)
 - glipizide, glyburide, glimepiride
 - glyburide **not** preferred in the elderly; renal dysfunction
- **Benefits:** Generally well tolerated

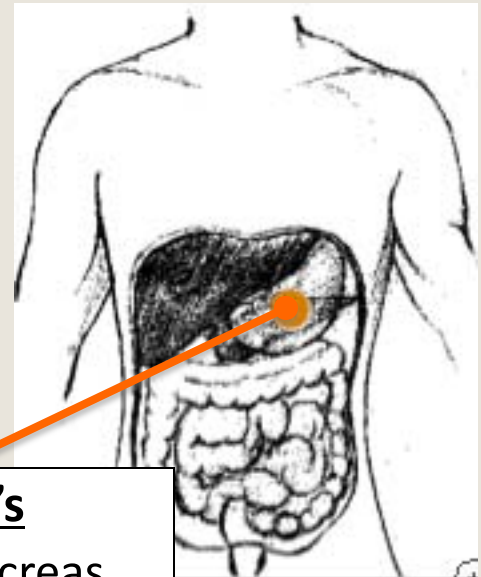


- ↓CVD events & mortality

- **Negatives**



- C/I severe sulfa allergy



Effect of SFU's

Stimulate Pancreas
to increase insulin
production

Glipizide



- **Dosing:**

- Start with 5mg qBreakfast then 5mg po BID; then 10mg po BID; possibility of 20mg po BID if no hypoglycemia and close to goal (qwk titration)

- **Pt Counseling:**



- Skip dose if not eating meal
- Know how to prevent and treat low sugar

- **Other:**

- **Good** for use in elderly
- Discontinue use if patient on basal-bolus insulin



Glyburide



- **Dosing:** (Micronized and regular versions are not interchangeable)
- **REGULAR** (Diabeta®): Start with 2.5 to 5mg qBreakfast then increase by 2.5mg qwk; max 20mg qday
 - Start with 1.25mg if pt is sensitive to hypoglycemia
- **MICRONIZED** (Glynase®; Prestab®): Start with 1.5 to 3mg qbreakfast, then increase by 1.5mg qwk; max 12mg qday
 - Start with 0.75mg if pt is sensitive to hypoglycemia

- **Pt Counseling:**



- Skip dose if not eating meal
- Know how to prevent and treat low sugar

- **Other:**

- Not great for use in elderly
- Discontinue use if patient on basal-bolus insulin



Glimepiride



- **Dosing:**

- Start with 2mg qBreakfast, then increase by 2mg qWk; max 4mg qDay (qWk dosing)
- Possibility of 8mg qDay if no hypoglycemia and close to goal

- **Pt Counseling:**



- Carry fast acting carbohydrate
- Know how to prevent and treat low sugar

- **Other:**

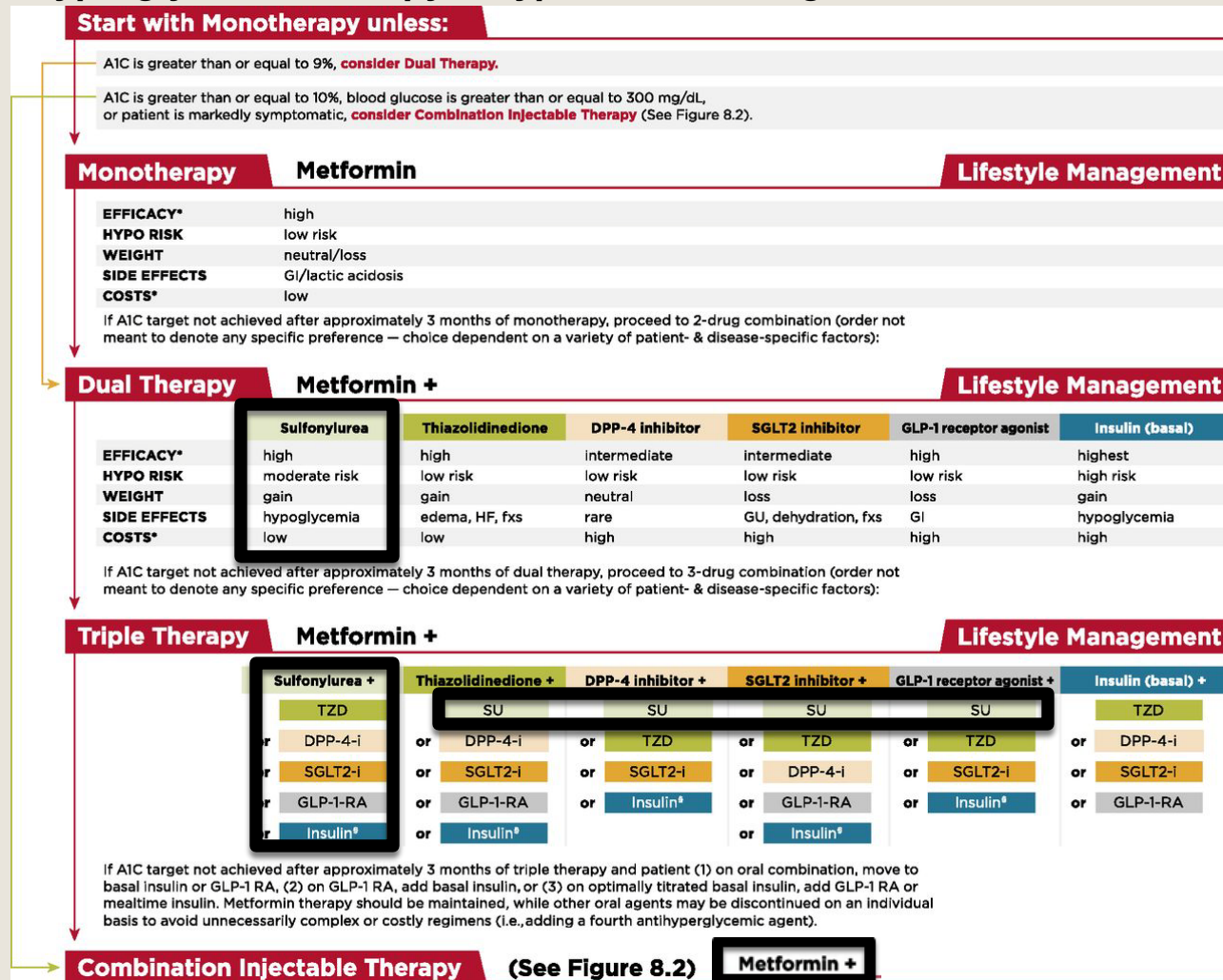
- **Good** for use in elderly
- Discontinue use if patient on basal-bolus insulin



Insulin Secretagogues: Glinides

~AWP \$150 to \$800/mo

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

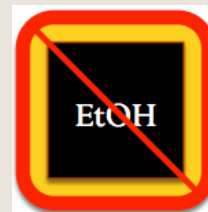
Glinides – shorter-acting than SFU's



- **Benefits:** Rapidly effective; benefits postprandial BGs; Useful in erratic eating schedule, renal dysfunction & patients with sulfa allergy or experiencing hypoglycemia with SFU
- **Negatives:**



- **Dosing:**
- **Repaglinide (Prandin®):** 1 to 2mg po TID or QID; 0.5mg if close to goal; double dose until 4mg per dose; max 16mg qday; ≥1 wk titrations
 - ↓ FPG 60 mg/dl; A1C by 1.7%
- **Nateglinide (Starlix®):** 120mg PO TID with meals; 60mg PO TID if close to goal
 - ↓ A1C by 0.5%; PPG control
- **Pt Counseling:**



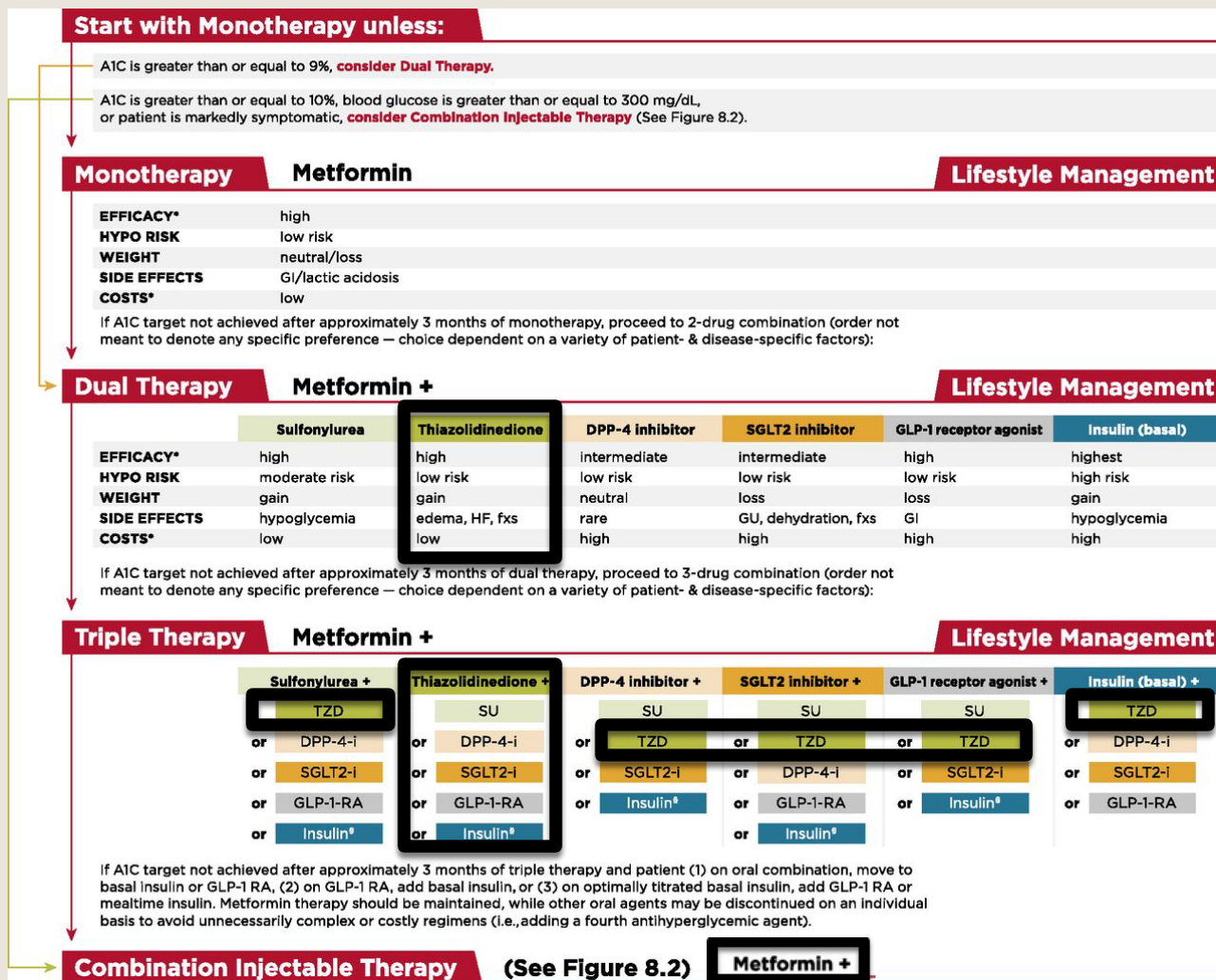
Storage: 25° C (77° F); repaglinide: protect from moisture

Other: Discontinue use if patient on basal-bolus insulin

Thiazolidinediones (TZDs)

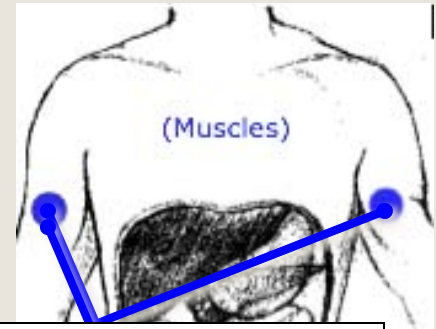
~AWP \$350/mo

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

Thiazolidinediones (TZDs)



Decrease peripheral insulin resistance (enhance glucose uptake by muscle); decreases hepatic glucose output

- **Benefits:**

- Activate peroxisome proliferator-activated receptors gamma (PPAR γ) nuclear receptors: muscle & fat tissue
- CV effects
($\downarrow$ vascular inflammation & smooth muscle cell proliferation;
 $\downarrow$ BP; $\downarrow$ microalbuminuria)
- Positive effects on lipids ($\downarrow$ TG, $\uparrow$ HDL-C, less-dense LDL-C)
- Preservation of beta-cell function
- $\downarrow$ restenosis after angioplasty & stent placement (rosiglitazone); $\downarrow$ progression of heart atherosclerosis (pioglitazone)

Parulkar. Ann Intern Med. 2001;134:61-71.

Spiegelman. Diabetes. 1998;47:507-514.

TZDs: Side Effects and CIs

- **SE:**



- Bone loss and risk of fractures primarily in women.

- **Contraindications**



- Check LFTs before starting, then periodically q 6 months



Thiazolidenediones (TZDs)



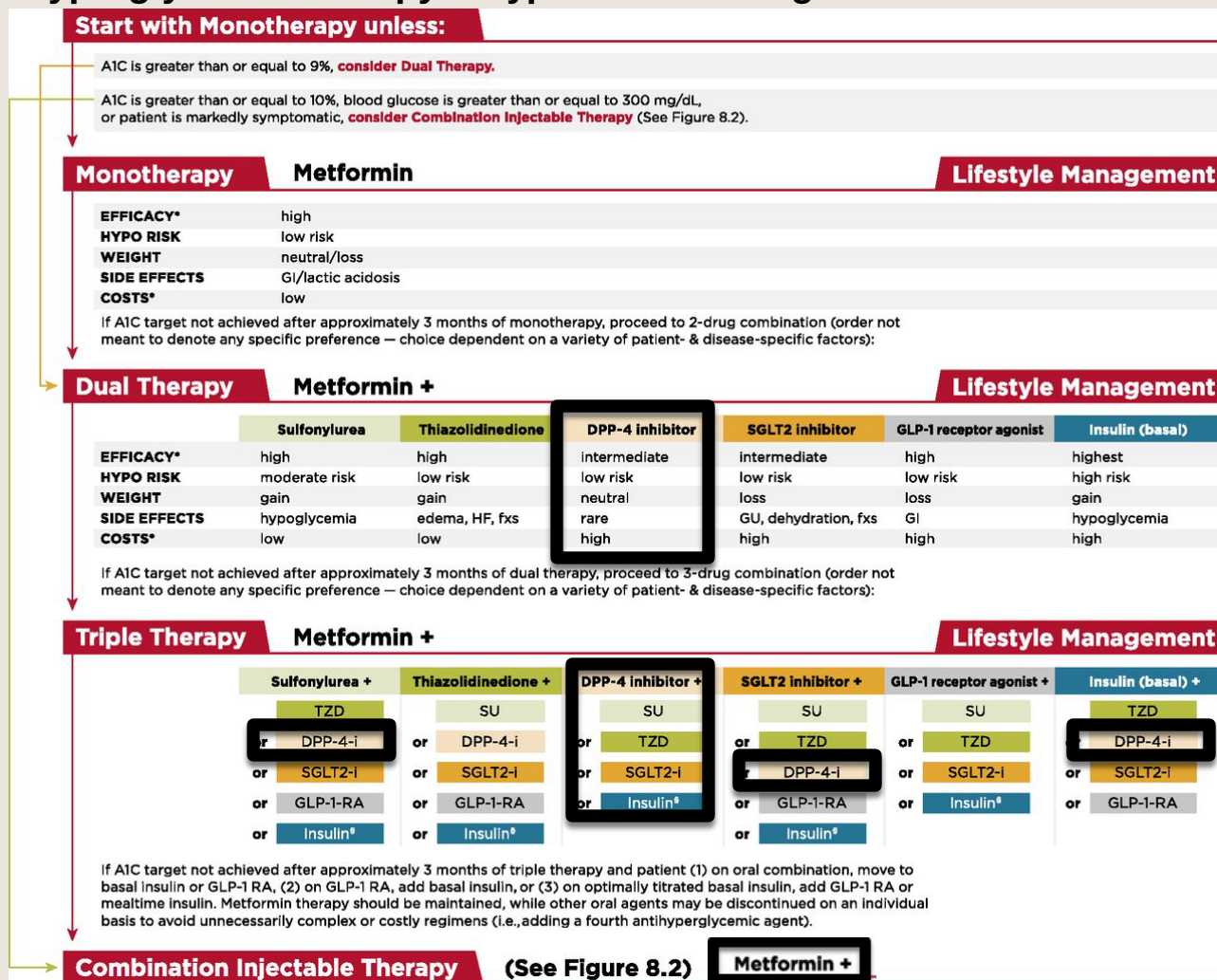
- **Dosing:** (up to 3-4 months to see full effect of dose)
- **Pioglitazone (Actos®):** 15 to 30mg PO qDay; can titrate to 45mg daily (titrate q8 to 12 wks; but caution bladder cancer risk)
- **Rosiglitazone (Avandia®):** 4mg po qDay; can titrate to 8mg daily (titrate q8 to 12 wks)
 - Enrollment in Avandia-Rosiglitazone Medicines Access Program
- **Pt Counseling:**
- Report problems with lower extremity swelling, unusual fatigue
- **Storage:** 15 to 30° C (59 to 86° F); protect from light
- **Other:**
 - Expensive
 - Avandia associated with increased CVD risk
 - Actos: Risk for Heart failure, macular edema
 - Unlikely associated with bladder cancer



DPP-4 Inhibitors: Sitagliptin; Saxagliptin; Linagliptin, Alogliptin

~AWP \$400/mo

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

DPP-4 Inhibitors

- **Gliptins:** Monotherapy ($\downarrow$ A1C $\sim 0.7\%$) Ideal if close to A1c goal / high PPG
 - **Advantages:** oral; weight neutral; little nausea or hypoglycemia, No hepatic adjustment
- **Disadvantages:** UTIs (can lead to renal failure), arthralgias (rare but disabling), bone fractures (due to falls/hypotension), expensive (select formulary choice), low evidence for CV outcomes
- **Storage:** 15 to 30° C (59 to 86° F)



DPP-4 Inhibitors

Sitagliptin (Januvia®)

- Dose: 100 mg po daily
 - 50 mg daily if CrCl 30-50 ml/min
 - 25 mg daily if CrCl <30 ml/min
- P-glycoprotein substrate
- Low CYP3A4 DDI



Saxagliptin (Onglyza®)

- 5 mg po daily (2.5 mg if Cyp3A4 drug interactions or CrCl ≤50 ml/min)
- Cyp 3A4 and P-glycoprotein substrates
- Increased heart failure risk



Alogliptin (Nesina®)

- Dose: 25 mg po daily
 - 12.5 mg daily if CrCl 30 to <60 ml/min
 - 6.25 mg daily if CrCl <30 ml/min
- Low CYP3A4 DDI



Linagliptin (Tradjenta®)

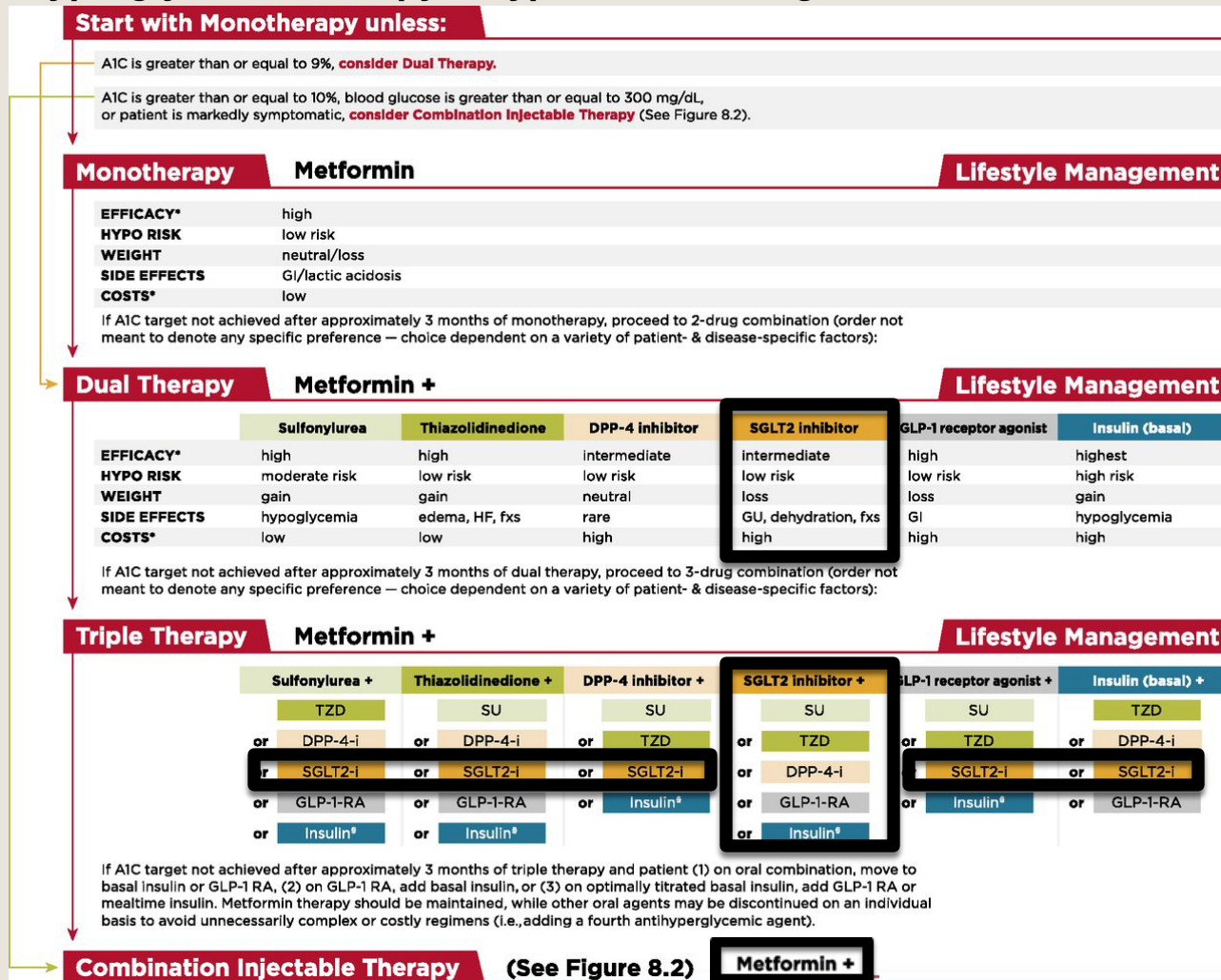
- 5 mg po daily
- Lipids, TGs increase
- No need for renal adjustment
- Cyp 3A4 and P-glycoprotein substrate



SGLT2 Inhibitors

~AWP \$500/mo

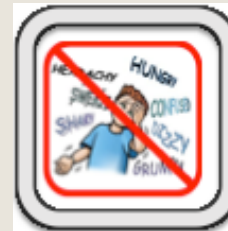
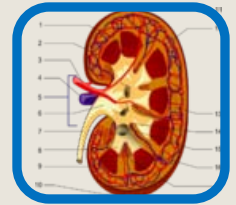
Antihyperglycemic therapy in type 2 diabetes: general recommendations.



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SGLT2 Inhibitors

- **MOA:** Inhibits sodium-glucose co-transporter 2 in the kidneys. Allows more glucose to spill into the urine instead of being reabsorbed
- Monotherapy ($\downarrow$ A1C ~1%)
- **Advantages:** oral, weight loss, lower BP, low hypoglycemia, no hepatic dosage adjustment



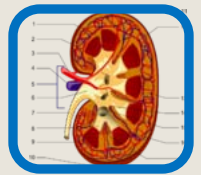
- **Disadvantages:** UTI, genital yeast infections, ketoacidosis, increases LDL, increased urination, dehydration, hyperkalemia, transient increase of creatinine, potential increased risk of stroke (Canagliflozin®), expensive



Storage: 15 to 30° C (59 to 86° F)

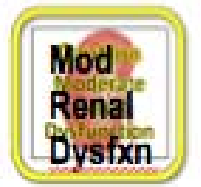


SGLT2 Inhibitor



- **Dapagliflozin (Farxiga®)**

- Dosing: 5mg AM with or w/o food; may increase to 10mg daily
 - Avoid if eGFR <60 ml/min; C/I if eGFR <30 ml/min
 - No hepatic dose adjustment (not studied in severe hepatic impairment)
 - May ↑ LDL-C
 - Increased bladder cancer risk; C/I bladder cancer



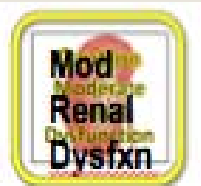
- **Empagliflozin (Jardiance®)**

- Dosing: 10mg in AM with or w/o food; may increase to 25mg qday
 - Avoid if eGFR <45 ml/min; C/I if eGFR <30 ml/min
 - No hepatic dose adjustment
 - Frequent hypo's with insulin
 - Lowers risk of CV death – new FDA labeling



- **Canagliflozin (Invokana®)**

- Dosing: 100mg/day with or w/o food but best 30min AC first meal
 - May increase to 300mg/day (if GFR >60ml/min)
 - 100mg/day if eGFR 45 to 59 ml/min
 - Avoid if eGFR <45 ml/min; C/I if eGFR <30 ml/min
 - Potential increased risk of stroke





Combination Therapy

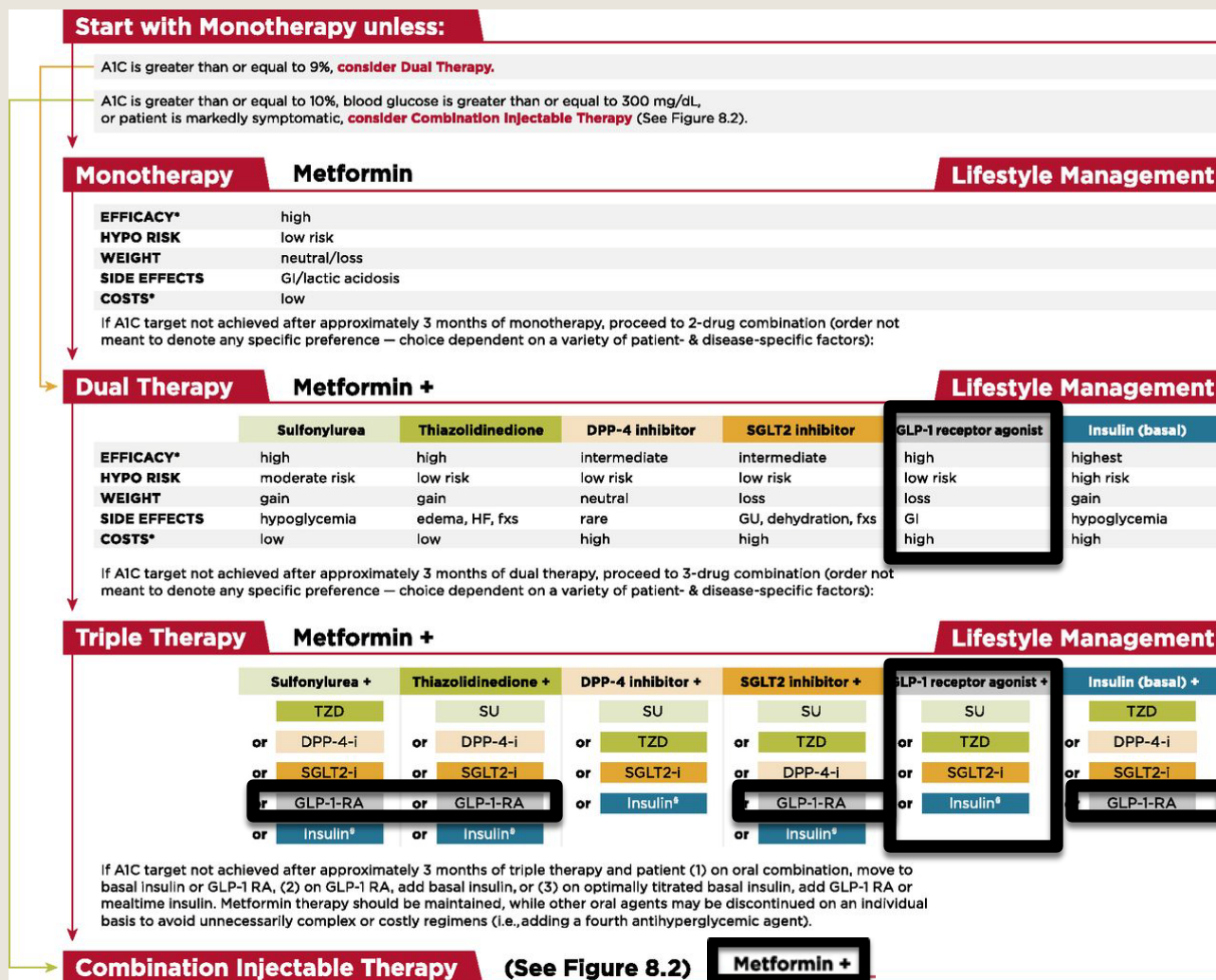
Combine Agents with Different Mechanisms of Action

- **Consider initiating two agents especially when A1c $\geq$ 9%**
- Combination Oral Therapy
 - Metformin plus Sulfonylurea
 - Metformin plus Repaglinide/Nateglinide
 - Metformin plus DPP-4 inhibitor
 - Metformin plus Thiazolidinedione
 - SFU plus Acarbose
 - SFU plus Thiazolidinedione
 - SFU plus DPP-4 inhibitor
 - Others
 - Triple oral therapy
- Combination therapy: oral agents or basal insulin with GLP-1 RA (e.g., exenatide, liraglutide, insulin glargine plus lixisenatide and insulin degludec plus liraglutide)

GLP-1 Receptor Agonists: Exenatide, Liraglutide, Albiglutide, Dulaglutide

~AWP \$500 to \$700/mo

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



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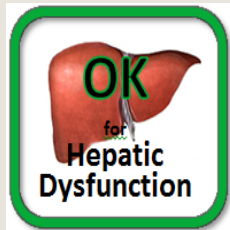


Exenatide (Byetta®)



- Indication: type 2 DM adults
 - Monotherapy (10/09); Combination therapy
- Peak concentration post injection: 2.1 hr
- A1C ↓ ~1%

Resistant to DPP-IV degradation; similar binding affinity at GLP-1 receptors



Do not use in:



- patients with severe GI disease (e.g., gastroparesis)



Exenatide (Byetta®)



- SE:



- Storage: 2 to 8° C (36 to 46° F); after opening: ≤25° C (≤77° F); do not freeze (discard if frozen); protect from light; discard after 30 days from initial use
- Increased risk of hypoglycemia when combined with SFU or SFU + metformin → consider decreasing SFU therapy upon initiation of Exenatide
 - No hypoglycemia if combined with only metformin

Exenatide (Byetta®) Dosing



- Start 5 mcg subQ BID before (within 60 mins) morning and evening meal (at least 6hr apart). Inject in upper arm, thigh, or abdomen.
- When added to SFU, consider ↓ dose of SFU
- After 1 month, can ↑ to 10 mcg SQ BID
- Available in prefilled pen
 - 5 mcg and 10 mcg for 60 doses (1 month supply)
 - **Pen in use: can be stored up to 25° C (77° F)**
- For oral medications dependent on threshold concentrations or rapid onset, take them 1 hour before (i.e., BCPs, antibiotics); post marketing case reports ↑ INR with warfarin (monitor closely)
- When using with insulin, inject in non-adjacent site to insulin injection and do not mix injections



~AWP \$500 to \$700/mo

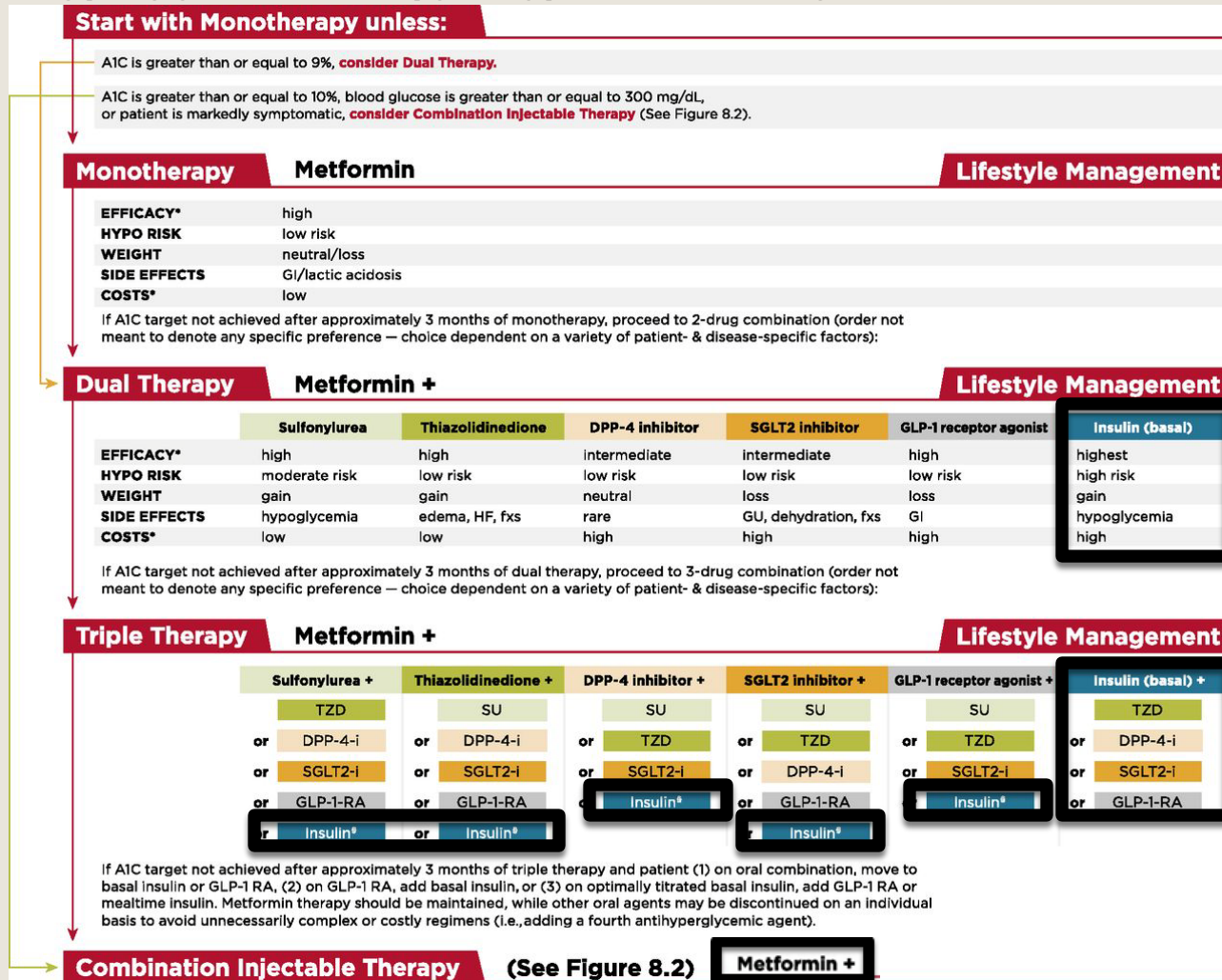
GLP Receptor Agonists

- **Exenatide (Byetta®)**
 - 5mcg SQ BID. May increase to 10mcg SQ BID after 1 mo
 - Not Rec'd use in severe renal impairment
- **Liraglutide (Victoza®, Saxenda®)**
 - 0.6mg SQ qDay. May increase to 1.2mg qDay weekly until 1.8mg qDay
 - Not Rec'd use in mod-to-severe renal impairment
- **Albiglutide (Tanzeum®)**
 - 30mg SQ qWk. May increase to 50mg qWk after 12 wks monothx or 4wks combo thx
 - No renal or hepatic dosage adjustment
- **Dulaglutide (Trulicity®)**
 - 0.75mg SQ qWk. May increase to 1.5mg qWk
 - No renal or hepatic dosage adjustment

Insulin

~AWP \$150 to \$400/1,000 units; ~\$600/inhaled insulin

Antihyperglycemic therapy in type 2 diabetes: general recommendations.



American Diabetes Association Dia Care 2017;40:S64-S74

Insulin Considerations

- Start insulin therapy when:
 - Severely uncontrolled DM
 - $A1c \geq 10\%$
 - Random BG ≥ 300
 - Presence of ketoacidosis
 - Pregnant
 - Contraindicated to other DM meds
- Avoid use as threat or describing it as a failure or punishment
- Patient self-titration of insulin based on SMBGs improves glycemic control



Insulin Pharmacokinetics

Type of Insulin	Onset	Peak	Duration	Appearance
Rapid-acting Humalog/Novolog/ Glulisine	5-15 min	1-2 hr	3-5hr	clear
Inhaled insulin Afrezza®	12-15 min	53min	2.5-3hr	powder
Short-acting Regular	30-60 min	2-4hr	6-8+hr	clear
Intermediate-acting NPH	1-2hr	6-10hr	12+hr	cloudy
Long-acting Detemir Glargine Degludec Basaglar	1 hr 1.5hr 1h 1h	flat flat flat flat	6-24hr 24+hr 24+hr 24+hr	clear clear

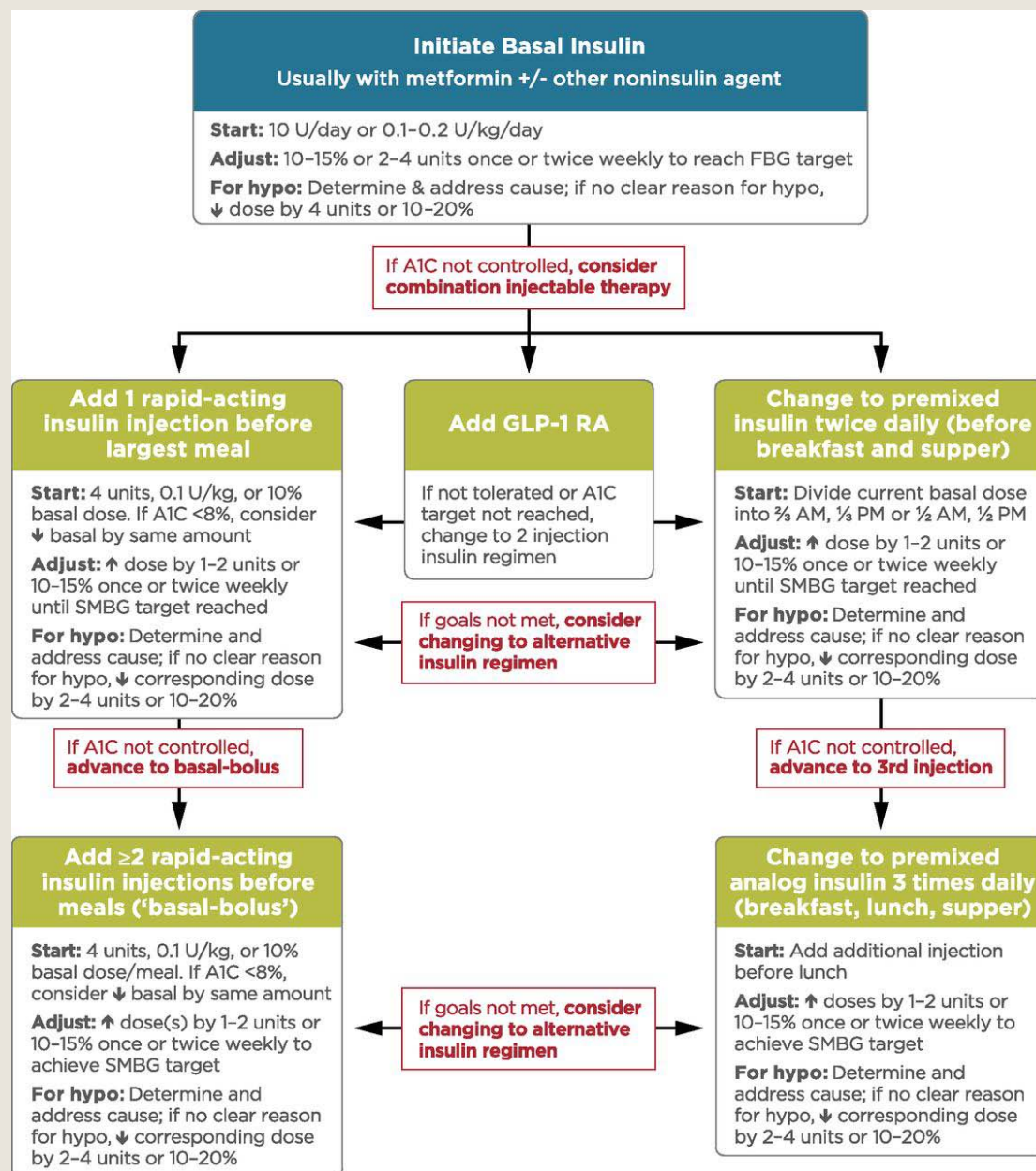


Insulin Pre-Mixes



- **Insulin Mixtures (all are cloudy)**
 - Humalog[®] Mix 75/25
75% insulin lispro protamine susp/25% insulin lispro
 - Humalog[®] Mix 50/50
50% insulin lispro protamine susp/50% insulin lispro
 - NovoLog[®] Mix 70/30
70% insulin aspart protamine susp/ 30% insulin aspart
 - Novolog[®] Mix 50/50
70% insulin aspart protamine susp/ 30% insulin aspart

Combination injectable therapy for type 2 diabetes.



Insulin Titration

Initiate Basal Insulin

Usually with metformin +/- other noninsulin agent

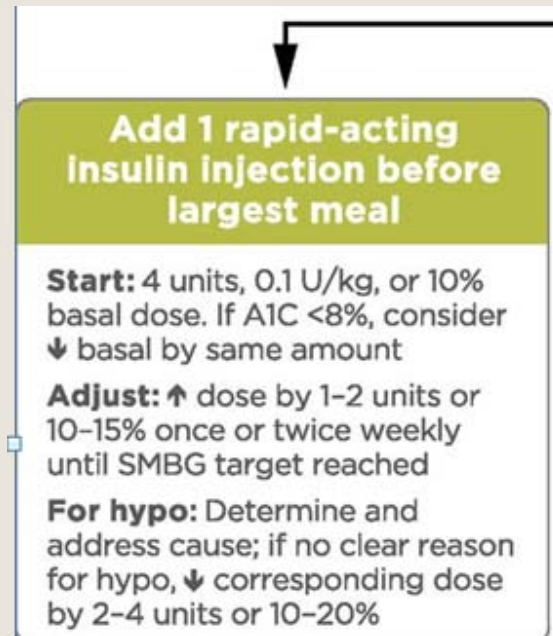
Start: 10 U/day or 0.1-0.2 U/kg/day

Adjust: 10-15% or 2-4 units once or twice weekly to reach FBG target

For hypo: Determine & address cause; if no clear reason for hypo,
↓ dose by 4 units or 10-20%

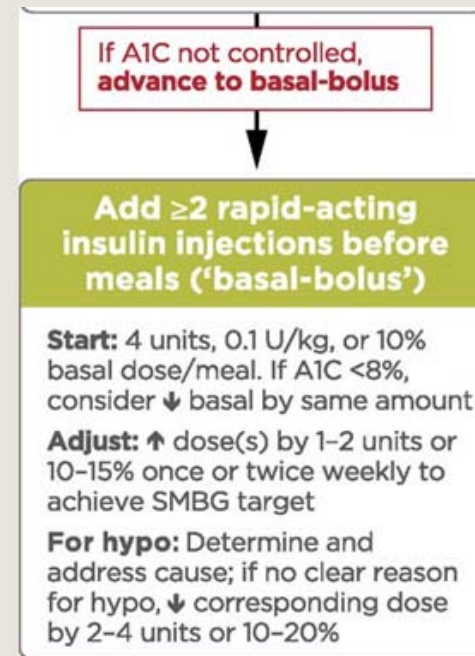
- Example titration: A1c 13.7
 - 10 u basal insulin, e.g., Basaglar, at bedtime
 - +1wk: 12 u
 - +1wk: 14 u
 - +1wk: 16 u
 - +1wk: **Hypo's**: Decrease by 4 u to 12 u
 - +1wk: 14 u
 - Continued weekly titration to 32 u → 3-month A1c 10.2 and not at FBG goal

Insulin Titration



- Example Titration Continued: 32 u Basaglarat bedtime. A1c 10.2
 - **Add 4 u Novolog pre-dinner (largest meal)**
 - +1wk: 5 u Novolog PM and 32 u Basaglar
 - +1wk: 6 u Novolog PM and 32 u Basaglar
 - +1wk: 8 u Novolog PM and 32 u Basaglar
 - **Continued weekly titration to 12 u Novolog PM → Both bedtime and FBGs near goal. BGs continued elevated especially afternoon BGs**

Insulin Titration



- Example Titration Continued:
 - **Add 4 u Novolog pre-breakfast** to 12 u Novolog PM and 32 u Basaglar
 - +1wk: 5 u Novolog AM, 12 u Novolog PM, and 32 u Basaglar
 - +1wk: 6 u Novolog AM, 12 u Novolog PM, and 32 u Basaglar
 - +1wk: 8 u Novolog AM, 12 u Novolog PM, and 32 u Basaglar
 - +1wk: **Hypo's**: Decrease by 2 u to 6 u
 - **Titrate to 10 u Novolog AM, 12 u Novolog PM, and 32 u Basaglar. 3-month A1c 8.4**

Concentrated Insulins

- U-500 regular (Humulin R®)
 - Pen or vial with dedicated syringe
 - Regular insulin syringe could lead to a 5-fold dosing error



- U-200 lispro (Humalog KwikPen®)



- U-200 degludec (Tresiba FlexTouch®)
 - Opened at RT good for 8 wks (56 days)
 - Also comes in U-100



- U-300 glargine (Toujeo Solostar®)



Basaglar Insulin

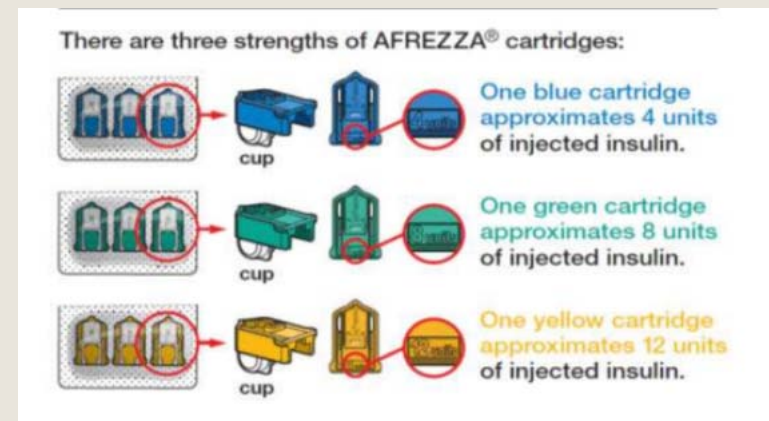
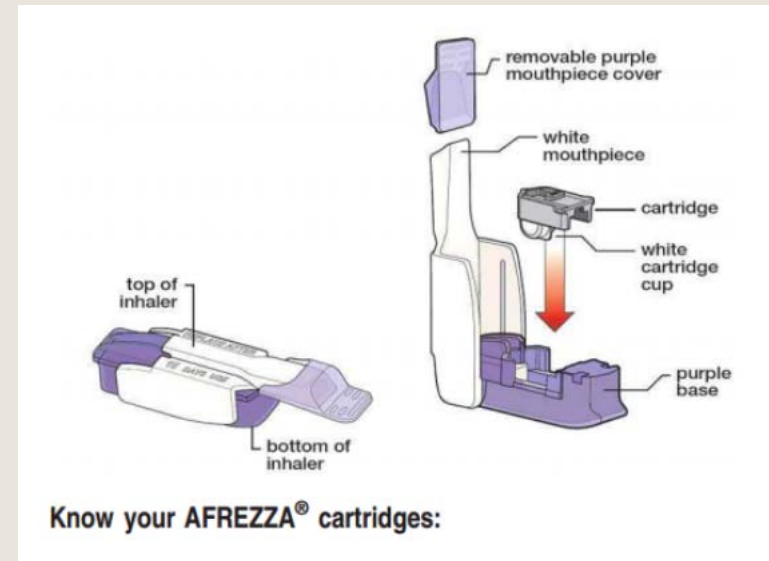
- Many patients will switch from *Lantus* to *Basaglar* (BAY-zuh-glar).
- *Basaglar* is a new brand of glargine U-100...NOT a *Lantus* generic.
- But *Lantus* will be dropped from some 2017 formularies since it costs about \$370 per 5-pen box...compared to about \$320 for *Basaglar*. *Basaglar* will only come in a *KwikPen*.
- If needed, help patients switch to *Basaglar* appropriately.
- Request a new Rx when switching from ANY long-acting insulin to *Basaglar*...since *Basaglar* isn't AB-rated and usually can't be automatically substituted.
- And advise patients to monitor blood glucose more frequently when making a switch...especially between different types of insulin.

Basaglar Insulin

- When switching from *Lantus* (glargine U-100) to *Basaglar*, generally suggest the same daily dose and dosing frequency.
- When switching from *Levemir* (detemir U-100) to *Basaglar*, suggest giving the same daily dose. But point out that some patients on Levemir TWICE-daily can switch to *Basaglar* ONCE-daily...because glargine is a little longer-acting than detemir.
- When switching from *Toujeo* (glargine U-300) to *Basaglar*, suggest starting with 80% of the daily Toujeo dose in well-controlled patients.
 - Explain that patients will likely need about a 10% lower dose of *Basaglar* than *Toujeo*...but starting 20% lower decreases hypoglycemia risk

Inhaled Insulin

- Afrezza® (rapid-acting insulin)
 - Less A1c lowering (~0.8%)
 - Limited strengths
 - Not for those who smoke or stopped within 6 mo; asthma, COPD
 - Need lung function test BL, 6mo, annual



Glucagon (Glucagen®)



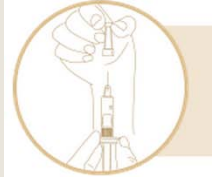
- **Benefits:** Treat severe hypoglycemia
- **Side Effects:** Nausea, Headache
- **DDI:** oral anticoagulants (increase bleeding risk)
- **Negatives:** C/I pheochromocytoma, insulinoma
- **Dosing:** 1mg IM, subQ prn severe hypoglycemia
- **Notes:**
 - Train family, co-workers, close friends on use
 - Rx multiple kits as many insurance cover in one copay



Glucagon Administration



1. Flip off the seal from the vial of Glucagon powder.



2. Remove the needle cover from the syringe. **DO NOT REMOVE THE PLASTIC CLIP FROM THE SYRINGE**, as this may allow the push rod to come out of the syringe.



3. Insert the needle into the rubber stopper on the vial, then inject the entire contents of the syringe into the vial of Glucagon powder.



4. Remove the syringe from the vial, then gently swirl the vial until the liquid becomes clear. Glucagon should not be used unless the solution is clear and of a water-like consistency.



5. Insert the same syringe into the vial and slowly withdraw all of the liquid. In children weighing less than 44 pounds, withdraw half the liquid (0.5 mark on the syringe).



Glucagon Administration



6. Cleanse site on buttock, arm or thigh and inject Glucagon immediately after mixing. Inject the Glucagon and then withdraw the needle. Apply gentle pressure against the injection site.



7. Turn the person on his/her side. When an unconscious person awakens, he/she may vomit.

Call 911 immediately after administering Glucagon. If the person does not awaken within 15 minutes, you may administer a second dose of Glucagon, if previously instructed by your healthcare provider to do so.

As soon as the person is awake and able to swallow, give him/her a fast-acting source of sugar (such as fruit juice) followed by a snack or meal containing both protein and carbohydrates (such as cheese and crackers, or a peanut butter sandwich).



8. Discard any unused reconstituted Glucagon.



Diabetes Medicines

When initiating drug therapy, REMEMBER to assess:

- A1c:
 - $\geq 10\%$ think insulin (combo insulin therapy)
 - $\geq 9\%$ think combo therapy
 - $< 9\%$ can be monotherapy (usually metformin)
 - Each non-insulin agent lowers A1c by $\sim 0.9\%$ to 1.1%
- Contraindications
- Potential side effects, e.g., hypoglycemia?
- Weight considerations
- Barriers to adherence and patient preferences
- Drug formulary, i.e., Cost
- Drug-drug, drug-disease interactions

Diabetes Medicines

When adjusting drug therapy, REMEMBER to assess:

- Is your patient **administering** the medications correctly?
- Does your patient have any barriers to **adherence** including **cost**?
- Are the current medications **dosed** appropriately?
- Is your patient experiencing **side effects** from any of the diabetes medications?
- Does your patient have any **conditions** that warrant modification of therapy?
- Are there drug-drug, drug-food, drug-herb **interactions** of concern?

SPECIAL THANKS

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- Note: Philip Chan does not claim copyright to images or slides protected under copyright