

Metformin

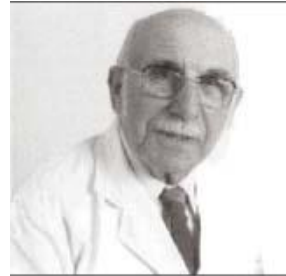
By pharmacist:
Rasha Barhoum

Contents

- History
- Mechanism of action
- Metformin in Guidelines
- Dosing
- Side effects
- Contraindications
- Pharmacokinetics

Historical Overview

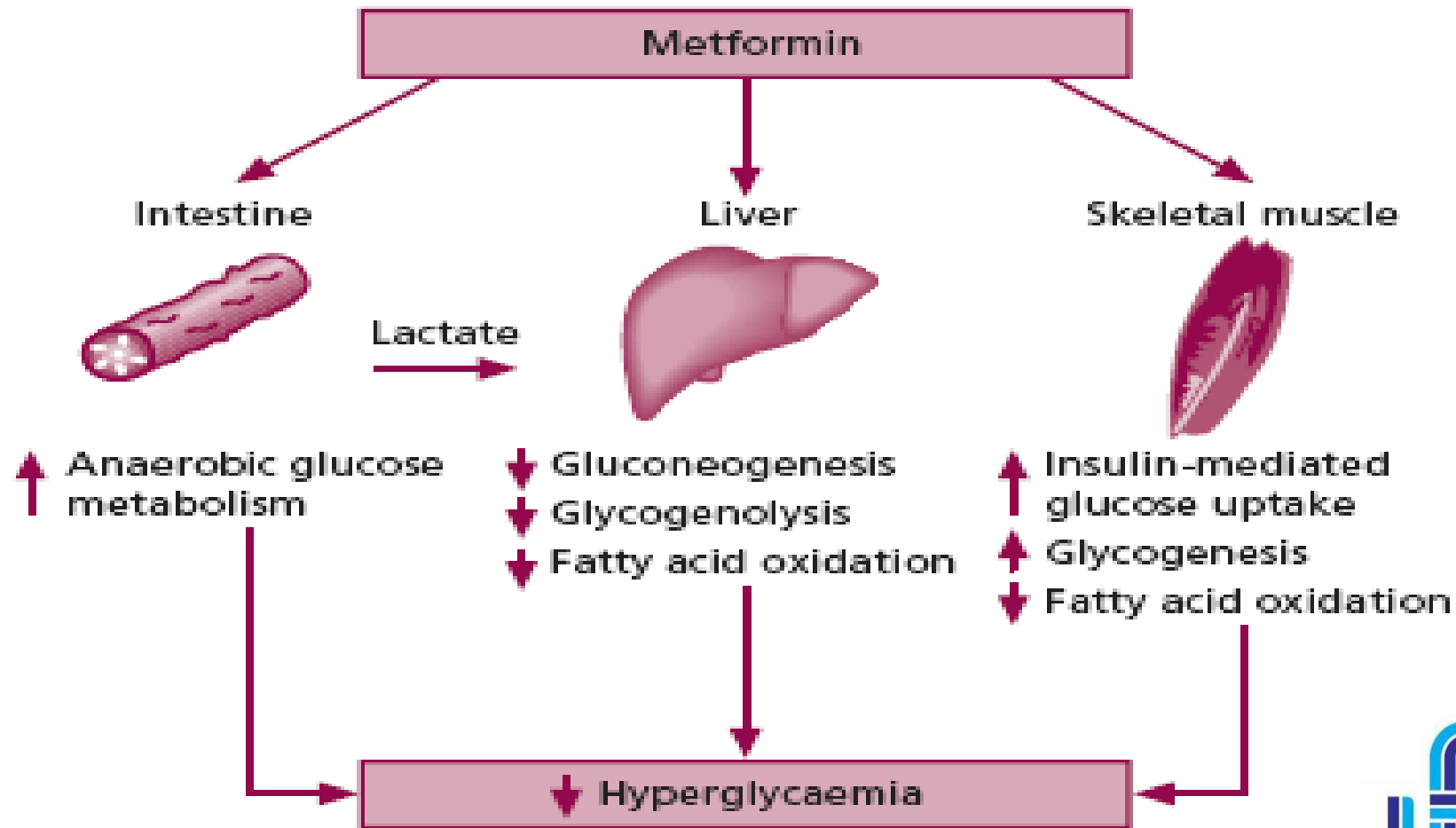
- *Galega officinalis (Middle ages) reduce DM*
- *Synthalin A&B less toxic 1920's*
- *Advent of insulin 1930's*
- *Jean Sterne (Paris) 1956*
- *UK 1958*
- *Canada 1972*
- *US 1995*
- *FDA approved 1994 !!!*



Mechanism of action

- Insulin sensitizer
- Increases glucose uptake and utilization by target tissues
- Decreases insulin resistance
- Lower risk of hypoglycemia due to its mechanism of action

Metformin Mechanism of action



Metformin in Guidelines

- First line agent
- >50 year old molecule
- Current guidelines from the **ADA/EASD** and the **AACE/ACE** recommend early **initiation of metformin as a first-line drug** for monotherapy and combination therapy for patients with T2DM

Guidelines 2016

Mono-therapy

Efficacy[†]
Hypo risk
Weight
Side effects
Costs[†]



Dual therapy[†]

Efficacy[†]
Hypo risk
Weight
Side effects
Costs[†]

Healthy eating, weight control, increased physical activity, and diabetes education

Metformin

high
low risk
neutral / loss
GI / lactic acidosis
low

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

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea	Thiazolidine- dione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
high	high	Intermediate	Intermediate	high	highest
moderate risk	low risk	low risk	low risk	low risk	high risk
gain	gain	neutral	loss	loss	gain
hypoglycemia	edema, HF, fxs	rare	GU, dehydration	GI	hypoglycemia
low	low	high	high	high	variable

Guidelines 2018

Antihyperglycemic Therapy in Adults with Type 2 Diabetes

At diagnosis, initiate lifestyle management, set A1C target, and initiate pharmacologic therapy based on A1C:

A1C is less than 9%, **consider Monotherapy.**

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy

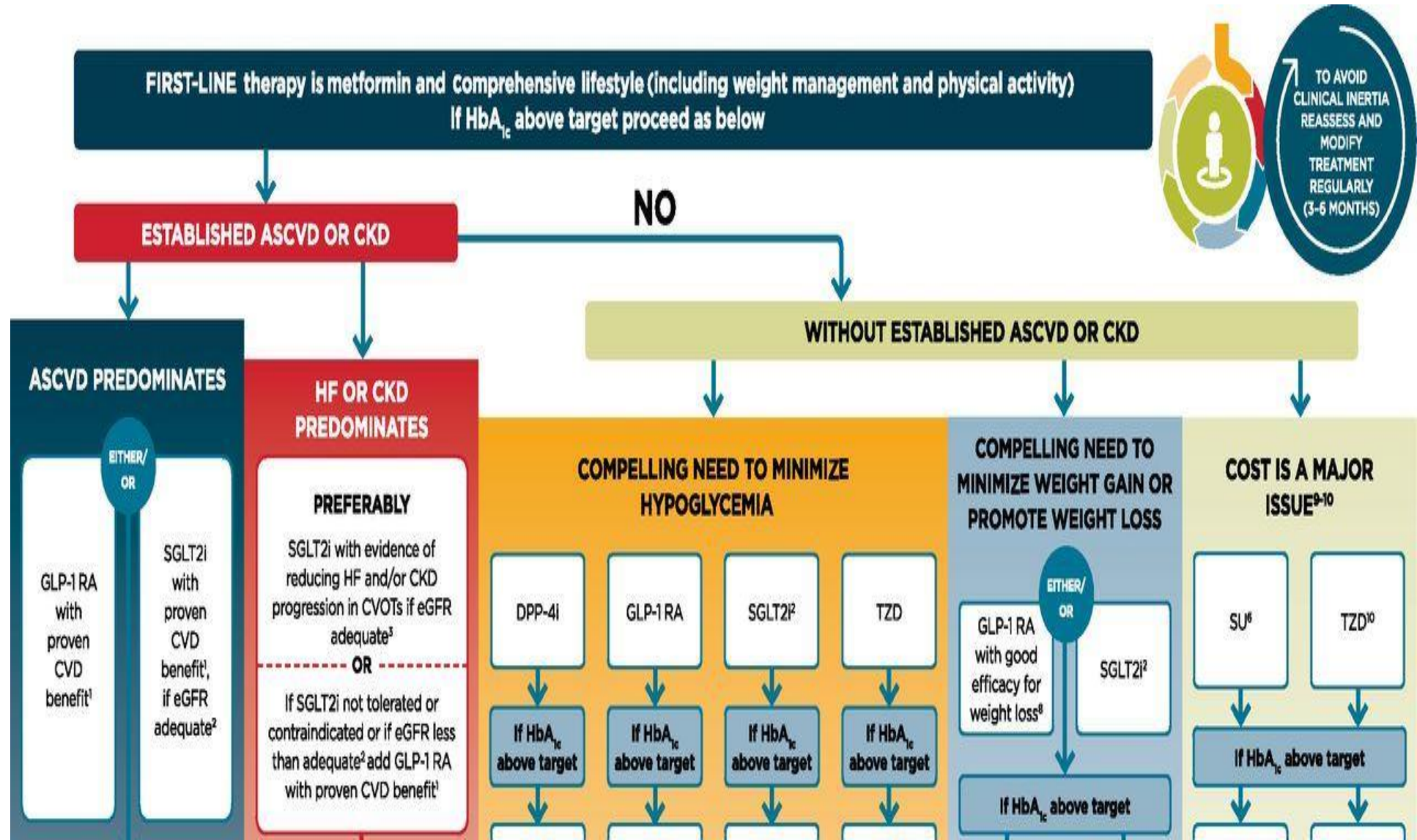
Lifestyle Management + Metformin

Initiate metformin therapy if no contraindications* (See Table 8.1)

**A1C at target
after 3 months
of monotherapy?**

- Yes:** - Monitor A1C every 3–6 months
- No:** - Assess medication-taking behavior
- Consider Dual Therapy

Guidelines 2019



Dosing

- *T2DM*
- Initial 500mg po q12 hr or 850mg po qDay with meals; increase dose in increments of 500 mg/week or 850mg/ 2 weeks
- Maintenance dose 1500-2550 mg/day
- *PCO (off-label)*
- 500 mg for 1-2 weeks then 500mg twice a day for 1-2 weeks then 500mg three times a day or 850mg twice a day for 1-2 weeks then 1g twice a day or 850mg three times a day

Common side effects of Metformin

- Stomach pain
- Nausea and vomiting
- Bloating
- Gas
- Diarrhea
- Constipation
- Heartburn
- Weight loss
- Headache



Contraindication and cautious use

- **Contraindicated:**
 - Renal / hepatic disease
 - Acute MI
 - Diabetic ketoacidosis
- **Caution:**
 - 80 years old patient
 - History of CHF

pharmacokinetics

- Bioavailability: 50-60%
- Peak plasma: 2-3 hr
- Metabolism: Not by liver
- Half-life: 4-9 hr
- Excretion: urine (90% by tubular secretion)





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Thanks for listening