EXTRACORPOREAL NEPHROLOGY GROUP

ORAL HYPOGLYCEMIC DRUGS IN CKD

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INTRODUCTION

- Metformin – reduces hepatic glucose production, increases insulin sensitivity and insulin mediated peripheral glucose utilization and decreases intestinal glucose absorption.[1st line OHA].
- Shorter-acting sulfonylurea medications with mostly inactive metabolites are preferred - Glipizide, Glimepride and Gliclazide.
- DPP-IV I -Inhibit the enzyme DPP-4 , deactivates GLP-1 and glucose-dependent insulinotropic polypeptide (GIP).[less hypoglycemia events].
- Meglitinides: Repaglinide - acts at the sulfonylurea receptor to increase insulin secretion .Much shorter acting than sulfonylureas. Nateglenide not used in CKD.

INTRODUCTION

- Alfa glucosidade inhibitors: decreases glucose uptake after food intake. Voglibose - very low systemic absorption (<10–20%) ; excreted unchanged in feces. Renal excretion is negligible.

- SGLT2I : Cardio renal benefits. First line drugs. Decreases proteinuria and can be given up to egfr 20.
- [Kidney trials – Credence, Empa- kidney, Dapa Ckd
  Cardiovascular trials – Empareg, Canvas, Declare –Timi, Vertis-CV, Scored
  Heart failure trials – Dapa HF , Emperor reduced, Deliver].

- GLP-1 :DM /CKD/Obesity profile patients benefitted most. Decreases all cause mortality ,albuminuria .weight loss and reduces cardiac events.

METFORMIN DOSE ADJUSTEMENT

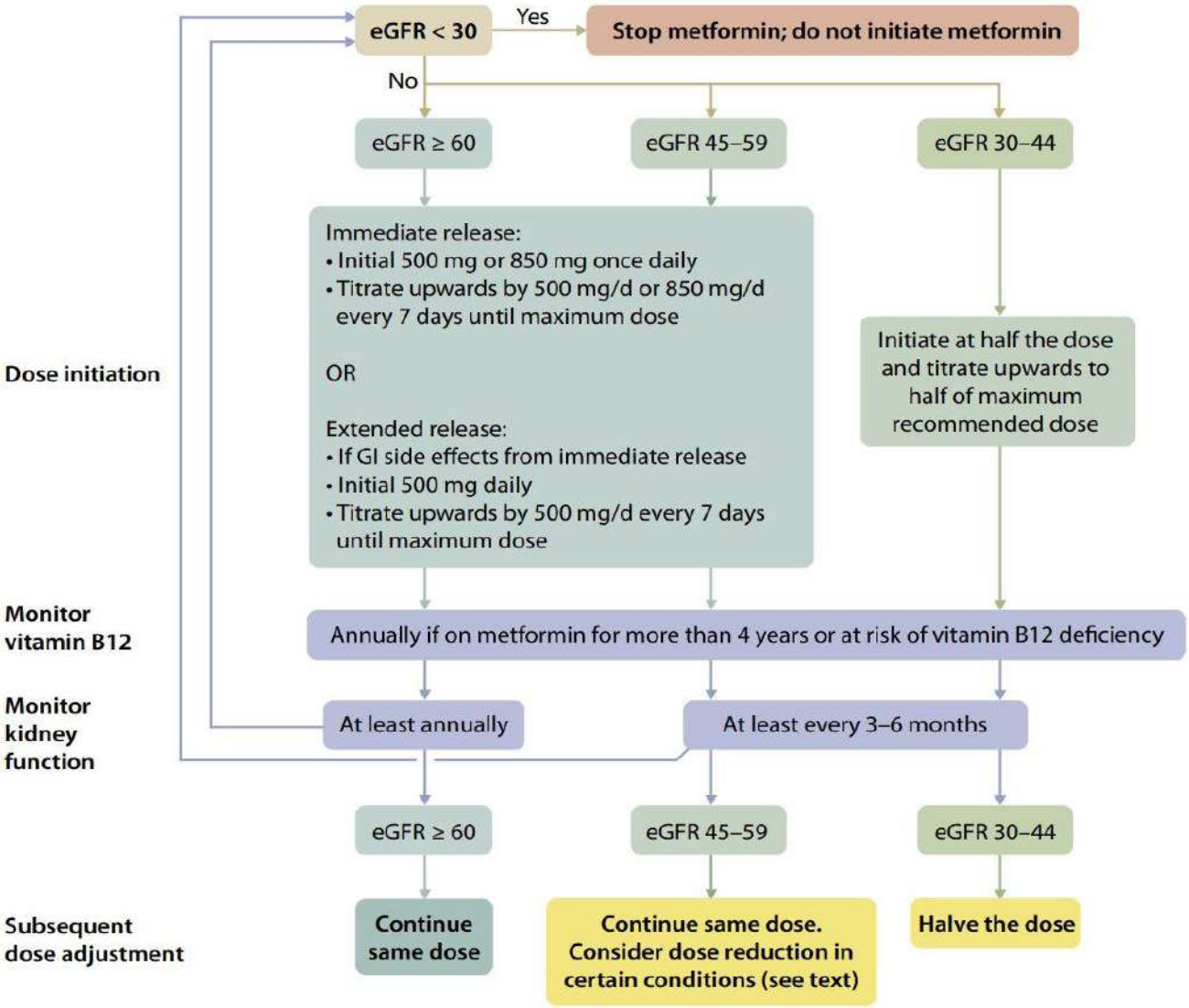
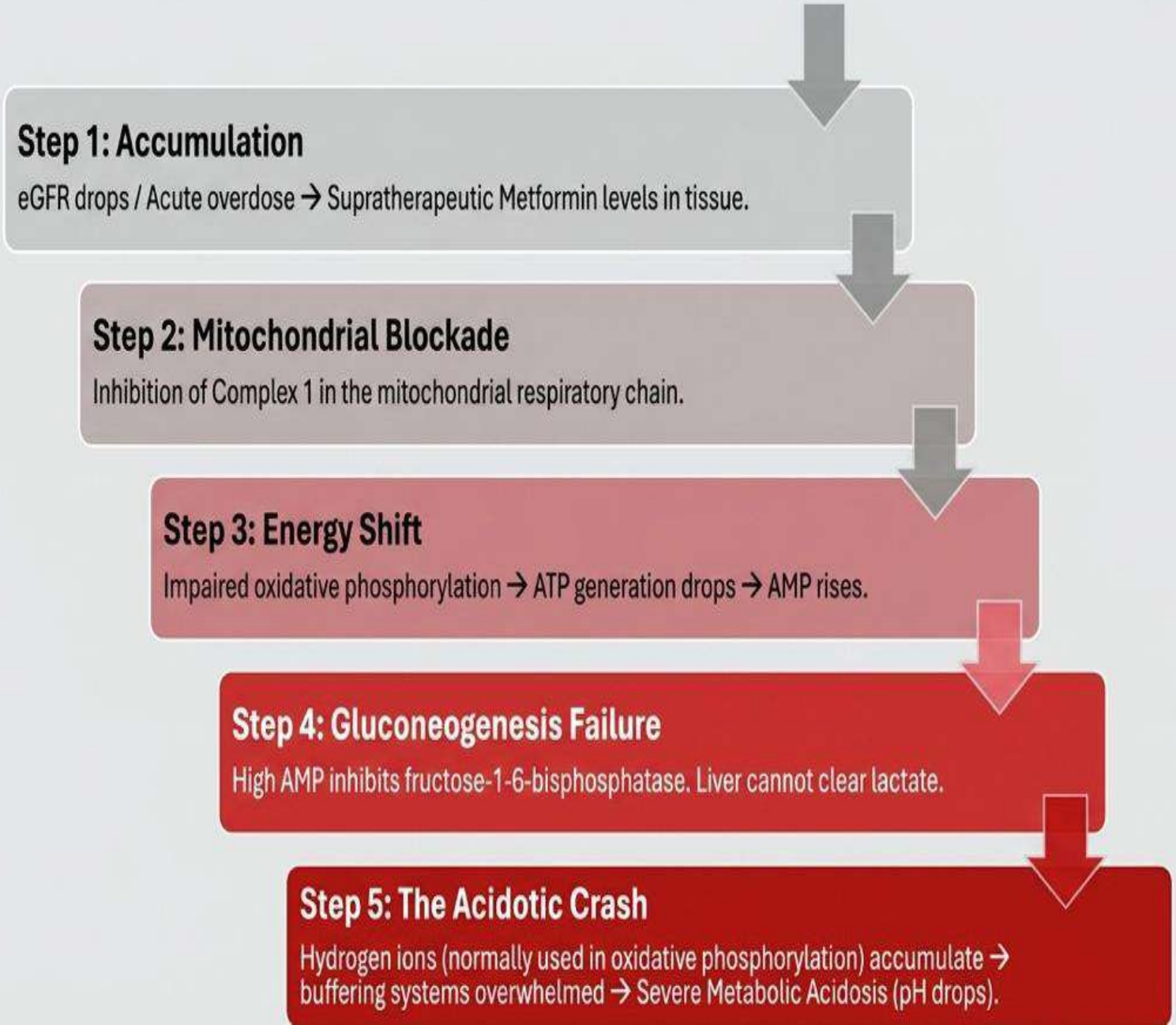


Figure 22 | Suggested approach in dosing metformin based on the level of kidney function. eGFR, estimated glomerular filtration rate (in ml/min per 1.73 m^2); GI, gastrointestinal.

The Anatomy of Metformin-Associated Lactic Acidosis (MALA)



DPP IV USE IN RENAL IMPAIRMENT

DPP-IV Inhibitor	Renal impairment Mild (Crcl >50ml/min) Moderate (Crcl >30 <50 ml/min) Severe- (Crcl <30ml/min)	Hepatic impairment	Renal & Liver function monitoring	Use with other drugs (Dose reduction with sulphonyl urea & Insulin)
Sitagliptin	50 mg – moderate - OD 25 mg – severe - OD	Yes	Yes	-
Vidagliptin	50 mg – Moderate & Severe - OD	No	Yes	Dose reduction (50mg once daily) when used with sulphonylurea
Saxaglitpin	2.5 mg OD	Yes	Yes	Dose reduction (2.5mg once daily) when used with strong CYP3A4/5 inhibitors (e.g. ketoconazole, ritonavir)
Alogliptin	12.5 mg –moderate-OD 6.25 mg –severe-OD	Yes	Yes	-
Linagliptin	Yes	Yes	No	Efficacy may be reduced if used with CYP3A4 inducer (e.g. rifampin)
Gemigliptin	Yes with caution	Presently not recommended	-	May require dose reduction when used with drugs which alter CYP3A4 activity
Teneligliptin	Yes	Yes with care	No	-

Holistic approach for improving outcomes in patients with diabetes and chronic kidney disease.