DESIDUSTAT

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INTRODUCTION

- Desidustat is an orally bioavailable, small molecule, hypoxia inducible factor -prolyl hydroxylase inhibitor(HIF-PHI) resulting in the stabilisation of HIF which stimulates erythropoietin production and erythropoiesis.
- Mobilises iron and may reduce IV iron needs.
- Works better in ESA hypo responsive states.
- Safety similar to ESAs.
- 2019 Nobel prize medicine - HIF: William Kaelin , Peter Radicliffe and Greg Semenza.

DOSAGE

- **Dialysis-dependent (DD) patients** - 100 mg administered thrice weekly post dialysis.
- **Non dialysis dependent patients (NDD)**
  - Erythrocyte stimulating agent (ESA) naive - 100 mg three times weekly,
  - Switching from an ESA -100, 125 or 150 mg thrice weekly, depending on the previous dose of ESA (epoetin, darbepoetin or methoxy polyethylene glycol-epoetin beta).
- **Maintenance dose** - based on haemoglobin levels assessed every 4 weeks, with a maximum dosage of 150 mg three times weekly

ESAs Compared to HIF-PHIs

	ESAs	HIF-PHIs
MOA	• Stimulate RBC production	• HIF stimulates EPO production & erythropoiesis, improves iron uptake • HIF-PHI prevents HIF degradation
Benefits	• Raise Hb, reduced need for RBC transfusion • Improved HRQoL (inconsistent)	• Raise Hb, reduced need for RBC transfusion • Improve HRQoL (?); network meta-analysis: daprodustat associated with reduced fatigue vs roxadustat[1]
Effectiveness	• Same if given in equivalent doses • epoetin and darbepoetin more effective SC	• No head-to-head clinical trials, but network meta-analysis showed no difference[1]
Safety	• HTN • Access thrombosis, thromboembolic events, MACE • Enhance some malignancies	• HTN • Access thrombosis, thromboembolic events, MACE • Enhance malignancies?

Acknowledgement-Slide contributed by –DR JAISON GEORGE ,Nephrologist [MOSC Kolanchery.]

KDIGO 2025 DRAFT GUIDELINES ON ANEMIA

Recommendation 3.1.1: In people with anemia and CKD in whom correctable causes of anemia have been addressed, we suggest using an ESA rather than a HIF-PHI as first-line therapy for treatment of anemia (*2D*).

3.5. HIF-PHI treatment initiation and maintenance

Practice Point 3.5.1: In people with anemia and CKD, including those with ESA hyporesponsiveness, do not use ESAs and HIF-PHIs in combination.

Practice Point 3.5.2: In people with anemia and CKD, the Hb thresholds for the initiation and maintenance of HIF-PHIs are unknown, but it is reasonable to use the same Hb thresholds as those recommended or suggested for ESA therapy (Recommendations 3.2.1, 3.2.2, 3.3.1).

Practice Point 3.1.3: In people with anemia and CKD, HIF-PHIs should be avoided in those at increased risk of adverse events (Table 6).

Table 6 | Considerations for people with anemia and CKD at risk for adverse events with hypoxia-inducible factor-prolyl hydroxylase inhibitors (HIF-PHI) therapy

Theoretical risk or experimental evidence of risk for disease development or progression	Concern for risk based on adverse event profiles in clinical trials	Insufficient data for risk assessment; dedicated studies needed
• Active cancer or with a history of cancer not in complete remission for at least 2–5 years (based on trial exclusion criteria)[223] • Polycystic kidney disease[224] • Proliferative retinal disease[225, 226] • Pulmonary arterial hypertension[227-229] • Pregnancy*	• Prior cardiovascular events (i.e., stroke, myocardial infarction)[223] • Prior thromboembolic events (i.e., deep venous thrombosis, pulmonary embolism)[223] • Prior vascular access thrombosis[223] • Hepatic impairment† • Seizures, exfoliative dermatitis, hypothyroidism, bacterial infections/sepsis (roxadustat)[230]	• Post-kidney transplant anemia[223] • Children[231]