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| **Royal Infirmary of Edinburgh**  **Renal Directorate Guideline** |

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**Drug name: Roxadustat (Evrenzo®)**

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| **Indication and additional Information** | Management of symptomatic anaemia in patients with chronic renal failure NOT on haemodialysis.  Anaemia in chronic kidney disease (CKD) is primarily due to erythropoietin deficiency. It is characterised by haemoglobin (Hb) level below 100g/L on 2 or more consecutive readings in a patient with known CKD. Roxadustat is an oral hypoxia-inducible factor, prolyl hydroxylase inhibitor (HIF-PHI), which stimulates a coordinated erythropoietic response, thereby increasing haemoglobin production and improving iron bioavailability. It is the only drug for this indication *not* given by injection. Other causes of anaemia (B12 & folate) should be investigated and addressed prior to commencing roxadustat. Adequate iron stores should be ensured prior to initiating treatment. |
| **Dosage and administration** | Recommended oral starting dose for patients NOT currently on dialysis or an erythropoiesis-stimulating agent (ESA):  70 mg three times per week in patients weighing less than 100kg.  100 mg three times per week in patients weighing 100kg and over.  Dose adjustments and monitoring see Table 1 on page 3.  Dosing should be on non-consecutive days.  Maximum dose - 3mg/kg body weight or 300mg three times a week (whichever is lower) in non-dialysis patients.  See Summary of Product Characteristics (SmPC) if converting from an ESA. |
| **Contraindications** | Allergies to peanuts or soya.  Lactase deficiency/galactose intolerance/glucose-galactose malabsorption.  Pregnancy and breastfeeding.  Severe hepatic impairment (Child-Pugh class C). |
| **Precautions** | History of seizures/epilepsy.  Ensure reliable contraception in women of child-bearing age.  Moderate hepatic impairment (Child-Pugh class B) – reduce starting dose by half. |
| **Side Effects** | **Common**  Hypertension, thrombotic vascular events, gastrointestinal disorders, peripheral oedema, hyperkalaemia, sepsis and seizures, headaches, insomnia.  **Uncommon/unknown**  Hyperbilirubinaemia, secondary hypothyroidism, skin reactions.  This medicinal product is subject to additional monitoring (black triangle). This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to:  [mhra - Yellow card](https://yellowcard.mhra.gov.uk/) |
| **Drug Interactions** | Sevelamer carbonate or calcium acetate or products containing calcium, iron or magnesium (see patient counselling section).  Statins (increased AUC of statins, monitor for side effects and consider dose reduction).  When initiating or discontinuing treatment with strong inhibitors (gemfibrozil) or inducers (rifampicin) of CYP2C8 or inhibitors (probenecid) of UGT129, Hb should be monitored closely. |
| **Patient Counselling** | Roxadustat should be taken at least 1 hour after administration of sevelamer or calcium acetate or other medicinal products or supplements containing calcium, iron or magnesium.  Missed dose advice:  If it is more than 24 hours until next dose, take the dose and then the next scheduled dose.  If it is less than 24 hours until next dose, do not take dose, take the next scheduled dose. |
| **Other Information** | The Scottish Medicines Consortium has approved its restricted use in patients who are non-dialysis-dependent at the time of treatment initiation. It may be continued if dialysis is then started.  Refer all new patients to the renal anaemia co-ordinators and the hospital will supply the first 4 weeks of treatment.  Refer to the Roxadustat Shared Care Agreement for information regarding ongoing treatment and monitoring in primary/secondary care.  For further information please refer to SmPC and East Region Formulary  [SmPC](http://www.medicines.org.uk/emc/product/12835)  [Formulary | East Region Formulary (nhs.scot)](https://formulary.nhs.scot/east) |

**TABLE 1**

**Roxadustat monitoring and dose adjustment rules**

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| Aim to maintain Hb in target range of 100-120g/L.  Titrate up or down in stepwise manner: 20 mg - 40 mg - 50 mg - 70 mg - 100 mg - 150 mg - 200 mg - 250 mg - 300 mg | | | | |
| Change in Hb over previous 4 weeks | Current Hb Level g/L | | | |
| <105 | 105-119 | 120-129 | >130 |
| Hb has increased by >10g/L | No change | Reduce dose by 1 step | Reduce dose by 1 step | Withhold dosing, monitor Hb and resume dosing when Hb is less than  120g/l, at a dose that is reduced by 2 steps |
| Hb not significantly changed over 4 weeks | Increase dose by 1 step | No change | Reduce dose by 1 step |
| Hb has fallen by >10g/L | Increase dose by 1 step | Increase dose by 1 step | No change |

* Monitor Hb every 2 weeks.
* Dose adjustments can be stepped up or down every 4 weeks.
* Only adjust dose after 2 weeks if there is an increase in Hb of more than 20g/L, when the dose should be decreased by 1 step immediately.
* Once Hb is stable monitor monthly.
* If additional dose reduction is necessary for a patient on the lowest dose (20mg) three times per week, do not break tablets, reduce dose frequency to twice weekly or once weekly if further dose reduction is required.
* Failure to achieve target Hb levels within 24 weeks should prompt search for other causes of anaemia, including blood film, reticulocyte count and consideration of bone marrow biopsy. Roxadustat should be discontinued.

**References**

1. [Evrenzo (roxadustat) film coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)](https://www.medicines.org.uk/emc/product/12835/smpc)
2. SMC advice Roxadustat (Evrenzo) [roxadustat (Evrenzo) (scottishmedicines.org.uk)](https://www.scottishmedicines.org.uk/medicines-advice/roxadustat-evrenzo-full-smc2461/)
3. National Institute for Health and Clinical Excellence quick reference guide (June 2015) Anaemia management in people with chronic kidney disease.
4. Roxadustat for the treatment of anaemia in chronic kidney disease patients not on dialysis; a phase 3, randomized, open-label, active-controlled study (DOLOMITES) Jonathan Barratt et al. Nephrol Dial Transplant (2021) 1–13 doi: 10.1093/ndt/gfab191 Advance Access publication 2 June 2021