Renustat™ 50

Roxadustat INN 50 mg

COMPOSITION
Renustat™ 50 Tablet: Each Film coated tablet contains Roxadustat INN 50 mg.

PHARMACOLOGY
Roxadustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI). The activity of HIF-PH enzymes controls intracellular levels of HIF, a transcription factor that regulates the expression of genes involved in erythropoiesis. Activation of the HIF pathway is important in the adaptative response to hypoxia to increase red blood cell production. Through the reversible inhibition of HIF-PH, Roxadustat stimulates a coordinated erythropoietic response that includes the increase of plasma endogenous erythropoietin (EPO) levels, regulation of iron transporter proteins and reduction of hepcidin (an iron regulator protein that is increased during inflammation in CKD). This results in improved Iron bioavailability, increased Hb production and increased red cell mass.

INDICATION
Renustat™ is indicated for treatment of adult patients with symptomatic anemia associated with chronic kidney disease (CKD).

DOSAGE & ADMINISTRATION
The appropriate dose of Roxadustat must be taken orally three times per week and not on consecutive days.
The dose should be individualized to achieve and maintain target Hb levels of 10 to 12 g/dL as described below:
Patients not on erythropoiesis-stimulating agent treatment:
For adults, the usual starting dose is 50 mg three times weekly. The recommended starting dose of Roxadustat is 70 mg three times per week in patients weighing less than 100 kg and 100 mg three times per week in patients weighing 100 kg and over.
Patients switching from erythropoiesis-stimulating agents:
For adults, the usual starting dose is 70 or 100 mg three times weekly. The dosage thereafter should be adjusted according to the patient's condition.

Conversion table:

Erythropoetin dose (IU/week)	Darbepoetin alfa dose (micrograms/week)	Methoxy polyethylene glycal-epoetin beta dose (micrograms/monthly)	Roxadustat dose (Miligrams three Times per week)
Less than 5, 000	Less than 25	Less than 80	70
5,000 up to 8,000	25 to less than 40	80 up to and including 120	100
More than 8,000 up to and including 16,000	40 up to and including 80	More than 123 up to and including 200	150
More than 16,000	More than 80	More than 200	200

Renustat™ treatment should not be continued beyond 24 weeks of therapy if a clinically meaningful increase in Hb levels is not achieved.
Dose adjustment:
When dose adjustments are required, increase or decrease the dose according to the "dose increase/decrease table' and 'stepwise dose adjustment sequence" below. Once adjusted, maintain the dose level for ≥4 weeks. If the hemoglobin concentration increases rapidly (>2.0 g/dL) within 4 weeks of a dose increase, decrease the dose or suspend the treatment immediately.
The stepwise dose adjustments up or down should follow the sequence of the available doses:
20 mg - 40 mg - 50 mg - 70 mg - 100 mg - 150 mg - 200 mg - 250 mg - 300 mg - 400 mg (only for CKD patients on dialysis).

Dose increase/decrease rules:

Change in Hb over the previous 4 weeks	Current Hb level (g/dl):			
	Lower than 10.5	10.5 to 11.9	12.0 to 12.9	13.0 or higher
Change in value of more than + 1.0 g/dl	No change	Reduce dose by one step	Reduce dose by one step	Withhold dosing, monitor Hb level and resume dosing when Hb is less than 12.0 g/dL at a dose that is reduced by two steps
Change in value between -1.0 and +1.0 g/dL	Increase dose by one step	No change	Reduce dose by one step	
Change in value of less than 1.0 g/dL	Increase dose by one step	Increase dose by one step	No change	
Change in value of more than 20 g/dL	Decrease by one step			

Missed dose:
When there is ≥24 hour interval until the next scheduled dosing time, take the missed dose immediately and follow the prescribed schedule for subsequent doses. If there is <24 hours until the next scheduled dosing time, skip the missed dose, and take the next dose as scheduled. Do not take 2 doses on the same day.
Method of administration:
Renustat™ tablets are to be taken orally with or without food.

CONTRAINDICATION
Roxadustat is contraindicated in the following conditions:
- Hypersensitivity to the active substance, peanut, soya or to any of the excipients
- Third trimester of pregnancy
- Breast-feeding

WARNING AND PRECAUTION
Renustat™ **50** tablets should be used with caution in-
- Patients with pre-existing risk factors for TVE, including obesity and prior history of TVES.
- Patients with a history of seizures.
- Patient having serious signs and symptoms of an infection.
- Patient having liver disorder.
- Pregnant women.

SIDE EFFECT
Hypertension, blood clot, diarrhoea, peripheral edema, hyperkalaemia and nausea are the side effects of **Renustat**™**.**

USE IN PREGNANCY & LACTATION
Renustat™ is contraindicated during the first, second and third trimester of pregnancy. Do not administer to women that may be pregnant or breast-feeding women.

DRUG INTERACTION
Roxadustat may have drug-drug interaction with Phosphate binders which decrease Roxadustat AUC. This drug should be taken at least 1 hour after administration of phosphate binders. Roxadustat may also have drug-drug interactions with gemfibrozil or probenecid which increases Roxadustat AUC and Cmax.

Coadministration	Risk	Recommendation
Roxadustat with Phosphate binders and other products containing multivalent cation (EXCEPT) lanthanum carbonate	Decreased roxadustat AUC by 67% and 46% and Cmax by 66% and 52%	Roxadustat should be taken at least 1 hour after administration of phosphate binders or other medicinal products or supplements containing multivalent cation
Roxadustat with gemfbrozil (CYP2C8 and OATP1B1 inhibitor) or or probenecid (UGT and OAT1/OAT3 inhibitor)	Increased roxadustat AUC by 2.3 fold and Cmax by 1.4-fold	Adjust the dose of roxadustat folowing dose adjustment rule based on Hb montoring
Roxadustat with OATP1B1 or BCRP Substrales (simvastatin, rosuvastatin & atorvastatin)	AUC and Cmax incre ased	Adjust the dose of roxadustat folowing dose adjustment rules based on Hb montoring.

OVERDOSE
When this drug is administered to a healthy adult about 5 mg/kg (510 mg), this increases musculo-skeletal pain, heart rate etc. Overdose of **Renustat**™ can elevate the level of haemoglobin above the desire level.

STORAGE
Store below 30°C, in a cool & dry place. Keep away from light. Keep out of the reach of children.

HOW SUPPLIED
Renustat™ 50 Tablet: Each box contains 3 tablets in Alu-PVDC blister pack.

Manufactured by

SQUARE
PHARMACEUTICALS PLC.
BANGLADESH