VELETRI 0.5mg and 1.5mg, powder for solution for infusion PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): Epoprostenol

Please refer to Summary of Product Characteristics (SmPC) before prescribing.

INDICATION(S):
Pulmonary Arterial Hypertension (PAH): Veletri is indicated for the treatment of PAH (idiopathic or heritable PAH and PAH associated with connective tissue diseases) in patients with WHO Functional Class III–IV symptoms to improve exercise capacity.

Renal Dialysis: Veletri is indicated for use in haemodialysis (HD) in emergency situations when use of heparin carries a high risk of causing or exacerbating bleeding or when heparin is otherwise contraindicated.

DOSAGE & ADMINISTRATION: Veletri is only indicated for continuous infusion by intravenous route (i.v).

PAH: Treatment should only be initiated and monitored by a physician experienced in the treatment of PAH.

Short-term (acute) dose ranging: This procedure should be conducted in a hospital with adequate resuscitation equipment. A short-term dose-ranging procedure administered via a peripheral or central venous line is required to determine the long-term infusion rate. The infusion is initiated at 2 ng/kg/min and increased by increments of 2 ng/kg/min every 15 min or longer until maximum haemodynamic benefit or dose-limiting pharmacological effects are elicited. If the initial infusion rate of 2 ng/kg/min is not tolerated, a lower dose that is tolerated by the patient should be identified.

Long-term continuous infusion: Long-term continuous infusion of Veletri should be administered through a central venous catheter (CVC). Long-term infusions should be initiated at 4 ng/kg/min less than the maximum tolerated infusion rate, determined during short-term dose-ranging. If the maximum tolerated infusion rate is 5 ng/kg/min or less, the long-term infusion should be started at 1 ng/kg/min.

Dosage adjustments: Changes in the long-term infusion rate should be based on persistence, recurrence or worsening of the patient's symptoms of PAH or the occurrence of adverse reactions (AEs) due to excessive doses of Veletri. Increase infusion rate by 1- 2 ng/kg/min increments at a minimum interval of 15 min to allow assessment of clinical response. After establishing a new infusion rate, observe patient and monitor erect and supine blood pressure and heart rate for several hours to ensure new dose is tolerated. Dosage decreases should be made in 2 ng/kg/min decrements every 15 min or longer until the dose-limiting effects resolve. Abrupt withdrawal of Veletri or sudden large reductions in infusion rates should be avoided due to the risk of potentially fatal rebound effect. Except in life-threatening situations e.g. unconsciousness, collapse, infusion rates of Veletri should be adjusted only under the direction of a physician.

Suitable ambulatory pumps and accessories to be used for the administration of VELETRI are provided in section 6.6 of the SmPC.

Renal Dialysis: Veletri is suitable for continuous infusion only, either intravascularly or into the blood supplying the dialyser. Adult infusion rate: Pre-dialysis: 4 ng/kg/min i.v for 15 mins. During dialysis: 4 ng/kg/min into the arterial line to the dialyser. Stop infusion at the end of dialysis. If exceeding the recommended dose carefully monitor the patient's blood pressure.

CONTRAINDICATIONS:
Hypersensitivity to the active substance or excipients. In congestive heart failure arising from severe left ventricular dysfunction. Veletri must not be used chronically in patients who develop pulmonary oedema during dose-ranging.

SPECIAL WARNINGS & PRECAUTIONS:
The pH of the diluted solution decreases with dilution, and ranges from 12.0 for a concentration of 90,000 ng/mL, 11.7 for a concentration of 45,000 ng/mL to 11.0 for a concentration of 3,000 ng/mL. Therefore, peripheral intravenous use should be restricted to short duration only, using low concentrations. Avoid extravasation during administration.

Veletri is a potent pulmonary and systemic vasodilator. The cardiovascular effects during infusion disappear within 30 min of the end of administration. Veletri is a potent inhibitor of platelet aggregation, hence, potential risk for bleeding, particularly for patients with other risk factors for bleeding. If excessive hypotension occurs during administration the dose should be reduced or the infusion discontinued. Hypotension may be profound in overdose and may result in loss of consciousness.

Blood pressure and heart rate should be monitored during administration of Veletri. Veletri may either decrease or increase heart rate. The change is thought to depend on both the basal heart rate and the infusion rate of Veletri administered. The effects of Veletri on heart rate may be masked by concomitant use of drugs which affect cardiovascular reflexes. Extreme caution is advised in patients with coronary artery disease. Elevated serum glucose levels have been reported.

PAH: Some patients may develop pulmonary oedema during dose-ranging, which may be associated with pulmonary veno-occlusive disease. Veletri must not be used chronically in patients who develop pulmonary oedema. Avoid abrupt withdrawal or interruption of infusion except in life-threatening situations. Abrupt interruption of therapy can induce a rebound of PAH, resulting in dizziness, asthenia, increase dyspnoea, and death.

Renal dialysis: The hypotensive effect of Veletri may be enhanced by the use of acetate buffer in the dialysate. Veletri is not a conventional anticoagulant. Epoprostenol has been successfully used instead of heparin in renal dialysis, but in a small proportion of dialyses clotting has developed in the dialysis circuit, requiring termination of dialysis. When epoprostenol is used alone, measurements such as activated whole blood clotting time may not be reliable.

SIDE EFFECTS: **Very common**; headache, facial flushing, nausea, vomiting, diarrhoea, jaw pain and pain (unspecified). **Common**; sepsis, septicaemia, decreased platelets, potential bleeding from various sites, anxiety, nervousness, tachycardia, bradycardia, hypotension, abdominal colic, rash, arthralgia, injection site pain and chest pain.
Refer to SmPC for other side effects.

LEGAL CATEGORY: Prescription Only Medicine (POM)

PRESENTATIONS, PACK SIZES, MARKETING AUTHORISATION NUMBER(S)

PRESENTATIONS	PACK SIZES	MARKETING AUTHORISATION NUMBER(S)
Veletri 0.5 mg	x 1	PA0885/001/001
Veletri 1.5 mg	x 1	PA0885/001/002

FURTHER INFORMATION IS AVAILABLE FROM THE MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium. Tel: 1800 709122

Prescribing information last revised: April 2020.

Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse events via:
HPRA Pharmacovigilance
Website: www.hpra.ie

Adverse events should also be reported on 1800 709 122 or at dsafety@its.jnj.com.