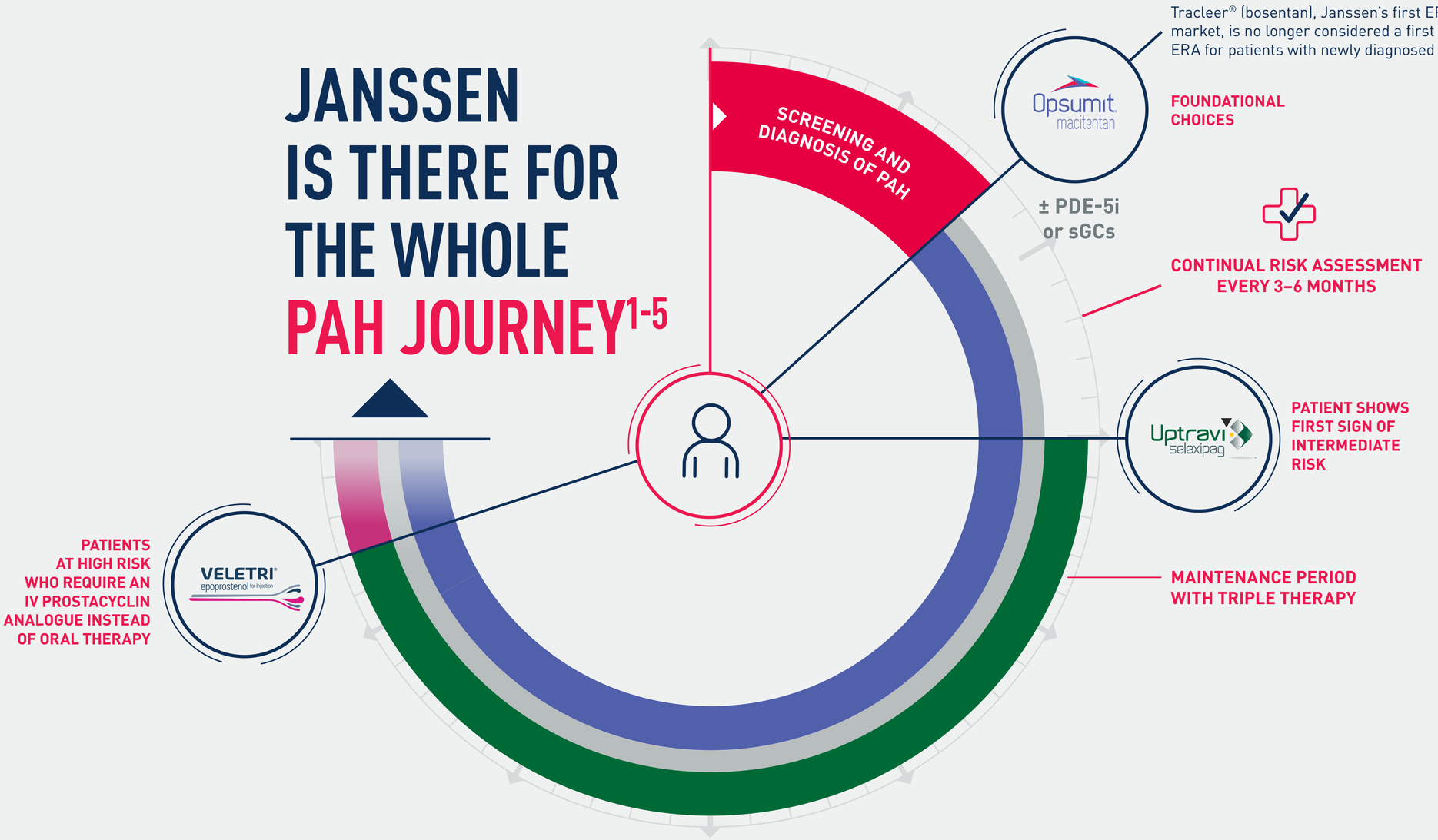
JANSSEN IS THERE FOR THE WHOLE PAH JOURNEY[1-5]



Tracleer® (bosentan), Janssen's first ERA to market, is no longer considered a first choice ERA for patients with newly diagnosed PAH[6]

FOUNDATIONAL CHOICES

CONTINUAL RISK ASSESSMENT EVERY 3–6 MONTHS

PATIENT SHOWS FIRST SIGN OF INTERMEDIATE RISK

MAINTENANCE PERIOD WITH TRIPLE THERAPY

PATIENTS AT HIGH RISK WHO REQUIRE AN IV PROSTACYCLIN ANALOGUE INSTEAD OF ORAL THERAPY

The indications for OPSUMIT, UPTRAVI, VELETRI and TRACLEER can be found in the SmPC of each treatment available at **www.medicines.ie**.
Opsumit, Uptravi, Veletri and **Tracleer** are registered trademarks of Actelion Pharmaceuticals Ltd.
ERA, Endothelin Receptor Antagonist; IV, intravenous; PAH, pulmonary arterial hypertension; PDE-5i, phosphodiesterase type-5 inhibitor; sGCs, soluble guanylate cyclase stimulator
Prescribing information can be found at the end of the document.

References: 1. Galie N *et al. Eur Respir J* 2016; 37(1):67–119. **2.** VELETRI Summary of Product Characteristics, Available at www.medicines.ie. **3.** Galie N *et al. Eur Respir J* 2019; 53(1):1801889. **4.** OPSUMIT Summary of Product Characteristics, Available at www.medicines.ie. **5.** UPTRAVI Summary of Product Characteristics, Available at www.medicines.ie. **6.** Hoeper M *et al. Int J Cardiol* 2018;272:37-45.

CP-193513 | November 2020

ABBREVIATED PRESCRIBING INFORMATION: OPSUMIT®

OPSUMIT 10mg film-coated tablets PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): Macitentan. Please refer to Summary of Product Characteristics (SmPC) before prescribing.

INDICATION(S): Mono or combination therapy for long-term treatment of pulmonary arterial hypertension (PAH), in adults of WHO Functional Class (FC) II & III. Efficacy shown in idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

DOSAGE & ADMINISTRATION: Treatment should only be initiated and monitored by a physician experienced in the treatment of PAH. To be administered orally, once daily with/without food. Tablets should be swallowed whole, with water. *Elderly patients:* No dose adjustment required in patients >65 years. Limited clinical experience in patients >75 years, use with caution. *Paediatric patients:* Safety and efficacy not yet established in children and adolescents below 18 years. *Hepatic impairment:* Mild/moderate: no dose adjustment. Severe: contraindicated. *Renal impairment:* Caution advised in in PAH patients with severe renal impairment. Not recommended in dialysis patients.

CONTRAINDICATIONS: Hypersensitivity to active substance, soya or to any of the excipients. Pregnancy, women of childbearing potential not using reliable contraception, breastfeeding, severe hepatic impairment or baseline hepatic aminotransferase (AST/ALT) >3X upper limit of normal (ULN).

SPECIAL WARNINGS & PRECAUTIONS: Benefit/risk not established in WHO FC I. Patients with rare hereditary galactose intolerance, total lactase deficiency or glucose-galactose malabsorption or hypersensitivitity to soya, should not take macitentan. *Hepatic insufficiency:* Record baseline hepatic AST/ALT prior to initiation of Opsumit with monthly monitoring recommended. *Haemoglobin (Hgb):* Record baseline Hgb and monitor as clinically indicated. Treatment not recommended in patients with severe anaemia. *Renal impairment:* Monitoring of blood pressure and Hgb should be considered in patients with renal impairment. *Pulmonary veno-occlusive disease (PVOD):* If signs of pulmonary oedema, consider possibility of PVOD. *Women of child bearing potential:* Only initiate treatment in women of childbearing potential, using reliable contraception, who have a negative pregnancy test immediately prior to treatment and thereafter monthly during treatment. *CYP3A4 inducers/inhibitors:* Avoid concomitant use with strong CYP3A4 inducers (e.g. rifampicin, St. John's wort, carbamazepine, and phenytoin) as efficacy could be reduced. Use caution with concomitant use of strong CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, clarithromycin, telithromycin, nefazodone, ritonavir, and saquinavir).

SIDE EFFECTS: *Very common:* nasopharyngitis, bronchitis, headache, anaemia, haemoglobin decrease, oedema, fluid retention. *Common:* pharyngitis, influenza, urinary tract infection, leukopenia, thrombocytopenia, AST/ALT elevations, hypotension, nasal congestion. Other side effects: hypersensitivity. **Refer to SmPC for other side effects.**

LEGAL CATEGORY: Prescription Only Medicine (POM).

PRESENTATIONS, PACK SIZES & MARKETING AUTHORISATION NUMBER(S): 10mg tablets, 30 Tablets, EU/1/13/893/002.

MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium.

FURTHER INFORMATION IS AVAILABLE FROM: Actelion, a division of Janssen-Cilag International NV. Tel: 1800 709 122.

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 to Actelion, a division of Janssen-Cilag International NV on 1800 709 122 or at dsafety@its.jnj.com.

ABBREVIATED PRESCRIBING INFORMATION: UPTRAVI®

UPTRAVI®▼ 200-1600 µg film-coated tablets PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): selexipag. **Please refer to the Summary of Product Characteristics (SmPC) before prescribing.**

INDICATION(s): Long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO FC II-III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist and/or a phosphodiesterase type 5inhibitor, or as monotherapy in patients who are not candidates for these therapies. Efficacy has been shown in idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

DOSAGE & ADMINISTRATION: Only a PAH experienced physician should initiate and monitor treatment. Individualised dose titration: Up-titrate patients to the highest individually tolerated dose, which can range from 200 to 1600 microgram (µg) given twice daily (BD). The recommended starting dose is 200 µg BD approximately 12 hours apart. Increase dose in increments of 200 µg BD, usually at weekly intervals, based on tolerability. During titration some adverse reactions reflecting the mode of action of Uptravi may occur, these are usually transient or manageable with symptomatic treatment. If a patient reaches a dose that cannot be tolerated, the dose should be reduced to the previous dose level. Individualised maintenance dose: Maintain the highest tolerated dose a patient can take with tolerable adverse events. Administration: Take each tablet orally, morning and evening with food to improve tolerability. During the up-titration phase take the first increased dose in the evening.

CONTRAINDICATIONS: Hypersensitivity to active substance/excipients, severe coronary heart disease, unstable angina, myocardial infarction within 6 months, decompensated cardiac failure, severe arrhythmias, cerebrovascular events within 3 months, congenital or acquired valvular defects, concomitant use with strong CYP2C8 inhibitors (e.g. gemfibrozil).

SPECIAL WARNINGS & PRECAUTIONS: Hypotension: Vasodilatory properties may reduce blood pressure. Before prescribing Uptravi, carefully consider whether patients with certain underlying conditions could be adversely affected by vasodilatory effects. Hyperthyroidism: has been observed, monitor thyroid function if clinically indicated. Pulmonary veno-occlusive disease: If signs of pulmonary oedema occur consider possibility of pulmonary veno-occlusive disease which has been reported with vasodilators (mainly prostacyclins), if confirmed discontinue treatment. Elderly (≥65 yrs): There is limited clinical experience in patients over 75 yrs, therefore Uptravi should be used with caution in this population. Renal impairment: Caution should be exercised during dose titration in patients with severe renal impairment. Hepatic impairment: Do not treat patients with severe liver impairment (Child-Pugh class C). In patients with moderate hepatic impairment, Uptravi should be dosed once daily. Women of childbearing potential: should practice effective contraception while taking selexipag. Co-administration of Moderate CYP2C8 Inhibitors: When co-administered with moderate CYP2C8 inhibitors, reduce the dosing of Uptravi to once daily.

SIDE EFFECTS: Very common: Headache, flushing, nasopharyngitis, diarrhoea, vomiting, nausea, jaw pain, myalgia, arthralgia & pain in extremity. **Common:** Anaemia, decreased haemoglobin, hyperthyroidism, decreased thyroid-stimulating hormone, decreased appetite, weight decrease, hypotension, nasal congestion, abdominal pain, rash, urticaria, erythema, pain. **Refer to SmPC for other side effects.**

LEGAL CATEGORY: POM

PRESENTATIONS, PACK SIZES & MARKETING AUTHORISATION NUMBER(S): 200 µg tablets (Titration pack), 140 tablets, EU/1/15/1083/003; 200 µg tablets, 60 tablets, EU/1/15/1083/002; 400 µg tablets, 60 tablets, EU/1/15/1083/004; 600 µg tablets, 60 tablets, EU/1/15/1083/005; 800 µg tablets, 60 tablets, EU/1/15/1083/006; 1000 µg tablets, 60 tablets, EU/1/15/1083/007; 1200 µg tablets, 60 tablets, EU/1/15/1083/008; 1400 µg tablets, 60 tablets, EU/1/15/1083/009; 1600 µg tablets, 60 tablets, EU/1/15/1083/010.

MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B 2340 Beerse, Belgium.

FURTHER INFORMATION IS AVAILABLE FROM: Actelion, a division of Janssen-Cilag International NV. Tel: 1800 709122

Prescribing information last revised: April 2020

Adverse events should be reported. ▼ This medicinal product is subject to additional monitoring and it is therefore important to report any suspected adverse events related to this medicinal product. Healthcare professionals are asked to report any suspected adverse events via: HPRA Pharmacovigilance Website: www.hpra.ie.

Adverse events should also be reported to Actelion, a division of Janssen-Cilag International NV on 1800 709 122 or at dsafety@its.jnj.com.

ABBREVIATED PRESCRIBING INFORMATION: VELETRI®

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): 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.

ABBREVIATED PRESCRIBING INFORMATION: TRACLEER®

TRACLEER 62.5 & 125 mg film-coated tablets PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): Bosentan

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

INDICATION(S): Treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity and symptoms in patients with WHO functional class III. Efficacy shown in: Primary (idiopathic and heritable) PAH, PAH secondary to scleroderma without significant interstitial pulmonary disease, PAH associated with congenital systemic-to-pulmonary shunts and Eisenmenger's physiology. Some improvements shown in patients with PAH functional class II. Tracleer is also indicated to reduce the number of new digital ulcers in patients with systemic sclerosis (SSc) and ongoing digital ulcer disease.

DOSAGE & ADMINISTRATION: Treatment should only be initiated and monitored by physician experienced in the treatment of PAH or SSc. **Adults:** Initial dose 62.5mg twice daily (b.d.) for 4 weeks, maintenance dose 125mg b.d. Take with or without food. **Paediatrics:** Recommended starting and maintenance dose in children with PAH aged 1 year and older is 2 mg/kg morning and evening. There are no data on the safety and efficacy in patients under 18 years with SSc with ongoing digital ulcers.

CONTRAINDICATIONS: Hypersensitivity to the active substance or excipients. Moderate to severe hepatic impairment. Baseline values of liver aminotransferases (AST and/or ALT), greater than 3 times the upper limit of normal (ULN). Concomitant use of cyclosporine A. Pregnancy, women of childbearing potential not using reliable methods of contraception.

SPECIAL WARNINGS & PRECAUTIONS: Tracleer should only be initiated if the systemic systolic BP >85 mmHg. Efficacy of Tracleer not established in patients with severe PAH. Benefit/risk balance of bosentan not established in patients with WHO class I functional status of PAH. ***Liver function:*** Liver aminotransferase levels must be measured prior to initiation of treatment and subsequently at monthly intervals for duration of treatment. In addition, aminotransferase levels must be measured 2 weeks after any dose increase. ***Haemoglobin (Hgb) concentration:*** Tracleer has been associated with dose-related decreases in Hgb concentration. Hgb concentrations should be checked prior to initiation of treatment, and monthly for the first 4 months and quarterly thereafter. ***Pulmonary veno-occlusive disease (PVOD):*** Should signs of pulmonary oedema occur in PAH patients, consider possibility of associated veno-occlusive disease. ***PAH patients with concomitant left ventricular failure:*** monitor patients for signs of fluid retention. Should this occur, treat with diuretics, or increase the dose of existing diuretics. Treatment with diuretics should be considered in patients with evidence of fluid retention before starting Tracleer treatment. ***PAH associated with HIV infection:*** Due to potential for interactions related to the inducing effect of bosentan on CYP450, monitor patients carefully regarding their HIV infection and HIV therapy.

SIDE EFFECTS: Very common: headache, abnormal liver function test, oedema and fluid retention. **Common:** anaemia, haemoglobin decrease, hypersensitive reactions, syncope, palpations, flushing, hypotension, nasal congestion, gastro-oesophageal reflux, diarrhoea, erythema. **Other side effects:** anaphylaxis and/or angioedema, blurred vision, liver cirrhosis and liver failure have been reported. **Refer to SmPC for other side effects.**

LEGAL CATEGORY: Prescription Only Medicine (POM)

PRESENTATIONS, PACK SIZES & MARKETING AUTHORISATION NUMBER(S): Tracleer 62.5mg, 56 Tablets, EU/1/02/220/002; Tracleer 125mg, 56 Tablets, EU/1/02/220/004. **MARKETING AUTHORISATION HOLDER:** Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium

FURTHER INFORMATION IS AVAILABLE FROM: Actelion, a division of Janssen-Cilag International NV. Tel: 1800 709 122

Prescribing information last revised: April 2020

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