SSc-PAH: AN INVISIBLE BUT FATAL DISEASE

YOUR EARLY INTERVENTION COULD EXTEND LIVES

PAH, pulmonary arterial hypertension; SSc, systemic sclerosis

PATIENTS WITH SSc ARE AT HIGH RISK OF DEVELOPING PAH[1]

Pulmonary arterial hypertension (PAH) is a severe, progressive and fatal disease characterised by elevated pulmonary arterial pressure, leading to right heart failure and death[2]

APPROXIMATELY 1 IN 10 PATIENTS WITH SYSTEMIC SCLEROSIS (SSc) ARE ESTIMATED TO DEVELOP PAH[3]

PAH IS A SEVERE AND OFTEN FATAL COMPLICATION OF SSc[4]

PAH, pulmonary arterial hypertension; SSc, systemic sclerosis

PAH IS A LEADING CAUSE OF DEATH IN PATIENTS WITH SSc[5]

PAH ACCOUNTS FOR

>50%

OF DEATHS IN SSc-PAH PATIENTS[5]

EARLIER DIAGNOSIS OF SSc-PAH IS ESSENTIAL TO IMPROVING OUTCOMES FOR YOUR PATIENTS[6]

PAH, pulmonary arterial hypertension; SSc, systemic sclerosis

EARLY SCREENING AND REFERRAL IMPROVE SURVIVAL OUTCOMES[6]

AT 8 YEARS, THERE IS A DIFFERENCE OF

47%

IN SURVIVAL RATES BETWEEN PATIENTS DIAGNOSED DURING ROUTINE CLINICAL PRACTICE AND THOSE DIAGNOSED USING SCREENING[6]

GUIDELINES RECOMMEND ANNUAL SCREENING FOR PAH IN SSc

2015 ESC/ERS PH guidelines:
Resting echo is recommended as a screening test in asymptomatic patients with SSc, followed by **annual screening** with echo, DLCO and biomarkers[7]

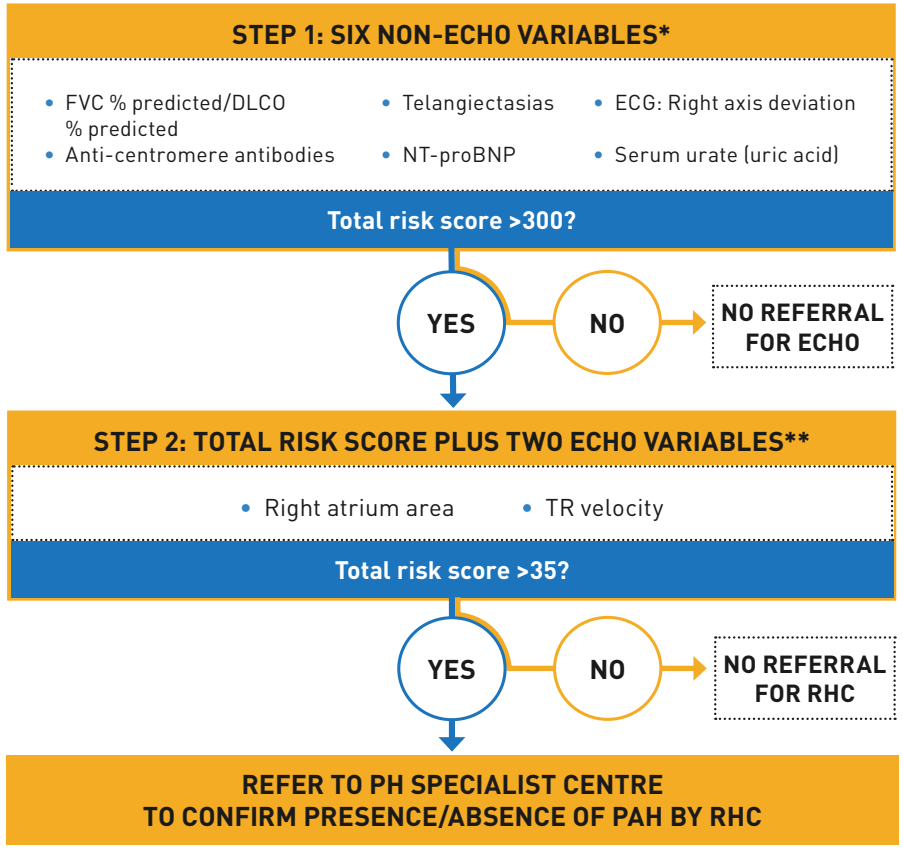
6th World Symposium on Pulmonary Hypertension:
Supports recommendation for **annual screening** for PAH in patients with scleroderma spectrum diseases[8]

Recommendations for screening and detection of CTD-PAH:
Every patient with SSc should be **screened annually** for PAH due to the high prevalence of PAH in SSc[9]

CTD, connective tissue disease; DLCO, carbon monoxide diffusing capacity; ERS, European Respiratory Society; ESC, European Society of Cardiology; PAH, pulmonary arterial hypetension; PH, pulmonary hypertension; SSc, systemic sclerosis

USING THE DETECT ALGORITHM[10]

A screening model like the DETECT algorithm can provide guidance on which SSc patients to refer for echo and then right heart catheterisation (RHC), the diagnostic gold standard for PAH[7,10]



Adapted from Coghlan *et al.* 2014[10]

DLCO, carbon monoxide diffusing capacity; ECG, electrocardiogram; FVC, forced vital capacity; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; RHC, right heart catheterisation; SSc, systemic sclerosis; TR, tricuspid regurgitation
*If a single Step 1 variable is missing, it should be assigned 50 risk points, with the exception of current/past telangiectasias which should be assigned 65 points.
**If a single Step 2 variable is missing, it should be assigned 10 points.

The objective of this PAH risk calculator is to provide an evidence-based screening tool for PAH in SSc patients. The PAH risk calculator may not be used to make a diagnosis of PAH and does not replace specialist PAH clinical judgement. This PAH risk calculator is intended for use only by healthcare professionals. This PAH risk calculator has been developed based on the DETECT study under the auspices of an Actelion Pharmaceuticals Ltd, Switzerland, sponsored Study Scientific Committee, comprised of SSc and PAH experts and specialists. It is recommended to use the PAH risk calculator in centres specialised in the management of SSc, and/or centres that work closely with these specialised SSc centres.

START AHEAD WITH OPSUMIT – AN ORAL ERA WITH PROVEN BENEFICIAL AND SUSTAINED LONG-TERM OUTCOMES IN PAH[11–14]

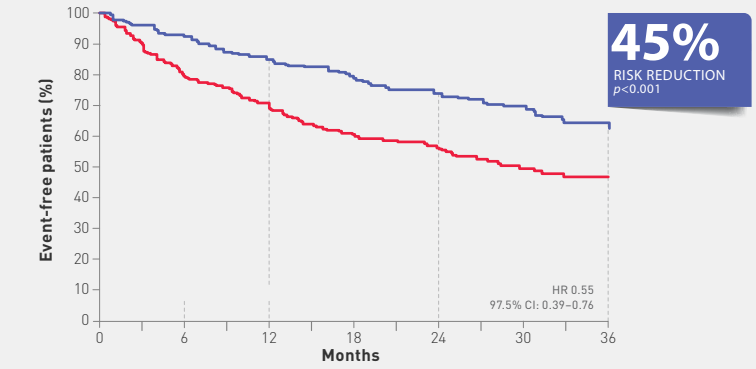
Opsumit® macitentan

The SERAPHIN study is the first and only study to demonstrate a statistically significant long-term benefit with an endothelin receptor antagonist (ERA) vs placebo in PAH based on a composite morbidity-mortality primary endpoint*[11]

31% of patients in SERAPHIN had CTD-PAH[11]

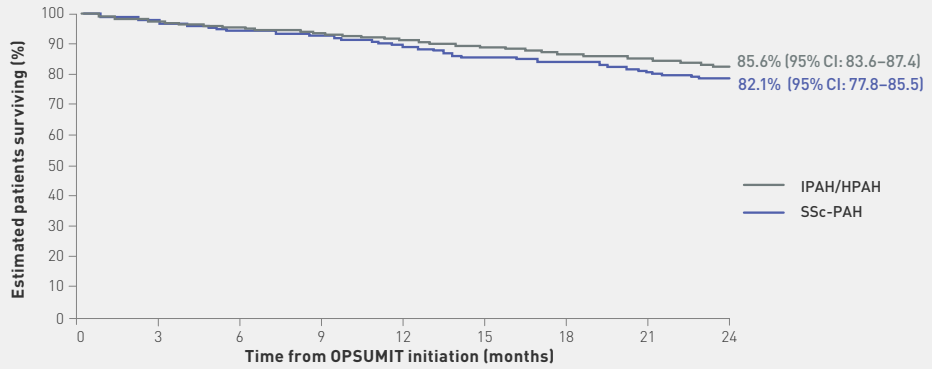
Real-world data from the OPUS and OrPHeUS registries* support the use of OPSUMIT in SSc-PAH, showing similar clinical outcomes in patients with SSc-PAH and patients with idiopathic PAH (IPAH)/heritable PAH (HPAH)[16,17]

OPSUMIT REDUCES THE RISK OF A MORBIDITY OR MORTALITY EVENT* IN PATIENTS WITH PAH VS PLACEBO[11]



Adapted from Pulido *et al.* 2013[11]

REAL-WORLD DATA SUPPORT THE EFFECTIVENESS OF OPSUMIT IN PATIENTS WITH SSc-PAH[17]



Adapted from McLaughlin *et al.* 2019[17]

CONSISTENT WITH THE PRIMARY ENDPOINT, OPSUMIT REDUCED THE RISK OF A MORBIDITY-MORTALITY EVENT* IN **PATIENTS WITH CTD-PAH BY 42% VS PLACEBO****[15]

CI, confidence interval; CTD, connective tissue disease; ERA, endothelin receptor antagonist; HR, hazard ratio; PAH, pulmonary arterial hypertension
*As measured by a composite primary morbidity-mortality endpoint. Results were driven by a decrease in PAH worsening and do not apply to mortality on its own.[11]
**HR 0.58; 95% CI: 0.33–1.02.[15]

OPSUMIT IMPROVES LONG-TERM OUTCOMES IN PAH AND SHOWS **EFFECTIVENESS IN A BROAD PATIENT POPULATION**, INCLUDING PATIENTS WITH **SSc-PAH**[11,12–22]

Adverse events observed in SERAPHIN that were more frequently associated with OPSUMIT included anaemia, bronchitis, headache, oedema and nasopharyngitis.[12] For full safety and tolerability information, please consult the OPSUMIT Prescribing Information.

CI, confidence interval; HPAH, heritable pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; PAH, pulmonary arterial hypertension; SSc, systemic sclerosis
*The OPUS registry included PAH patients with comorbidities including hypertension, oedema, diabetes mellitus, anaemia, signs of right heart failure, autoimmune disease and renal insufficiency.[21,22]

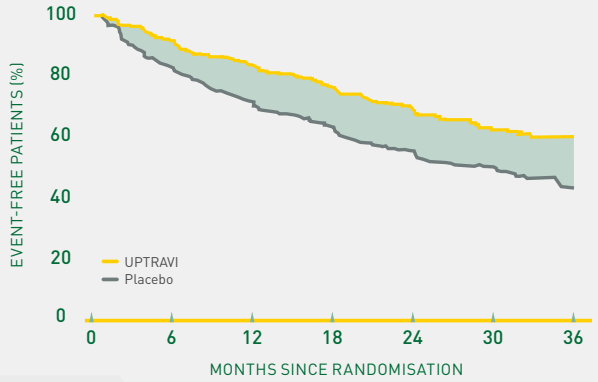
CHANGE THE COURSE OF PAH WITH UPTRAVI – AN ORAL IP RECEPTOR AGONIST SHOWN TO DELAY DISEASE PROGRESSION[23–25]

The GRIPHON trial assessed the effect of UPTRAVI on long-term outcomes in PAH using a robust composite primary endpoint that reflects recommendations from the World Symposium on Pulmonary Hypertension[23,26]

Patients with CTD-PAH comprised **29% of the GRIPHON patient population**[23]

UPTRAVI reduced the risk of morbidity-mortality* in patients with SSc-PAH vs placebo. This response was consistent with that observed in the overall GRIPHON population[28]

TIME TO FIRST MORBIDITY-MORTALITY EVENT* IN GRIPHON (OVERALL POPULATION)[23]

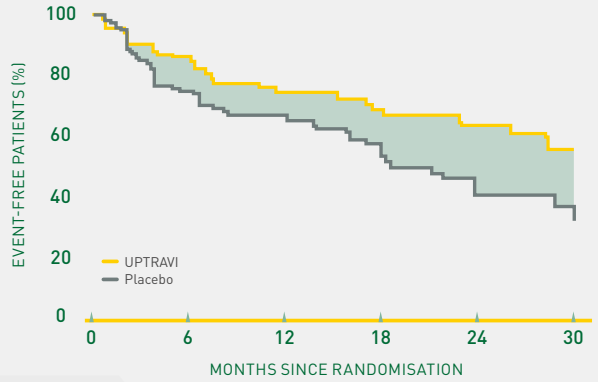


PATIENTS AT RISK							
UPTRAVI	574	455	361	246	171	101	40
Placebo	582	433	347	220	149	88	28

40%
RISK REDUCTION
HR 0.60; 99% CI: 0.46–0.78; $p<0.001$

Adapted from Sitbon *et al.* 2015[23]

TIME TO FIRST MORBIDITY-MORTALITY EVENT* IN GRIPHON (SSc-PAH POPULATION)[28]



PATIENTS AT RISK						
UPTRAVI	77	56	42	34	20	9
Placebo	93	60	47	30	19	9

44%
RISK REDUCTION
HR 0.56; 95% CI: 0.34–0.91

Adapted from Gaine *et al.* 2017[28]

EARLY USE OF UPTRAVI PROVIDES A **LASTING BENEFIT FOR PAH PATIENTS**[23,27]

CI, confidence interval; CTD, connective tissue disease; HR, hazard ratio; IP, prostacyclin; PAH, pulmonary arterial hypertension
*As measured by a composite primary endpoint. Results were driven by a decrease in hospitalisation and other disease progression events and not by mortality on its own.[23]

UPTRAVI DELAYS **DISEASE PROGRESSION AND IMPROVES LONG-TERM OUTCOMES IN SSc-PAH**, A POPULATION PREVIOUSLY CONSIDERED DIFFICULT TO TREAT[28]

In GRIPHON, the most common adverse events were headache, flushing, nasopharyngitis, diarrhoea, vomiting, nausea, jaw pain, myalgia, arthralgia and pain in extremity.[24] For full safety and tolerability information, please consult the UPTRAVI Prescribing Information.

CI, confidence interval; HR, hazard ratio; PAH, pulmonary arterial hypertension; SSc, systemic sclerosis
*As measured by a composite primary endpoint. Results were driven by a decrease in hospitalisation and other disease progression events and not by mortality on its own.[28]

PRESCRIBING INFORMATION

Opsumit® macitentan

OPSUMIT ABBREVIATED PRESCRIBING INFORMATION BASED ON THE EU SUMMARY OF PRODUCT CHARACTERISTICS

OPSUMIT® 10 mg film-coated tablets. ACTIVE INGREDIENT(S): macitentan. Please refer to Summary of Product Characteristics (SmPC) before prescribing. **INDICATION(S):** Opsumit, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III. Efficacy has been shown in a PAH population including 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. *Posology*: Opsumit is to be taken orally at a dose of 10 mg once daily, with or without food. *Elderly patients*: No dose adjustment is required in patients over the age of 65 years. There is limited clinical experience in patients over the age of 75 years. Therefore Opsumit should be used with caution in this population. *Patients with hepatic impairment*: Based on PK data, no dose adjustment is required in patients with mild, moderate or severe hepatic impairment. However, there is no clinical experience with the use of macitentan in PAH patients with moderate or severe hepatic impairment. *Patients with renal impairment*: Based on PK data, no dose adjustment is required in patients with renal impairment. There is no clinical experience with the use of macitentan in PAH patients with severe renal impairment. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, soya or to any of the excipients, pregnancy, women of childbearing potential who are not using reliable contraception, breastfeeding, patients with severe hepatic impairment (with or without cirrhosis), baseline values of hepatic aminotransferases (AST and/or ALT > 3 × ULN). **SPECIAL WARNINGS & PRECAUTIONS:** *Liver function*: Elevations of liver aminotransferases (AST, ALT) have been associated with PAH and with endothelin receptor antagonists (ERAs). Opsumit is not to be initiated in patients with severe hepatic impairment or elevated aminotransferases (> 3 × ULN), and is not recommended in patients with moderate hepatic impairment. Liver enzyme tests should be obtained prior to initiation of Opsumit. Patients should be monitored for signs of hepatic injury and monthly monitoring of ALT and AST is recommended. If sustained, unexplained, clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin > 2 × ULN, or by clinical symptoms of liver injury (e.g., jaundice), Opsumit treatment should be discontinued. Reinitiation of Opsumit may be considered following the return of hepatic enzyme levels to within the normal range in patients who have not experienced clinical symptoms of liver injury. The advice of a hepatologist is recommended. *Haemoglobin concentration*: Decrease in haemoglobin concentrations has been associated with endothelin receptor antagonists (ERAs) including macitentan. Initiation of Opsumit is not recommended in patients with severe anaemia. It is recommended that haemoglobin concentrations be measured prior to initiation of treatment and tests repeated during treatment as clinically indicated. *Pulmonary veno-occlusive disease*: If signs of pulmonary oedema occur when macitentan is administered in patients with PAH, the possibility of pulmonary veno-occlusive disease should be considered. *Patients with renal impairment*: Patients with renal impairment may run a higher risk of experiencing hypotension and anaemia during treatment with macitentan. Therefore, monitoring of blood pressure and haemoglobin should be considered. There is no clinical experience with the use of macitentan in PAH patients with severe renal impairment. Caution is recommended in this population. There is no experience with the use of macitentan in patients undergoing dialysis, therefore Opsumit is not recommended in this population. *Excipients*: Opsumit contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Opsumit contains lecithin. If a patient is hypersensitive to soya, Opsumit must not be used. This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'. **SIDE EFFECTS:** Very common (≥ 1/10): nasopharyngitis, bronchitis, anaemia, haemoglobin decrease, headache, oedema, fluid retention*. Common (≥ 1/100 to < 1/10): pharyngitis, influenza, urinary tract infection, hypotension, nasal congestion, leukopenia, thrombocytopenia, aminotransferase elevations. Uncommon (< 1/10): hypersensitivity reactions (e.g., angioedema, pruritus, rash). Consult SmPC in relation to less common side effects. * In a large, long-term clinical study in PAH, rates of oedema adverse events were similar in patients on macitentan and placebo. In clinical studies conducted in other non-approved indications of idiopathic pulmonary fibrosis and digital ulcers associated with systemic sclerosis, the observed rates of oedema AEs were higher for macitentan than for placebo. **Refer to the SmPC for other side effects. PREGNANCY:** Opsumit is contraindicated during pregnancy. Opsumit treatment should only be initiated in women of childbearing potential when the absence of pregnancy has been verified, appropriate advice on contraception provided, and reliable contraception is practised. Women should not become pregnant for 1 month after discontinuation of Opsumit. Monthly pregnancy tests during treatment with Opsumit are recommended to allow the early detection of pregnancy. **LACTATION:** Opsumit is contraindicated during breastfeeding. **MALE FERTILITY**: A deterioration of spermatogenesis cannot be excluded. **INTERACTIONS:** *CYP3A4 inhibitors*: Caution should be exercised when macitentan is administered concomitantly with strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, voriconazole, clarithromycin, telithromycin, nefazodone, ritonavir, and saquinavir). *CYP3A4 inducers*: Reduced efficacy in the presence of strong CYP3A4 inducers (e.g., rifampicin, St. John's wort, carbamazepine, and phenytoin) could occur and combination with macitentan should be avoided. *Sildenafil*: When macitentan and sildenafil are given concomitantly, sildenafil exposure may increase and the exposure to the macitentan active metabolite may decrease. These changes are not considered clinically relevant. *Cyclosporine A and warfarin*: The pharmacokinetics of macitentan and its active metabolite are not affected by cyclosporine A and warfarin. *Hormonal contraceptives*: Macitentan 10 mg once daily did not affect the pharmacokinetics of an oral contraceptive (norethisterone 1 mg and ethinyl estradiol 35 µg). *Breast cancer resistance protein (BCRP) substrate drugs*: Macitentan 10 mg once daily did not affect the pharmacokinetics of a BCRP substrate drug (riociguat 1 mg; rosuvastatin 10 mg). **LEGAL CLASSIFICATION:** Subject to restricted medical prescription. **MARKETING AUTHORISATION NUMBER(S):** EU/1/13/893/001/2/3. **MARKETING AUTHORISATION HOLDER:** Janssen-Cilag International NV, Turnhoutseweg 30, B 2340 Beerse, Belgium. **PACKS & PRICE:** *country specific (no need to include further details here).* Blister packs containing 15 or 30 film-coated tablets, bottles containing 30 film-coated tablets. Products mentioned in this document may not be registered in all countries. Prescribing Information may vary per country. Health Care Providers must refer to their country prescribing information. Prescribing information generation date or last revised: May 2020. Based on 17 April 2020 EU Summary of Product Characteristics.

Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in section 4.8 of the SmPC.

PRESCRIBING INFORMATION

Uptravi selexipag

UPTRAVI® 200 microgram, 400 microgram, 600 microgram, 800 microgram, 1,000 microgram, 1,200 microgram, 1,400 microgram, and 1,600 microgram Film-coated Tablets ABBREVIATED PRESCRIBING INFORMATION BASED ON THE EU SUMMARY OF PRODUCT CHARACTERISTICS ACTIVE INGREDIENT: Each film-coated tablet contains either 200 microgram or 400 microgram or 600 microgram or 800 microgram or 1,000 microgram or 1,200 microgram or 1,400 microgram or 1,600 microgram selexipag. Please refer to Summary of Product Characteristics (SmPC) before prescribing. **INDICATION(S):** Long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II–III, as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist and/or a phosphodiesterase type 5 inhibitor, 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:** *Individualised dose titration:* Only a PAH experienced physician should initiate and monitor treatment. Up titrate patients to the highest individually tolerated dose, which can range from 200 micrograms to 1,600 micrograms given twice daily (BD). The recommended starting dose is 200 micrograms BD approximately 12 hours apart. Increase dose in increments of 200 micrograms BD, usually at weekly intervals, based on tolerability. During titration some adverse reactions reflecting the mode of action of selexipag may occur, these are usually transient or manageable with symptomatic treatment. *Individualised maintenance dose:* Maintain the highest tolerated dose a patient can take with tolerable adverse events. *Interruptions and discontinuations:* Missed doses should be taken as soon as possible, unless the next dose is scheduled within 6 hrs. If treatment is missed for 3 days or more, restart at a lower dose and then up-titrated. There is limited experience with abrupt discontinuation. No evidence for acute rebound has been observed. If it is necessary to stop treatment withdraw gradually. *Dose adjustment with co-administration of moderate CYP2C8 inhibitors:* Uptravi dosing should be reduced to once daily when co-administered with moderate CYP2C8 inhibitors (e.g., clopidogrel, deferasirox and teriflunomide). If the therapy is not tolerated at a given dose, symptomatic treatment and/or a dose reduction to the next lower dose should be considered. Uptravi dosing should be reverted to twice daily when coadministration with moderate CYP2C8 inhibitors is stopped. **Special populations:** *Elderly:* (≥ 65 years): No dose adjustment required. Limited experience in patients over 75 years. *Paediatrics:* No data are available. *Renal Impairment:* No dose adjustment required in mild or moderate renal impairment. No change in dose initiation is required in severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2); dose titration should be done with caution in these patients. *Hepatic impairment:* Do not treat patients with severe liver impairment (Child-Pugh class C). Moderate hepatic impairment (Child-Pugh class B), starting dose 200 micrograms once daily, increase weekly in increments of 200 micrograms, until patient reaches 1,600 microgram daily or experiences adverse reactions, reflecting the mode of action of selexipag, that cannot be tolerated or medically managed. Reduce dose by 200 micrograms daily to alleviate adverse reactions and maintain dosage. Mild hepatic impairment (Child-Pugh class A) no dose adjustment required. **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 the last 6 months, decompensated cardiac failure, severe arrhythmias, cerebrovascular events within the last 3 months, congenital or acquired valvular defects, concomitant administration with strong inhibitors of CYP2C8 (e.g., gemfibrozil). **SPECIAL WARNINGS & PRECAUTIONS:** *Hypotension:* Selexipag has vasodilatory properties that may reduce blood pressure. *Hyperthyroidism:* Hyperthyroidism has been observed, monitor thyroid function if clinically indicated. *Pulmonary veno-occlusive disease:* If signs of pulmonary oedema occur on administering selexipag, consider pulmonary veno-occlusive disease which has been reported with vasodilators (mainly prostacyclins), if confirmed discontinue treatment. *Elderly:* (≥ 65 years): Limited experience in patients over 75 years. So, selexipag should be used with caution in this population. *Hepatic impairment:* In patients with severe liver impairment (Child Pugh class C), selexipag should not be administered. In subjects with moderate hepatic impairment (Child Pugh class B), the exposure to selexipag and its active metabolite is increased. In patients with moderate hepatic impairment, Uptravi should be dosed once daily. *Renal impairment:* In patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2), caution should be exercised during dose titration. There is no experience with Uptravi in patients undergoing dialysis, therefore Uptravi should not be used in these patients. *Women of childbearing potential:* Women of childbearing potential should practise effective contraception while taking selexipag. **SIDE EFFECTS:** *Very common:* Headache, flushing, nasopharyngitis, diarrhoea, vomiting, nausea, jaw pain, myalgia, arthralgia, pain in extremity. *Common:* anaemia, decreased haemoglobin, hyperthyroidism, decreased appetite, weight decrease, hypotension, decreased thyroid-stimulating hormone, nasal congestion, abdominal pain, rash, urticaria, erythema, pain. **Refer to the SmPC for other side effects. PREGNANCY:** Uptravi is not recommended during pregnancy and in women of childbearing potential not using contraception. No data in pregnant women. Animal studies do not indicate reproductive toxicity. **LACTATION:** It is unknown if selexipag or its metabolites are excreted in human milk. Uptravi should not be used during breast feeding. **INTERACTIONS:** Concomitant administration of Uptravi with strong inhibitors of CYP2C8 (e.g., gemfibrozil) is contraindicated as when co-administered, exposure to the active metabolite, the major contributor to the drug effect, increased approximately 11-fold. Concomitant administration of Uptravi with a moderate inhibitor of CYP2C8, increased the exposure to the active metabolite up to 2.7-fold. Refer **"Dose adjustment with co-administration of moderate CYP2C8 inhibitors"** for more information on dose adjustment when co-administered with moderate CYP2C8 inhibitors. Co-administration of selexipag with rifampicin, an inducer of CYP2C8, reduced exposure to the active metabolite to half, hence dose adjustment of selexipag may be required when it is administered concomitantly with inducers of CYP2C8 (e.g., rifampicin, carbamazepine, phenytoin). Effect of strong inhibitors of UGT1A3 and UGT2B7 (valproic acid, probenecid, and fluconazole) on selexipag was not studied, therefore caution is required when co-administering as a potential interaction cannot be excluded. PAH specific therapies: In the phase 3 placebo-controlled trial in patients with PAH, the use of selexipag in combination with both an ERA and a PDE 5 inhibitor resulted in a 30% lower exposure to the active metabolite. **LEGAL CLASSIFICATION:** Local information on classification, prescription conditions, reimbursement, as applicable. **MARKETING AUTHORISATION NUMBER:** EU/1/15/1083 001-011. **MARKETING AUTHORISATION HOLDER:** JANSSEN-CILAG INTERNATIONAL NV, Turnhoutseweg 30, B 2340 Beerse, Belgium. **PACKS & PRICE:** Country specific. Products mentioned in this document may not be registered in all countries. Prescribing Information may vary per country. Health Care Providers must refer to their country prescribing information. Prescribing information generation date or last revised: December 2020. Based on 12 May 2016 EU Summary of Product Characteristic.

Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in section 4.8 of the SmPC.

HELP FACILITATE EARLIER TREATMENT AND IMPROVED OUTCOMES FOR YOUR PATIENTS WITH SSc-PAH

- PAH is a silently progressive disease and a leading cause of death in SSc-PAH patients[5]
- Early identification of PAH is critical to improving patient outcomes[6]
  - Guidelines recommend annually screening SSc patients for PAH[7–9]
  - The DETECT algorithm can be used to screen for PAH in SSc[7,10]
  - Refer patients to PH centres early to confirm PAH diagnosis
- Early PAH treatment with OPSUMIT and UPTRAVI makes a difference
  - Proven to delay disease progression and improve long-term outcomes in a broad range of patients, including those with SSc-PAH[11–13,15–25,28,29]
  - Both OPSUMIT and UPTRAVI are recommended in combination therapy[7] and have been shown to reduce morbidity-mortality* vs placebo when used as combination therapy**[20,25]

ERA, endothelin receptor antagonist; PAH, pulmonary arterial hypertension; PDE-5i, phosphodiesterase type-5 inhibitor; PH, pulmonary hypertension; SSc, systemic sclerosis; WHO, World Health Organization

*As measured by a composite primary endpoint. Results were driven by a decrease in hospitalisation and other disease progression events and not by mortality on its own.[11,23]

**OPSUMIT in combination with PDE-5i or oral/inhaled prostanoid in the SERAPHIN trial.[11] UPTRAVI in combination with ERA and PDE-5i in GRIPHON.[23]

OPSUMIT, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO functional class (FC) II to III. Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.[12]

UPTRAVI is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II–III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type-5 (PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies. Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.[24]

REFERENCES

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