

PREPARING YOUR PATIENTS FOR TYVASO

Making an adverse event management plan

Give your patients specific instructions to help address adverse reactions. Below are some methods to consider for your patients.

The following approaches to managing adverse reactions are based on anecdotal evidence cited in Poms et al (2011) and should not be construed as medical advice. United Therapeutics does not recommend or endorse using healthcare products other than as directed or prescribed.

Considerations for adverse reactions¹:



Cough

- Inhaled anticholinergics
- Inhaled steroids
- OTC or prescription cough medicines
- Before treatment, drink very cold water for numbing effect or warm water to soothe and relax
- Reduce the number of breaths per treatment and/or titrate slower (eg, by 1 breath, 4x per day)



Throat irritation

- Oral phenol-based analgesic sprays to numb throat before treatment



Headaches

- OTC pain relievers (acetaminophen, short-term ibuprofen, aspirin)
- Temporary dose reductions (eg, by 1 breath, 4x per day)



Nausea

- Swish and spit after treatment
- Eat a small meal before next treatment
- Temporary dose reductions (eg, by 1 breath, 4x per day)



Flushing

- If severe, decrease by 1 breath, 4x per day, and increase when symptom improves

OTC=over the counter.

Remind patients to talk to you or your staff about any adverse reactions and not to discontinue treatment without your direction

IMPORTANT SAFETY INFORMATION FOR TYVASO

WARNINGS AND PRECAUTIONS

- The efficacy of Tyvaso has not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease). Patients with acute pulmonary infections should be carefully monitored to detect any worsening of lung disease and loss of drug effect

Please see Important Safety Information on reverse side and visit www.tyvaso.com to see Full Prescribing Information, Patient Package Insert, and the TD-100 and TD-300 Tyvaso Inhalation System Instructions for Use manuals.

INDICATION

Tyvaso (treprostinil) is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).

The effects diminish over the minimum recommended dosing interval of 4 hours; treatment timing can be adjusted for planned activities.

While there are long-term data on use of treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.

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- Tyvaso is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, Tyvaso may cause symptomatic hypotension
- Titrate slowly in patients with hepatic or renal insufficiency, as exposure to treprostinil may be increased in these patients
- Tyvaso inhibits platelet aggregation and increases the risk of bleeding
- Co-administration of the cytochrome P450 (CYP) 2C8 enzyme inhibitor gemfibrozil may increase exposure to treprostinil. Co-administration of the CYP2C8 enzyme inducer rifampin may decrease exposure to treprostinil. Increased exposure is likely to increase adverse events, whereas decreased exposure is likely to reduce clinical effectiveness

DRUG INTERACTIONS / SPECIFIC POPULATIONS

- The concomitant use of Tyvaso with diuretics, antihypertensives, or other vasodilators may increase the risk of symptomatic hypotension
- Co-administration of the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to *oral treprostinil*. Co-administration of the CYP2C8 enzyme inducer rifampin decreases exposure to *oral treprostinil*. It is unclear if the safety and efficacy of *treprostinil by the inhalation* route are altered by inhibitors or inducers of CYP2C8
- Limited case reports of treprostinil use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. However, pulmonary arterial hypertension is associated with an increased risk of maternal and fetal mortality. There are no data on the presence of treprostinil in human milk, the effects on the breastfed infant, or the effects on milk production
- Safety and effectiveness in pediatric patients have not been established

ADVERSE REACTIONS

- The most common adverse reactions seen with Tyvaso in $\geq 4\%$ of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical study were cough (54% vs 29%), headache (41% vs 23%), throat irritation/ pharyngolaryngeal pain (25% vs 14%), nausea (19% vs 11%), flushing (15% vs <1%), and syncope (6% vs <1%). In addition, adverse reactions occurring in $\geq 10\%$ of patients were dizziness and diarrhea

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Reference: 1. Poms A, Kingman M. Inhaled treprostinil for the treatment of pulmonary arterial hypertension. *Crit Care Nurse*. 2011;31(6)ce1-e10.



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