VENTAVIS® (iloprost)
Dosing and Administration of VENTAVIS in Pulmonary Arterial Hypertension

SUMMARY

- VENTAVIS is supplied in 1 mL ampules in two concentrations: 10 mcg/mL and 20 mcg/mL.[1]
- VENTAVIS therapy is initiated with 2.5 mcg via inhalation. If the 2.5 mcg dose is well tolerated, dosing should be increased to 5 mcg and maintained at the 5 mcg dose. If the 5 mcg dose is not well tolerated, the dose may be reduced to 2.5 mcg and maintained at the 2.5 mcg dose.[1]
- Patients who are maintained at the 5 mcg dose and who have repeatedly experienced extended treatment times may use the 20 mcg/mL concentration to decrease treatment times to help maintain patient adherence.[1]
- The primary support for the dosing regimen of 2.5 mcg or 5 mcg administered 6 to 9 times daily is based on clinical experience from the Phase 3 AIR study.[2]
- Patients receiving VENTAVIS experienced jaw pain and flushing more frequently than those on placebo in the pivotal study. Syncope was also more common in patients receiving VENTAVIS.[2]
- A search of the published literature identified a study evaluating the inhalation behavior in patients with pulmonary arterial hypertension switching from VENTAVIS 10 mcg/mL to 20 mcg/mL formulations.[3]

CLINICAL DATA

US Prescribing Information

Dosage and Administration

VENTAVIS is intended to be inhaled using the I-neb® Adaptive Aerosol Delivery (AAD®) System. The first inhaled dose should be 2.5 mcg (as delivered at the mouthpiece). If this dose is well tolerated, dosing should be increased to 5 mcg and maintained at that dose; otherwise maintain the dose at 2.5 mcg. VENTAVIS should be taken 6 to 9 times per day (no more than once every 2 hours) during waking hours, according to individual need and tolerability. The maximum daily dose evaluated in clinical studies was 45 mcg (5 mcg 9 times per day).[1]

Direct mixing of VENTAVIS with other medications in the I-neb AAD System has not been evaluated; do not mix with other medications. To avoid potential interruptions in drug delivery due to equipment malfunctions, the patient should have easy access to a back-up I-neb AAD System.[1]

Ampule Concentration	10 mcg/mL	20 mcg/mL
I-neb AAD delivered dose	2.5 or 5 mcg from one ampule	5 mcg from one ampule

It should take approximately 4-10 minutes to administer a 5 mcg dose using the 10 mcg/mL concentration. The 20 mcg/mL concentration is intended for patients who are maintained at the 5 mcg dose and who have repeatedly experienced extended treatment times which could result in incomplete dosing. Transitioning patients to the 20 mcg/mL concentration using the I-neb AAD System will decrease treatment times to help maintain patient compliance.[1]

For each inhalation session, the entire contents of each opened ampule of VENTAVIS should be transferred into the I-neb AAD System medication chamber immediately before use. After each inhalation session, any solution remaining in the medication chamber should be discarded. Use of the remaining solution will result in unpredictable dosing. Patients should follow the manufacturer's instructions for cleaning the I-neb AAD System components after each dose administration.[1]

Information From the Literature

Richter et al (2018)[3] conducted an observational, non-blinded, case-crossover study that evaluated the effect of switching from VENTAVIS V10 (10 mcg/mL) to V20 (20 mcg/mL) formulations for delivering a 5 mcg dose via the I-Neb AAD device. The co-primary endpoints were mean daily proportion of complete inhalations and mean daily inhalation frequency and the secondary endpoint was mean daily inhalation duration. Data was collected from 63 patients for 3 months before and after switching. Results showed that switching from the V10 to V20 formulation significantly increased the mean daily proportion of complete inhalations (92% vs 97%, $P<0.0001$) and mean daily inhalation frequency (4.6 versus 4.9 inhalations/day, $P=0.0430$) and reduced the mean daily inhalation duration (11.8 vs 6.5 minutes, $P<0.0001$). One adverse event (AE) was reported during the study observation period, which was a serious AE (hospitalization due to worsening of underlying disease) that was deemed unrelated to study drug and led to cessation of V20 treatment.

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, DERWENT® (and/or other resources, including internal/external databases) was conducted on 31 May 2024.

REFERENCES

1. VENTAVIS (iloprost) [Prescribing Information]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.;https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/VENTAVIS-pi.pdf.

2. Ghofrani HA, Wiedemann R, Rose F, et al. Combination therapy with oral sildenafil and inhaled iloprost for severe pulmonary hypertension. *Ann Intern Med*. 2002;136(7):515.

3. Richter MJ, Stollfuß B, Roitenberg A, et al. Switching inhaled iloprost formulations in patients with pulmonary arterial hypertension: the VENTASWITCH Trial. *Pulm Circ*. 2018;8(4):2045894018798921.