# Treprostinil Dry Powder Inhalation (DPI) (YUTREPIA)
# National Drug Mini-monograph
# August 2025

**VA Pharmacy Benefits Management Services and National Formulary Committee**

*The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.*

**FDA APPROVAL INFORMATION**

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| **Description / MOA** | Prostacyclin analogue |
| **Indication Under Review**[1] | ▪ Pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability<br>▪ Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability |
| **Dosage Regimen** | **Treatment naïve:** 26.5 mcg four times daily<br>**Target maintenance dose** 79.5 to 106 mcg four times daily<br>**Transitioning from treprostinil nebulized inhalation solution (TYVASO):** |

| Current TYVASO dose* (# breaths) | YUTREPIA DPI dose (mcg) |
|---|---|
| 5 or less breaths | 26.5 mcg |
| 6 to 8 breaths | 53 mcg |
| 9 to 11 breaths | 79.5 mcg |
| 12 to 14 breaths | 106 mcg |
| 15 to 17 breaths | 132.5 mcg (requires 2 capsules per dose) |
| 18 or more breaths | 159 mcg (requires 2 or more capsules per dose) |

*each breath of TYVASO delivers ~6 mcg Treprostinil

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| **Dosage Forms Under Review** | ▪ New DPI capsule formulation administered using a specialized capsule-based inhaler<br>▪ YUTREPIA DPI is formulated to provide uniform, small particles designed to enhance deep lung delivery with low inspiratory effort.<br>▪ *Of note, treprostinil nebulized solution, inhaled dry powder cartridge, parenteral infusion, and oral tablet are available in the U.S. but are not part of this review.* |

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| **Trial/Design** | **INSPIRE:** phase 3, open label **safety and tolerability** study of treprostinil DPI in **PAH**, mean duration 1 yr |
| **Population** | N=121; WHO Group 1 PAH patients who were either: 1) on stable doses of nebulized treprostinil (transition group); or 2) prostacyclin naïve and on ≤2 nonprostacyclin oral PAH agents. |
| **Intervention** | ▪ Prostacyclin naïve patients initiated treprostinil DPI at 26.5 mcg 4x daily, titrated weekly to max of 212 mcg 4x daily<br>▪ Transition patients initiated treprostinil DPI at comparable dose to treprostinil nebulized solution<br>▪ Primary safety endpoints: adverse events (AEs) and serious AEs |
| **Comparator** | none |
| **Demographics/ Baseline** | Mean age 54 yrs; female 86%; NYHA functional class II 66%; NYHA functional class III 34%; on ≥1 background oral meds 95%; mean dose at months 8 and 12: ~106 mcg 4x daily |
| **Results** | ▪ 99% of patients reported an AE, and 12% of patients discontinued due to AE.<br>▪ 17% of patients reported a serious AE, though none were considered treatment related.<br>▪ More patients in the treatment naïve group compared to the transitioning group reported treatment related and moderate to severe AEs |

| SAFETY CONSIDERATIONS | | |
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| | **Boxed Warnings** | None |
| | **Contraindications** | None |
| | **Other Warnings** | ▪ Risk of symptomatic hypotension (vasodilator)<br>▪ Risk of bleeding (inhibitor of platelet aggregation)<br>▪ Risk of bronchospasm, increased in patients with asthma, COPD, or other bronchial hyperreactivity<br>▪ Increased exposure of treprostinil when co-administered with CYP2C8 inhibitor (e.g., gemfibrozil); decreased exposure of treprostinil when co-administered with CYP2C8 inducer (e.g., rifampin) |
| | **Top AEs** | Cough, headache, throat irritation, dizziness |
| | **Pregnancy** | Insufficient human data; no adverse reproductive or developmental effects identified in animal studies |
| | **Lactation** | No data |

| PLACE IN THERAPY | DRUG | VANF | CFU | FDA | GUIDELINES |
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| | **Treprostinil DPI (YUTREPIA) capsule** | TBD | PAH<br>PH-ILD (proposed) | | |
| | **Treprostinil DPI (TYVASO DPI) cartridge** | NO | PAH<br>PH-ILD | | |
| | **Treprostinil inhalation solution (TYVASO) ampule** | NO | PAH<br>PH-ILD | | |

| VHA PLACE IN THERAPY | | |
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| | **Potential Use in VHA** | ▪ **PAH:** Inhaled treprostinil improves exercise ability as measured by 6MWD based on evidence from the TRIUMPH trial using the nebulized inhalation solution (TYVASO). No significant impact on clinical worsening or mortality has been shown in RCTs.<br>▪ **PH-ILD:** Inhaled treprostinil improves 6MWD, NT-proBNP, and clinical worsening based on evidence from the INCREASE trial using the nebulized inhalation solution (TYVASO).<br>▪ YUTREPIA DPI is the third inhaled treprostinil product approved in the U.S. The first approved product is TYVASO nebulized inhaled solution. TYVASO is administered via a nebulizer, requiring multiple breaths per dose and daily cleaning of the device (TYVASO). TYVASO DPI was approved in 2023 and uses a single-use cartridge in a portable inhaler device, improving patient satisfaction. YUTREPIA DPI uses a single-use capsule in a portable inhaler device. Both DPI products were FDA approved based on demonstration of safety and tolerability (not efficacy).<br>▪ YUTREPIA DPI was evaluated in the open-label INSPIRE trial in a PAH population comprised of a mix of treprostinil naïve and treprostinil experienced patients. Evaluated over a one-year period, no new safety or tolerability concerns with YUTREPIA DPI were identified. Overall, 12% of patients discontinued treatment due to AEs.<br>▪ Though there is no direct comparative data, the safety profile of YUTREPIA appears to be consistent with other forms of inhaled treprostinil in the PAH population. Common AEs include cough, headache, throat irritation, and dizziness (known AEs with inhaled prostacyclins). YUTREPIA DPI was not specifically evaluated in the PH-ILD population.<br>▪ Dosing: The mean YUTREPIA DPI dose in the INSPIRE trial was ~106 mcg, the highest strength capsule available. Doses greater than 106 mcg require 2 capsules and are double the cost.<br>▪ The clinical significance of the unique, uniform, small particle design of YUTREPIA DPI is unclear. YUTREPIA DPI requires low inspiratory effort and may be useful for patients who are unable to use DPIs that require strong inhalation for medication delivery.<br>▪ An open label extension study evaluating the long-term safety of YUTREPIA in PAH is ongoing (NCT 03992755). A separate open label study is ongoing evaluating safety and tolerability of YUTREPIA in a prostacyclin-naïve PH-ILD population (ASCENT).<br>▪ YUTREPIA DPI is a new formulation of treprostinil available as single-use capsules in a specialized inhaler that is discarded every 7 days. YUTREPIA DPI may be considered an alternative to treprostinil inhaled nebulized solution (TYVASO) or TYVASO DPI in patients with PAH and PH-ILD. |

Prepared: August 2025. Contact person: Lisa Longo, PharmD, BCPS, National PBM Clinical Pharmacy Program Manager, Formulary Management, VA Pharmacy Benefits Management Services (12PBM)

## References

1. YUTREPIA (treprostinil DPI) formulation [prescribing information online]. Morrisville, NC: Liquidia Technologies. May 2025. Available at: https://yutrepia.com/full-prescribing-information.pdf. Accessed August 12, 2025.
2. TYVASO (treprostinil inhalation powder) [prescribing information online]. Research Triangle Park, NC: United Therapeutics Corp. October 2024. Available at: https://www.tyvaso.com/pdf/TYVASO-DPI-PI.pdf . Accessed August 12, 2025.
3. Hill NS, Feldman JP, Sahay S, et al. INSPIRE: Safety and tolerability of inhaled Yutrepia (treprostinil) in pulmonary arterial hypertension. Pulm Circ. 2022;12:e12119. https://doi.org/10.1002/pul2.12119