University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-29 Pulmonary Arterial Hypertension (PAH) Drugs

Effective Date: 12/18/24

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plan and may not be covered by all UM Health Plan. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the situation.

Contact UM Health Plan Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

PAH medications [Endothelial Receptor Antagonists (ERA), Guanylate Cyclase Stimulants (sGCs), Phosphodiesterase Type-5 Inhibitors (PDE-5i), Prostacyclin Pathway Agonists (PCY), Activin Signaling Inhibitors (ASI)] are specialty drugs indicated for Pulmonary Arterial Hypertension and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and acceptable adverse effects.

3.0 Clinical Determination Guidelines:

Document the following with chart notes.

I. General considerations for use

   A. Appropriate medication use [must meet all listed below]:

      1. Diagnosis: meets standard diagnosis criteria that designate signs, symptoms, and test results to support specific diagnosis.
      2. Food and Drug Administration (FDA) approval status [must meet one listed below]:
         a. FDA approved: product, indication, and dosage regimen.
         b. Non-FDA approved use: Compendium support (UpToDate, Lexidrug) for the use of a drug for a non-FDA approved indication or dosage regimen)
      3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

   B. Grandfather status: patients currently on excluded PAH products may continue if appropriate.

C. Required site-of-care as determined by the Health Plan (see DDP-08 Site of Care for Administration of Parenteral Specialty Medications)

D. Dose Rounding: medication requests may be automatically rounded up or down by 10% of the requested dose in order to fit the nearest manufacturer's strength of the requested medication for patients weighing above 10 Kg (see DDP-21 Dose Rounding and Wastage).

E. Pharmaceutical sample use: The Health Plan does not recognize pharmaceutical samples as medication trials or for continuing therapy.

F. Formulary Status (see appendix II.)

1. Must try all preferred agents in a class before non-preferred agents will be approved
2. Excluded agents require a trial of all formulary agents before coverage will be considered

G. Approval:

1. Initial: six months
2. Re-approval: one year
    a. Decreased risk status or sustained low-risk status
        i. If not at low-risk status, escalate therapy (see section III.B.)
    b. Adherence to [must meet one listed below]:
        i. Medications processed on the medical benefit: consistent utilization (at least 80% of days covered) history in claims history or chart notes.
        ii. Medications processed on the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from the pharmacy.
    c. Activin Signaling Inhibitors only [must meet one below]:
        i. Improvement in 6-minute walk distance (6MWD) from baseline
        ii. Improvement in WHO functional class (see appendix I.)

II. Pulmonary Arterial Hypertension Diagnosis [must meet all listed below]:

A. Prescriber: cardiologist or pulmonologist (in consultation with a PAH center).

B. Diagnosis and severity [must meet all listed below]:

1. Pulmonary arterial hypertension (PAH) WHO Group I: Confirmed by right heart catheterization [must meet both listed below]:
    a. Mean pulmonary arterial pressure (mPAP): at least 20 mmHg at rest
    b. Pulmonary artery wedge pressure (PAWP): 15mmHg or below
    c. Pulmonary vascular resistance (PVR): greater than 2 wood units (WU)
2. Vasoreactivity test: completed or documented inappropriateness to test [must meet one listed below]:
    a. Positive acute vasodilator test (decrease in mPAP of at least 10mmHg to less than 40mmHg with unchanged or increased cardiac output)
        i. Using inhaled nitric oxide, IV epoprostenol, adenosine, or inhaled iloprost
        ii. Initiate calcium channel blockers (e.g., diltiazem or a dihydropyridine) unless all are contraindicated or have had an inadequate response or significant side effects
    b. Negative response test.
3. Risk status calculation using REVEAL 2.0 or REVEAL Lite 2 scale [must meet one below]:
    a. REVEAL 2.0
        i. Low-risk score: ≤6

ii. Intermediate-risk score: 7-8
iii. High-risk score: ≥9

b. Reveal Lite 2
i. Low-risk score ≤5
ii. Intermediate risk score: 6-7
iii. High-risk score: ≥8

III. Pulmonary Arterial Hypertension Treatment Options (see Appendix II.)

A. Baseline risk status and initial therapy

1. Low risk [must meet both below]:
a. Endothelin receptor antagonist (ERA)
b. Phosphodiesterase type 5 inhibitor (PDE-5i)

2. Intermediate risk [must meet both below]:
a. Endothelin receptor antagonist (ERA)
b. Phosphodiesterase type 5 inhibitor (PDE-5i)

3. High risk [must meet all below]:
a. Endothelin receptor antagonist (ERA)
b. Phosphodiesterase type 5 inhibitor (PDE-5i)
c. IV or SC prostacyclin pathway agonist (PCY)
i. Oral or Inhaled may be used if tolerated and effective

B. Follow-Up Risk Status and Therapy (after 3-6 months of initial therapy)

1. Low risk
a. Continue initial therapy (from section III.A.)

2. Intermediate-low risk
a. Add IV or SC prostacyclin pathway agonist (PCY)
i. Oral or Inhaled may be used if tolerated and effective
b. Switch from a Phosphodiesterase type 5 inhibitor (PDE-5i) to a soluble guanylate cyclase stimulant (sGCs)

3. Intermediate-high risk and High Risk
a. Add IV or SC prostacyclin pathway agonist (PCY)
i. Switch to IV or SC if currently using oral or inhaled
b. Evaluate for lung transplantation
c. May consider the addition of an activin signaling inhibitor [must meet all below]:
i. At least 18 years of age
ii. WHO functional class II or III symptoms (see appendix I.)
iii. Add on to at least 2 other lines of therapy (e.g., ERA, PDE-5i, sGCs, PCY)

4.0 Coding:

COVERED CODES – MEDICAL BENEFIT				
HCPCS Code	**Brand Name**	**Generic Name**	**Billing Units (1 unit)**	**Prior Approval**
J1325	Flolan/Veletri	epoprostenol	0.5mg	Y
J3285	Remodulin	treprostinil	1mg	Y
J3490	Uptravi	Selexipag	225mcg	Y
J3490	Winrevair	Sotatercept		Y

EXCLUDED CODES AND PRODUCTS			
HCPCS Code	**Brand Name**	**Generic Name**	**Benefit Plan Reference/Reason**
J7686	Tyvaso	treprostinil	Covered on the pharmacy benefit. with prior approval
Q4074	Ventavis	ilopprost	Covered on the pharmacy benefit. with prior approval

5.0 References, Citations & Resources:

1. ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. American College of Cardiology 2009; 53:573-1619.
2. Charles D. Burger, MD; Srinivas Murali, MD. Advances in Pulmonary Hypertension (2007) 6 (4): 176–179.
3. Chin KM, Gaine SP, Gerges C, et al. Treatment algorithm for pulmonary arterial hypertension. Eur Respir J 20241.
4. Guidelines for the treatment of pulmonary arterial hypertension. Lung 2020, 198:581-596
5. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Letaris, Tracleer, Opsumit, accessed November. 2024.
6. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Adempas, accessed November. 2024.
7. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Revatio, Adcirca accessed November. 2024.
8. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Flolan/Velitri, Ventavis, Remodulin. Tyvaso, Uptravi, Orenitram accessed November. 2024.
9. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Winrevair, accessed November. 2024.
10. Sahay S, Chakinala MM, Kim NH, Preston IR, Thenappan T, Mclaughlin VV. Contemporary Treatment of Pulmonary Arterial Hypertension: A U.S. Perspective. Am J Respir Crit Care Med. 2024 Sep 1;210(5):581-592.
11. Therapy for pulmonary arterial hypertension in adults: update of the CHEST guidelines and expert panel report. CHEST 2019;155(3):565-586.
12. UpToDate: Treatment of Pulmonary arterial hypertension in adults: Pulmonary HTN-specific Therapy Treatment of pulmonary arterial hypertension (group 1) in adults: Pulmonary hypertension-specific therapy - UpToDate accessed November 2024.

6.0 Appendices:

See pages 6-7.

7.0 Revision History:

Original Effective Date: 06/24/2010

Next Review Date: 11/10/2025

Revision Date	Reason for Revision
7/19	Moved to new format; replaced abbreviations and modified code table, complete revision of policy to follow 2019 CHEST guidelines
10/20	Annual review; formatting, replaced abbreviations, removed monitoring parameters for mono therapy, approved by P&T Committee 12/9/20
10/21	Annual review; reformatted, added appendix on treatment of pulm. HTN algorithm
10/22	Annual review, Added reference
9/23	Annual Review, updated coding section, fixed formatting
12/24	Annual review, reformatted, updated guidelines

Appendix I: World Health Organization (WHO) Functional Classifications of Pulmonary Hypertension

Class	Physical Limits	Symptoms (dyspnea, fatigue, chest pain, syncope)
I	No limitation	None upon ordinary physical activity
II	Slight limitation	Symptoms appear upon ordinary physical activity
III	Marked limitation	Symptoms appear upon less than ordinary activity
IV	Inability to carry on any physical activity	Symptoms appear upon any physical activity or may even be present at rest; signs of right heart failure present

Appendix II: Pulmonary Arterial Hypertension Therapeutic Agents

Class	Agent	Route	Dosing	Formulary Status
Endothelin Receptor Antagonists (ERA)	Letairis (ambrisentan)	PO	Initial: 5mg QD Max: 10mg QD	Generic: Preferred Brand: Excluded
	Opsumit (macitentan)	PO	10mg QD	Generic: NA Brand: Non-Preferred
	Tracleer (bosentan)	PO	Initial: 62.5mg BID Maintenance: 125mg BID (if >40kg)	Generic: Preferred Brand: Excluded
	Tracleer - dispersible (bosentan)	PO	Initial: 62.5mg BID Maintenance: 125mg BID (if >40kg)	Generic: NA Brand: Preferred
Phosphodiesterase type 5 Inhibitors (PDE-5i)	Adcirca/Tadliq (tadalafil)	PO	Initial: 20 – 40mg QD Max: 40mg QD	Generic: Preferred Brand: Non-Preferred
	Revatio (sildenafil)	PO/IV	Initial: 20mg TID / 10mg TID Max: 80mg BID / NA	Generic: Preferred Brand: Non-Preferred
Soluble Guanylate Cyclase Stimulants (sGCs)	Adempas (riociguat)	PO	Initial: 0.5-1mg TID Max: 2.5mg TID	Generic: NA Brand: Non-Preferred
Prostacyclin Pathway Agonists (PCY)	Uptravi (selexipag)	PO/IV	Initial: 200mcg BID / 225mcg BID Max: 1600mcg BID / 1800mcg BID	Generic: NA Brand: Non-Preferred
	Orenitram (Treprostinil)	PO	Initial: 0.125mg Q8h or 0.25mg Q12h Max: 8mg TID after 12 months	Generic: NA Brand: Non-Preferred
	Tyvaso (treprostenil)	INH	Initial: 18mcg (3 inhalations) QID Target: 54mcg QID	Generic: NA Brand: Preferred
	Tyvaso – dry powder (treprostenil)	INH	Initial: 16mcg QID Target: 48-64mcg QID	Generic: NA Brand: Preferred
	Remodulin (Treprostinil)	SQ/IV	Initial: 0.625-1.25ng/kg/min (CIV) Target: 40-80ng/kg/min (CIV)	Generic: Non-Preferred Brand: Excluded
	Flolan/Veletri (epoprostenol)	SQ/IV	Initial: 1-2ng/kg/min (CIV) Target: 25-40ng/kg/min (CIV)	Generic: Preferred Brand: Non-Preferred
	Ventavis (iloprost)	INH	Initial: 2.5mcg/dose 6-9 x daily Max: 5mcg/dose 9 x daily	Generic: NA Brand: Preferred
Activin Signaling Inhibitors (ASI)	Winrevair (sotatercept)	SQ	Initial: 0.3mg/kg Q 3 weeks Maintenance: 0.7mg/kg Q 3 weeks	Generic: NA Br`1and: Non-Preferred