VENTURA COUNTY
HEALTH CARE PLAN

# PRIOR AUTHORIZATION POLICY

**POLICY:** Pulmonary Arterial Hypertension – Adempas® (riociguat tablets – Bayer)

**TAC APPROVAL DATE:** 08/22/2018

## OVERVIEW

Adempas, a soluble guanylate cyclase (sGC) stimulator, is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) [World Health Organization {WHO} Group 4] after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.[1] Adempas is also indicated for the treatment of adults with pulmonary arterial hypertension (PAH) [WHO Group 1], to improve exercise capacity, WHO functional class and to delay clinical worsening. Efficacy in WHO Group 1 PAH was established in patients receiving Adempas as monotherapy or in combination with endothelin receptor antagonists (ERAs) or prostanoids. Studies establishing effectiveness included mainly patients with WHO functional class II or III and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (25%). The starting dose of Adempas is 1 mg three times daily (TID) and can be titrated to 2.5 mg TID. Pulmonary hypertension can be classified into five different groups (categories), which are in Table 1.[5]

**Table 1. Updated Classification of Pulmonary Hypertension.[5]**

| |
|---|
| **Group 1: Pulmonary Arterial Hypertension** |
| Idiopathic |
| Heritable |
| BMPR2 |
| ALK-1, ENG, SMAD9, CAV1, KCNK3 |
| Unknown |
| Drug and toxin-induced |
| Associated with |
| Connective tissue disease |
| Human immunodeficiency virus infection |
| Portal hypertension |
| Congenital heart diseases |
| Schistosomiasis |
| Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis |
| Persistent pulmonary hypertension of the newborn |
| **Group 2: Pulmonary Hypertension Due to Left Heart Disease** |
| Left ventricular systolic dysfunction |
| Left ventricular diastolic dysfunction |
| Valvular disease |
| Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies |
| **Group 3: Pulmonary Hypertension Due to Lung Diseases and/or Hypoxia** |
| Chronic obstructive pulmonary disease |
| Interstitial lung disease |
| Other pulmonary diseases with mixed restrictive and obstructive pattern |
| Sleep-disordered breathing |
| Alveolar hypoventilation disorders |
| Chronic exposure to high altitude |
| Developmental lung diseases |
| **Group 4: Chronic Thromboembolic Pulmonary Hypertension** |

**Table 1 (continued). Updated Classification of Pulmonary Hypertension.[5]**

| **Group 5: Pulmonary Hypertension with Unclear Multifactorial Mechanisms** |
|---|
| Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy |
| Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangiomyomatosis |
| Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders |
| Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure, segmental pulmonary hypertension |

BMPR2 – Bone morphogenic protein receptor type 2; ALK-1 – Activin-like receptor kinase-1; ENG – Endoglin; SMAD9 – Mothers against decapentaplegic; CAV1 – Caveolin-1; KCNK3 – Potassium channel super family K member-3.

The WHO classification of functional capacity, which is an adaptation of the New York Heart Association (NYHA) system, is in Table 2.[3] This provides a qualitative assessment of activity tolerance and is useful in monitoring disease progression and response to therapy in PAH.

**Table 2. WHO Classification of Functional Status of Patients with Pulmonary Hypertension.[3]**

| Class | Description |
|---|---|
| I | Patients in whom there is no limitation of usual physical activity. Ordinary physical activity does not cause increased dyspnea, fatigue, chest pain, or presyncope. |
| II | Patients who have mild limitation of physical activity. There is no discomfort at rest, but normal physical activity causes increased dyspnea, fatigue, chest pain, or presyncope. |
| III | Patients who have a marked limitation of physical activity. There is no discomfort at rest, but less than ordinary activity causes increased dyspnea, fatigue, chest pain, or presyncope. |
| IV | Patients who are unable to perform any physical activity at rest and who may have signs of right ventricular failure. Dyspnea and/or fatigue may be present at rest and symptoms are increased by almost any physical activity. |

WHO – World Health Organization.

## Guidelines

In 2004, the American College of Chest Physicians (ACCP) developed evidence-based clinical practice guidelines regarding the screening, early detection, and diagnosis of PAH. In patients with suspected pulmonary hypertension, right heart catheterization is required to confirm the presence of pulmonary hypertension, establish the specific diagnosis, and determine disease severity (grade A recommendation). In patients with suspected pulmonary hypertension, right heart catheterization is required to guide therapy (grade B recommendation).[3] The 2007 ACCP guidelines for medical therapy for PAH also restate these recommendations.[4]

In 2009, the American College of Cardiology Foundation (ACCF) Task Force on Expert Consensus Documents and the American Heart Association (AHA), developed in collaboration with the ACCP, American Thoracic Society (ATS) and the Pulmonary Hypertension Association, published an expert consensus document on pulmonary hypertension.[2] The guidelines state that the diagnosis of PAH requires confirmation with a complete right heart catheterization. The hemodynamic definition of PAH is a mean pulmonary artery pressure (mPAP) greater than 25 mmHg; a pulmonary capillary wedge pressure (PCWP), left atrial pressure (LAP) or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mmHg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units.

## POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Adempas. Because of the specialized skills required for evaluation and diagnosis of patients treated with Adempas as well as the monitoring required for adverse events and long-term efficacy, approval requires these agents to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 3 years in duration unless otherwise noted below.

**Documentation:** In the *Pulmonary Arterial Hypertension – Adempas Prior Authorization Policy*, documentation is required for initiation of therapy where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes and catheterization laboratory reports. For a patient case in which the documentation requirement of the right heart catheterization upon prior authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement in this *Pulmonary Arterial Hypertension – Adempas Prior Authorization Policy* is considered to be met.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Adempas is recommended in those who meet the following criteria:

### FDA-Approved Indications

1. **Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1].** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 years if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** The patient has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
     - **ii.** The agent is prescribed by, or in consultation with, a cardiologist or a pulmonologist; AND
     - **iii.** The patient meets the following criteria (a and b):
       - **a)** The patient has had a right heart catheterization **[documentation required]** (see documentation section above); AND
       - **b)** The results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; OR
   - **B)** Patients Currently Receiving Adempas. Approve for 3 years if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** The patient has a diagnosis of WHO Group 1 PAH; AND
     - **ii.** The agent is prescribed by, or in consultation with, a cardiologist or a pulmonologist; AND
     - **iii.** The patient meets the following criteria (a and b):
       - **a)** The patient has had a right heart catheterization; AND
       - **b)** The results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH.

   Adempas is indicated for the treatment of adults with PAH (WHO Group I) to improve exercise ability, WHO functional class, and to delay clinical worsening.[1] ACCP guidelines for the screening, early detection, and diagnosis of PAH, established in 2004, recommend to perform a right heart catheterization in patients with suspected pulmonary hypertension to confirm the presence of pulmonary hypertension, establish the diagnosis, and to determine disease severity.[3] An ACCF/AHA 2009 consensus document on pulmonary hypertension, developed in collaboration with the ACCP.

2. **Chronic Thromboembolic Pulmonary Hypertension (CTEPH).** Approve for 3 years if prescribed by, or in consultation with, a pulmonologist or a cardiologist.

   Adempas is indicated for the treatment of adults with persistent/recurrent CTEPH (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class. Adempas is the only medication specifically indicated for patients with CTEPH.[1] Reviews

note that Adempas is the first medication to demonstrate positive primary endpoints in a randomized controlled trial for this patient population.[6-7] However, patients with this diagnosis should be assessed if they could undergo pulmonary endarterectomy as this is the preferred treatment for CTEPH and it is curative for many patients.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Adempas has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

**1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Adempas® tablets [prescribing information]. Whippany, NJ: Bayer; January 2018.
2. McLaughlin VV, Archer SL, Badesch DB, et all; Writing committee members. ACCF/AHA 2009 Expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association: Developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *Circulation*. 2009;119:2250-2294.
3. McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *CHEST*. 2004;126:14-34.
4. Badesch, Abman SH, Simonneau G, et al. Medical therapy for pulmonary arterial hypertension. Updated ACCP Evidence-based clinical practice guidelines. *CHEST*. 2007;131:1917-1928.
5. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62(25 Suppl):D34-D41.
6. Hoeper MM, Madani MM, Nakanishi N, et al. Chronic thromboembolic pulmonary hypertension. *Lancet Respir Med*. 2014;2(7):573-582.
7. Kim NH. Group 4 pulmonary hypertension. Chronic thromboembolic pulmonary hypertension: epidemiology, pathophysiology and treatment. *Cardiol Clin*. 2016;34:435-441.

## HISTORY

| Type of Revision | Summary of Changes* | TAC Approval Date |
|---|---|---|
| Annual revision | For patients with PAH (WHO Group 1) who are currently receiving therapy, Uptravi was added to the list of other PAH medications. | 08/10/2016 |
| Annual revision | No criteria changes. | 08/30/2017 |
| Annual revision | For initial review, documentation is required for the right heart catheterization. For patients who are currently receiving Adempas, the wording "or who are receiving another medication for WHO Group 1 PAH" was removed, along with the cited alternatives. Also, the requirement was added that the patient has had a right heart catheterization and that the results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH. A note was added in the documentation section that for a patient case in which the documentation requirement of the right heart catheterization upon prior authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement is considered to be met. | 08/22/2018 |

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; PAH – Pulmonary arterial hypertension; WHO – World Health Organization.