RXADVANCE
2 Park Central Drive
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Clinical Policy Title:	tadalafil
Policy Number:	RxA.332
Drug(s) Applied:	Adcirca®, Alyq™
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Tadalafil (Adcirca®, Alyq™) is a phosphodiesterase-5 inhibitor.

Adcirca and Alyq are indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability.

Studies establishing effectiveness included predominately patients with New York Heart Association (NYHA) Functional Class II-III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Tadalafil (Adcirca, Alyq)	PAH	40 mg PO once daily	40 mg/day

Dosage Forms

- Tablets: 20 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. **Initial Approval Criteria**
   A. Pulmonary Arterial Hypertension (must meet all):
      1. Diagnosis of PAH;
      2. Prescribed by or in consultation with a cardiologist or pulmonologist;
      3. Failure of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (a or b):
         a. Inadequate response or contraindication to acute vasodilator testing;
         b. Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;

4. Dose does not exceed 40 mg (2 tablets) per day.

Approval duration
Commercial: 12 months
Medicaid: 6 months
HIM: 6 months

II. **Continued Therapy Approval**

A. Pulmonary Arterial Hypertension (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 40 mg (2 tablets) per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months
HIM: 12 months

I. Appendices

APPENDIX A: Abbreviation/Acronym Key
FC: functional class
FDA: Food and Drug Administration
NYHA: New York Heart Association
PAH: pulmonary arterial hypertension
PH: pulmonary hypertension
WHO: World Health Organization

APPENDIX B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
nifedipine (Adalat® CC, Afeditab® CR, Procardia®, Procardia XL®)	60 mg PO once daily; may increase to 120 to 240 mg/day	240 mg/day
diltiazem (Dilacor XR®, Dilt-XR®, Cardizem® CD, Cartia XT®, Tiazac®, Taztia XT®, Cardizem® LA, Matzim® LA)	720 to 960 mg PO once daily	960 mg/day
amlodipine (Norvasc®)	20 to 30 mg PO once daily	30 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant organic nitrates
  - Concomitant guanylat ecyclase stimulators
  - Hypersensitivity reactions

- Boxed Warning(s):
  - None Reported

APPENDIX D: General Information

Pulmonary Hypertension: WHO Classification

- Group 1: PAH (pulmonary arterial hypertension)
- Group 2: PH due to left heart disease
- Group 3: PH due to lung disease and/or hypoxemia
- Group 4: CTEPH (chronic thromboembolic pulmonary hypertension)
- Group 5: PH due to unclear multifactorial mechanisms

Appendix E: Pulmonary Hypertension: WHO/NYHA Functional Classes (FC)

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
Monitoring for progression of PH and treatment of co-existing conditions	I	Comfortable at rest	No limitation	Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope.	
Advanced treatment of PH with PH-targeted therapy - *see Appendix*	II	Comfortable at rest	Slight limitation	Ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	III	Comfortable at rest	Marked limitation	Less than ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	

*F***	IV	Dyspnea or	Inability to	Discomfort is	Signs
		fatigue may	carry out any	increased by any PA.	of right
		be present at	PA without		heart
		rest	symptoms		failure

*PH supportive measures may include diuretics, oxygen therapy, anticoagulation, digoxin, exercise, pneumococcal vaccination. **Advanced treatment options also include calcium channel blockers.

Appendix F: Pulmonary Hypertension: Targeted Therapies

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
Reduction of pulmonary arterial pressure through vasodilation	Prostacyclin* pathway agonist *Member of the prostanoid class of fatty acid derivatives.*	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) Remodulin (IV) Tyvaso (inhalation)
			Iloprost	Ventavis (inhalation)
		Non-prostanoid prostacyclin receptor (IP receptor) agonist	Selexipag	Uptravi (oral tablet)
	Endothelin receptor antagonist (ETRA)	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)
		Nonselective dual action receptor antagonist	Bosentan	Tracleer (oral tablet)
			Macitentan	Opsumit (oral tablet)
	Nitric oxide-cyclic guanosine monophosphate enhancer	Phosphodiesterase type 5 (PDE5) inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)
			Tadalafil	Adcirca (oral tablet)

		Guanylate cyclase stimulant (sGC)	Riociguat	Adempas (oral tablet)

References

1. Adcirca Prescribing Information. Indianapolis, IN: Eli Lilly and Company; August 2017. Available at: http://pi.lilly.com/us/adcirca-pi.pdf. Accessed July 09, 2020.
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3. McLaughlin VV, Archer SL, Badesch DB, et al. 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. J Am Coll Cardiol. 2009; 53(17): 1573-1619.
4. Taichman D, Ornelas J, Chung L, et. al. CHEST guideline and expert panel report: Pharmacologic therapy for pulmonary arterial hypertension in adults. Chest. 2014; 146 (2): 449-475.
5. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. Circulation. 2015 Nov 24; 132(21): 2037-99.
6. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. J Am Coll Cardiol 2013; 62(25): Suppl D92-99.
7. Galiè N, Humbert M, Vachiary JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension. European Heart Journal. Doi:10.1093/eurheartj/ehv317.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	03/06/2020
Policy was reviewed: **1.** Added alternative Authorized Generic (Alyq™) to the policy **2.** Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." **3.** Approval Duration for commercial updated to 12 months **4.** Added maximum quantity per day **5.** Reference reviewed and updated	07/09/2020	09/14/2020