Clinical Policy Title:	tadalafil
Policy Number:	RxA.332
Drug(s) Applied:	Adcirca®, Alyq™
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
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 orally 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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria;
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

III. APPENDICES

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

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
nifedipine (Adalat®CC, Procardia®, Procardia XL®)	60 mg PO once daily; may increase to 120 to 240mg/day	240 mg/day
diltiazem (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 generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Concomitant organic nitrates;
  - Concomitant guanylate cyclase 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
- Dividing the 40mg dose over the course of the day is not recommended.

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

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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. Accessed May 28, 2021.
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. Accessed May 28, 2021.
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. Accessed May 28, 2021.
6. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. J Am Coll Cardiol 2013; 62(25): Suppl D92-99. Accessed May 28, 2021.
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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 daily dosing. 5. References reviewed and updated.	07/09/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration. 3. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 5. Appendix B: Therapeutic Alternatives was updated to remove inactive/unavailable drugs Afeditab® CR and Dilacor XR®. 6. Statement about drug listing format in Appendix B is rephrased to "Therapeutic	05/28/2021	09/14/2021

alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 7. Appendix D was updated to include “Dividing the 40mg dose over the course of the day is not recommended”. 8. References were reviewed and updated.		