Clinical Policy: Epoprostenol (Flolan, Veletri)

Reference Number: LA.PHAR.192
Effective Date: 09.08.21
Last Review Date: 03.06.25~~04.29.24~~ Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description
Epoprostenol (Flolan®, Veletri®) is a prostacyclin.

FDA Approved Indication(s)
Flolan and Veletri are indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise capacity.

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

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

It is the policy of Louisiana Healthcare Connections that epoprostenol ~~is~~ , Flolan, and Veletri are **necessary** when the following criteria are met:

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. If request is for brand Flolan or brand Veletri, member must use generic epoprostenol sodium, unless contraindicated or clinically significant adverse effects are experienced;
5. Provider must submit treatment plan detailing pump rate, dose, and quantity (in mL).

Approval duration: 6 months

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B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

II. Continued Therapy

A. Pulmonary Arterial Hypertension (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for brand Flolan or brand Veletri, member must use generic epoprostenol sodium, unless contraindicated or clinically significant adverse effects are experienced;
4. Provider must submit treatment plan detailing pump rate, dose, and quantity (in mL).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CTEPH: chronic thromboembolic pulmonary hypertension
FC: functional class
FDA: Food and Drug Administration
NYHA: New York Heart Association
PA: physical activity
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.

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
nifedipine (Adalat® CC, Procardia XL~~®~~)~~®~~)†	~~60~~30 mg PO QD; may increase to 60 to 120 ~~to 240~~ mg~~/day~~ BID	240 mg/day
diltiazem (~~Dilacor XR®,~~ Dilt-XR®, Cardizem® CD, Cartia XT®, Tiazac®, ~~Taztia XT®,~~ Cardizem® LA, Matzim® LA~~)~~)†	~~720 to 960~~60 mg PO QD; may increase to 120 to 360 mg BID	~~960~~720 mg/day
amlodipine (Norvasc~~®~~)~~®~~)†	~~20~~5 mg PO QD; may increase to 15 to 30 mg ~~PO QD~~/day	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.
†Off-label

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Congestive heart failure due to severe left ventricular systolic dysfunction
  - Pulmonary edema (Veletri only)
  - Hypersensitivity to the drug or to structurally related compounds
- Boxed warning(s): none reported

Appendix D: Pulmonary Hypertension: WHO Classification
- Group 1: PAH
- Group 2: PH due to left heart disease
- Group 3: PH due to lung disease and/or hypoxemia
- Group 4: CTEPH
- 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 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	

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
				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)

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V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Epoprostenol (Flolan)	2 ng/kg/min IV, increased by 1-2 ng/kg/min at intervals of at least 15 minutes	Based on clinical response
Epoprostenol (Veletri)	2 ng/kg/min IV, increased by 2 ng/kg/min every 15 minutes or longer	Based on clinical response

VI. Product Availability

Drug Name	Availability
Epoprostenol (Flolan)	Vial with powder for reconstitution: 0.5 mg, 1.5 mg
Epoprostenol (Veletri)	Vial with powder for reconstitution: 0.5 mg, 1.5 mg

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VII. References

1. Epoprostenol Sodium Prescribing Information. Billerica, MA: Sun Pharmaceuticals Industries, Inc; ~~January 2021.~~October 2024. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=db57e498-db20-45e8-8298-b0cf0811d270. Accessed ~~October 3, 2023~~November 7, 2024.
2. Flolan Prescribing Information. ~~Research Triangle Park~~Durham, NC: GlaxoSmithKline; ~~August 2021~~October 2023. Available at: https://~~www.accessdata.fda.gov/drugsatfda_docs/label/2021/020444s025lbl.~~gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Flolan/pdf~~/~~/FLOLAN-PI-PIL.PDF Accessed ~~October 3, 2023~~November 7, 2024.
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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1325	Injection, epoprostenol, 0.5 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy.	03.21	09.08.21
Revised medical justification language to "must use" language for generic redirection; added generic redirection to continued therapy; references reviewed and updated.	09.22	09.15.22
Template changes applied to other diagnoses/indications and continued therapy section. References reviewed and updated. Added verbiage this policy is only for medical benefit.	06.02.23	10.24.23
Annual review; removed commercially unavailable branded products from Appendix B; clarified Veletri product availability description to describe a "powder for reconstitution" per PI; references reviewed and updated.	04.29.24	07.29.24
Annual review: in Policy/Criteria, clarified criteria also applies to brand Flolan and Veletri; in Appendix B per Clinical Pharmacology, removed commercially unavailable branded products, updated dosing regimens; clarified drugs used for off-label indications; references reviewed and updated.	03.06.25	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing

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The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

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This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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