Clinical Policy: Budesonide/Glycopyrrolate/Formoterol Fumarate (Breztri Aerosphere) and Fluticasone/Umeclidinium/Vilanterol (Trelegy Ellipta)

Reference Number: AZ.CP.PMN.1005
Effective Date: 11.08.19
Last Review Date: 10.20
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st) Revision Log

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

Description
Budesonide/glycopyrrolate/formoterol fumarate (Breztri Aerosphere™) is a combination of an inhaled corticosteroid (ICS), long-acting muscarinic antagonist (LAMA), and long-acting beta$_2$-adrenergic agonist (LABA).

Fluticasone/umeclidinium/vilanterol (Trelegy™ Ellipta®) is combination of an inhaled corticosteroid (ICS), long-acting anticholinergic (LAMA), and long-acting beta$_2$-adrenergic agonist (LABA).

FDA Approved Indication(s)
Breztri Aerosphere is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Trelegy Ellipta is indicated for the maintenance treatment of asthma in patients aged 18 years and older.

Limitation(s) of use: Not indicated for relief of acute bronchospasm.

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 Arizona Complete Health-Complete Care Plan and Care1st that Breztri Aerosphere and Trelegy Ellipta are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
A. Chronic Obstructive Pulmonary Disease (must meet all)**:**
1. Diagnosis of COPD;
2. Age ≥ 18 years;
3. Failure of one of the following (a or b) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
   a. One Preferred LABA (e.g., Serevent®) in combination with one Preferred LAMA (e.g., Tudorza® Pressair®, Spiriva Handihaler®) OR one Preferred LAMA/LABA combination* (Bevespi Aerosphere® and Stiolto Respimat®);
   **Prior Authorization required*

b. One Preferred inhaled corticosteroid (ICS) in combination with LABA* (e.g., Symbicort®, Advair Diskus®);
**Step therapy is required: member must have tried one steroid inhaler*

4. Dose does not exceed the following:
   a. Breztri Aerosphere: 4 inhalations per day (one canister per 30 days);
   b. Trelegy Ellipta: 1 inhalation per day (60 blisters per 30 days).

Approval duration: 12 months

B. Asthma (must meet all):
1. Diagnosis of asthma;
2. Age ≥ 18 years;
3. Request is for Trelegy Ellipta;
4. Failure of a formulary inhaled corticosteroid (ICS) in combination with LABA (e.g., Symbicort®, Dulera®, Advair® HFA/Diskus®);
5. Dose does not exceed 1 inhalation per day (60 blisters per 30 days).

Approval duration: 12 months

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid.

II. Continued Therapy

A. Asthma and Chronic Obstructive Pulmonary Disease (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the following:
   a. Breztri Aerosphere: 4 inhalations per day (one canister per 30 days);
   b. Trelegy Ellipta: 1 inhalation per day (60 blisters per 30 days).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid.

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 policies – AZ.CP.PMN.53 for Arizona Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COPD: chronic obstructive pulmonary disease
FDA: Food and Drug Administration
GOLD: Global Initiative for Chronic Obstructive Lung Disease
ICS: inhaled corticosteroid
LABA: long-acting beta$_2$ adrenergic agonist
LAMA: long-acting anticholinergic

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Dulera (mometasone furoate/formoterol)	2 inhalations (100/5 mcg or 200/5 mcg per inhalation) BID	800/20 mcg/day
fluticasone/salmeterol (Advair® Diskus®)	Asthma: 1 inhalation (100/50, 250/50, or 500/50 mcg) BID COPD: 1 inhalation (250/50 mcg) BID	Asthma: 1000/100 mcg/day COPD: 500/100 mcg/day
fluticasone/salmeterol (Advair® HFA)	Asthma: 2 inhalations (45/21, 115/21, or 230/21 mcg) BID	920/84 mcg/day
Incruse Ellipta (umeclidinium)	1 inhalation (62.5 mcg) QD	62.5 mcg/day
Symbicort (budesonide/ formoterol)	2 inhalations of 80/4.5 mcg BID	2 inhalations of 80/4.5 mcg BID
Serevent (salmeterol)	1 inhalation (50 mcg) BID	100 mcg/day
Spiriva Handihaler (tiotropium bromide)	2 inhalations (2.5 mcg) QD	2.5 mcg/day
Tudorza Pressair (aclidinium)	1 inhalation (400 mcg) BID	800 mcg/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):
  - Trelegy Ellipta: hypersensitivity to fluticasone furoate, umeclidinium, vilanterol, or any excipients of the products, severe hypersensitivity to milk proteins
  - Breztri Aerosphere: hypersensitivity to budesonide, glycopyrrolate, formoterol fumarate, or to any of the excipients

- Boxed warning(s): none reported

Appendix D: General Information

- Per the 2020 GOLD COPD guidelines, combination therapy (LAMA + LABA, ICS + LABA, or ICS + LAMA + LABA) is recommended for Group D patients (i.e., those who are very symptomatic and are at high risk of exacerbation). Selection of which combination to use depends on the individual patient:
  - For those with more severe symptoms, LAMA + LABA may be used.
  - For those with a history of asthma or blood eosinophil counts at least 300 cells/uL, LABA + ICS may be used.
  - For those who are inadequately controlled by dual therapy, triple therapy with ICS + LAMA + LABA may be used.

V. Dosage and Administration

Drug	Indication	Dosing Regimen	Maximum Dose
Breztri Aerosphere (budesonide/glycopyrrolate/formoterol fumarate)	COPD	2 inhalations by mouth BID	4 inhalations/day
Trelegy Ellipta (fluticasone/umeclidinium/vilanterol)	Asthma/COPD	1 inhalation by mouth QD	1 inhalation/day

VI. Product Availability

- Breztri Aerosphere
  - Inhalation aerosol: Pressurized metered dose inhaler containing a combination of budesonide (160 mcg), glycopyrrolate (9 mcg), and formoterol fumarate (4.8 mcg) per inhalation
- Trelegy Ellipta
  - Inhalation powder: disposable inhaler containing 2 foil strips of 30 blisters each: one strip with fluticasone furoate (100 or 200 mcg per blister), and the other strip with a blend of umeclidinium and vilanterol (62.5 mcg and 25 mcg per blister, respectively)

VII. References

1. Breztri Aerosphere Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; July 2020. Available at: www.breztri.com. Accessed August 14, 2020.
2. Trelegy Ellipta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; Sept 2020. Available at: www.trelegyellipta.com. Accessed October 19, 2020.
3. National Heart, Lung, and Blood Institute. Expert panel report 3: guidelines for the diagnosis and management of asthma. National Asthma Education and Prevention Program. Published August 28, 2007. Available from: http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report/. Accessed October 19, 2020.
4. Global Initiative for Asthma (GINA): Global strategy for asthma management and prevention (2020 report). Available from: www.ginasthma.org. Accessed October 19, 2020.

5. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2020 report). Published January 2020. Available at: http://www.goldcopd.org/. Accessed April 6, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created from Corporate CP.PMN.146. New name AZ.CP.PMN.146. Updated document with AHCCCS preferred products. No clinical changes made. Per AZCH P&T, non-clinical policy changes may be posted immediately and reviewed at the next P&T.	11.08.19	10.19
3Q 2020 annual review: no significant changes; updated FDA approved indication language to reflect most recent labeling; references reviewed and updated.	07.10.20	07.20
Combined Breztri Aerosphere and Trelegy Ellipta criteria; Added asthma indication for Trelegy Ellipta; Combined criteria I.A.3 and I.A.4 so that either one Preferred LABA (e.g., Serevent®) in combination with one Preferred LAMA (e.g., Tudorza® Pressair®, Spiriva Handihaler®) or one Preferred LAMA/LABA combination inhaler is required; Added language that Prior authorization is required for the preferred LAMA/LABA combination inhaler; Corrected off-label use policy from CP.PMN.53 to AZ.CP.PMN.53 which is specific to the Arizona Medicaid line of business; Removed examples of preferred ICS/LABA inhalers, Dulera and Advair HFA from COPD indication criteria due to lack of FDA-approved indications for COPD; Added Dulera, Advair HFA/Diskus, and Spiriva Handihaler for Appendix B: Therapeutic Alternatives; Updated Appendix C: Contraindications/Boxed Warnings and Appendix D: General Information; Added Breztri Aerosphere to Section V. Dosage and Administration and Section VI. Product Availability; Updated references; Updated criteria number from AZ.CP.PMN.146 to AZ.CP.PMN.1005	10.21.20	10.20
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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