09-J4000-14

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Reviewed: 01/10/24

Revised: 12/15/24

Subject: Budesonide (Tarpeyo)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Primary IgA nephropathy (IgAN) is due to the deposition of IgA immune complexes in the mesangial cells of the glomeruli, causing mesangial proliferation. It most commonly affects young adults and is more common in East or Pacific Asia. Patients may be asymptomatic, with microscopic hematuria and minimal proteinuria at first, but potential symptoms can include gross hematuria – hypertension, significant proteinuria, and decline in renal function may occur as the disease progresses. Definitive diagnosis requires a kidney biopsy showing IgA deposition in the mesangium confirmed by immunohistology.

In patients with normal blood pressure, normal estimated GFR, and consistent urinary protein-to-creatinine ratio of < 0.2, treatment may not be necessary. However, once proteinuria exceeds 1 g/day, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are recommended. In those with an inadequate response or rapidly progressive crescentic IgAN, a six-month course of corticosteroids, combination cyclophosphamide with corticosteroids, or single agent cyclophosphamide, azathioprine, or cyclosporine are recommended depending on severity of disease and GFR. Transplant is the treatment of choice for those with progressive kidney failure due to IgAN. Recurrence of IgAN after transplant appears to be time-dependent, with rates of recurrence increasing as time from transplant lengthens. A retrospective study from the ANZDATA registry showed that among a cohort of 2501 kidney transplant patients with biopsy-proven IgAN as the primary disease, 5% 10%, and 15% of recipients experienced disease recurrence at 5, 10 and 15 years after transplant, respectively. However, this may be underreported, and recurrence may be as high as 25% at 5 years and 50% at years.

Budesonide (Tarpeyo) delayed release capsules was approved by the U.S. Food and Drug Administration (FDA) in December 2021 to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g. This indication was approved under accelerated approval based on a reduction in proteinuria. It has not been established whether budesonide slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial. Tarpeyo's formulation allows budesonide to be released in a 'pulse-like' fashion only once it reaches the small intestine. This allows the drug to be delivered to the Peyer's patches in the ileum. Peyer's patches have been theorized to be the source of IgA production.

The safety and efficacy of budesonide were evaluated in patients with biopsy-proven primary immunoglobulin A nephropathy and proteinuria at risk of rapid disease progression (N=199, NCT: 03643965). Proteinuria was defined as either 1 g/day or greater or UPCR of 0.8 g/g or greater. Patients were randomized to receive budesonide 16 mg orally once daily or placebo for 9 months followed by a 2-week taper of either 8 mg once daily or placebo.

At baseline, the mean eGFR was approximately 58 mL/min/1.73 m2, with 62% of patients having an eGFR <60 mL/min/1.73 m2. The mean baseline UPCR was 1.6 g/g and 25% of patients had proteinuria >3.5 g/24 hours. The primary endpoint was the percentage reduction in UPCR at 9 months compared to baseline. Patients in the budesonide group had a 34% reduction in UPCR from baseline vs a 5% reduction observed in the placebo group (difference, 31%; 95% CI, 16% to 42%).

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, or emergency facility is not considered medically necessary.

Initiation of budesonide (Tarpeyo) **meets the definition of medical necessity** for members meeting the following criteria:

1. Member is diagnosed with IgA nephropathy – documentation from the medical record must be provided
2. Member's diagnosis is confirmed with kidney biopsy – biopsy report must be provided
3. **ONE** of the following:
    a. Member is on maximally tolerated dose of angiotensin-converting enzyme (ACE) inhibitors
    b. Member is on maximally tolerated dose of angiotensin receptor blockers (ARBs)
    c. Member has an intolerance, hypersensitivity, or FDA labeled contraindication to BOTH ACE inhibitors and ARBs - the specific intolerance, hypersensitivity, or FDA labeled contraindication must be provided
4. Member's current (within 90 days) urine protein-to-creatinine ratio (UPCR) is greater than or equal to 1.5 g/g – laboratory documentation must be provided
5. Member's eGFR must be equal to or greater than 35 mL/min per 1.73 m^2 AND equal to or less than 90 mL/min per 1.73 m^2 using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula

    CKD-EPI calculator is available here: https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/kidney-disease/laboratory-evaluation/glomerular-filtration-rate-calculators/ckd-epi-adults-conventional-units
6. Budesonide (Tarpeyo) is not used concomitantly with sparsentan (Filspari) or iptacopan (Fabhalta)

7. Budesonide (Tarpeyo) is prescribed by a nephrologist
8. Dose does not exceed 16 mg daily for 9 months

Approval duration: 9 months

Continuation of budesonide (Tarpeyo) **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years for IgA nephropathy OR the member has previously met all indication-specific initiation criteria
2. Member has (or maintains) a beneficial response to treatment with budesonide (Tarpeyo) as evidenced by a 20% or greater reduction in UPCR from baseline (i.e., prior to treatment with budesonide) – laboratory documentation must be provided
3. Budesonide (Tarpeyo) is not used concomitantly with sparsentan (Filspari) or iptacopan (Fabhalta)
4. Budesonide (Tarpeyo) is prescribed by a nephrologist
5. Dose does not exceed 16 mg daily

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 16 mg administered orally once daily, in the morning at least 1 hour before a meal.
- Swallow whole. Do not open, crush or chew
- When discontinuing, reduce dosage to 8 mg once daily for the last two week

Dose Adjustments

- None

Drug Availability

- Delayed release capsules: 4 mg.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Known hypersensitivity budesonide

Precautions/Warnings

- Hypercorticism and adrenal axis suppression
- Risk of immunosuppression
- Other corticosteroid effects

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

N02.B1	Recurrent and persistent immunoglobulin A nephropathy with glomerular lesion
N02.B2	Recurrent and persistent immunoglobulin A nephropathy with focal and segmental glomerular lesion
N02.B3	Recurrent and persistent immunoglobulin A nephropathy with diffuse membranoproliferative glomerulonephritis
N02.B4	Recurrent and persistent immunoglobulin A nephropathy with diffuse membranous glomerulonephritis
N02.B5	Recurrent and persistent immunoglobulin A nephropathy with diffuse mesangial proliferative glomerulonephritis
N02.B6	Recurrent and persistent immunoglobulin A nephropathy with diffuse mesangiocapillary glomerulonephritis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Calliditas Therapeutics AB. Tarpeyo (budesonide) capsule, delayed release. 2022 [cited 2/2/22]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=938cada4-d6bf-4252-836f-dd40f9eadb4d/.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 1/1/24]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 1/1/24]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 1/1/24]. Available online.
5. Fellström BC, Barratt J, Cook H, et al. Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial. Lancet. 2017;389(10084):2117-2127.
6. Infante B, Rossini M, et al. Recurrence of immunoglobulin A nephropathy after kidney transplantation: a narrative review of the incidence, risk factors, pathophysiology and management of immunosuppressive therapy. Clin Kidney J. 2020;13(5):758-767.
7. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 1/1/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/24.

GUIDELINE UPDATE INFORMATION:

04/01/22	New Medical Coverage Guideline.
10/01/23	Revised guideline; updated ICD10
02/15/24	Review and revision to guideline; updated references.
12/15/24	Revision to guideline; updated position statement