PRIOR AUTHORIZATION POLICY

POLICY: Nephrology – Tarpeyo Prior Authorization Policy
- Tarpeyo™ (budesonide delayed-release capsules – Calliditas)

REVIEW DATE: 01/31/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Tarpeyo, a corticosteroid, is indicated to reduce the loss of kidney function in adults with **primary immunoglobulin A nephropathy (IgAN)** at risk of rapid disease progression.[1]

The recommended dose is 16 mg orally once daily (QD) at least 1 hour before a meal for 9 months.[1] When discontinuing therapy, the dose is reduced to 8 mg QD for the last 2 weeks of therapy. Safety and efficacy of treatment with subsequent courses of Tarpeyo have not been established.

Clinical Efficacy

The efficacy of Tarpeyo was evaluated in one pivotal, 9-month trial (with 15 month observational follow-up [see below]) in patients ≥ 18 years of age with IgAN.[1,2,4] Eligible patients had biopsy-proven IgAN, proteinuria (defined as either ≥ 1 g/day) or a urinary protein-to-creatinine ratio (UPCR) ≥ 0.8 g/g despite optimized supportive care, and estimated glomerular filtration rate (eGFR) ≥ 35 mL/min/1.73 m^2 and ≤ 90 mL/min/1.73 m^2.[2,4] Optimized supportive care required that patients receive the maximum tolerated or maximum allowed dose of an angiotensin-converting enzyme inhibitor and/or angiotensin II type I receptor blocker for ≥ 3 months prior to randomization and continue the agent throughout the trial. Tarpeyo resulted in

statistically greater reduction in UPCR and less eGFR decline relative to placebo after 9 months of treatment.[2]

Following the 9-month randomized, treatment period, patients were followed for 15 months during an observational period in which no study medication was administered.[4] During the observational study period, all patients remained on optimized supportive care. At Year 2, the time-weighted average of eGFR (primary endpoint) showed a statistically significant treatment benefit in patients who received Tarpeyo vs. placebo (-2.47 mL/min/1.73 m^2 vs. -7.52 mL/min/1.73 m^2, respectively; $P < 0.0001$ for the difference). At the end of the original study period (Month 9), the mean change in eGFR in the Tarpeyo and placebo groups was +0.66 mL/min/1.73 m^2 and -4.56 mL/min/1.73 m^2, respectively; the eGFR benefit was maintained during the 15 month observational period. At Year 2, the change in eGFR from baseline was -6.11 mL/min/1.73 m^2 in the Tarpeyo group vs. -12.00 mL/min/1.73 m^2 in the placebo group corresponding to a difference in the 2-year total eGFR slope (supportive endpoint) of 2.95 mL/min/1.73 m^2/year ($P < 0.0001$). This represented approximately 50% less deterioration of kidney function in patients receiving Tarpeyo vs. placebo over the 2 year period. The 2-year eGFR treatment effect was consistent across subgroups including the baseline proteinuria and UPCR subgroups (< 1.5 g/g or ≥ 1.5 g/g). Time from randomization to confirmed 30% reduction eGFR or kidney failure (secondary endpoint) was significantly delayed with Tarpeyo vs. placebo (12% of patients vs. 21% of patients, respectively; hazard ratio [HR] 0.45; 95% confidence interval [CI]: 0.26, 0.75). In a *post-hoc* analysis, the benefit for this secondary endpoint was observed for patients with baseline UPCR < 1.5 g/g or ≥ 1.5 g/g, although the magnitude of effect was larger in patients with UPCR ≥ 1.5 g/g (18% vs. 36 for Tarpeyo vs. placebo, respectively; HR 0.51; 95% CI: 0.21, 1.12) vs. UPCR < 1.5 g/g (8% vs. 14% for Tarpeyo vs. placebo, respectively; HR 0.42; 95% CI: 0.21, 0.83). There was a durable reduction in proteinuria with Tarpeyo, the maximal effect of Tarpeyo vs. placebo was observed at 1 year (reduction in UPCR of approximately 50% with Tarpeyo); at Year 2, from baseline, UPCR reduction was similar to that observed at Month 9 (~ 30%).

Guidelines

Tarpeyo is recognized as new therapy "in development" for high-risk IgAN patients by the Kidney Diseases Improving Global Outcomes (KDIGO) guidelines for the management of glomerular diseases (2021).[3] According to the guidelines, a number of new therapies for high-risk IgAN patients are being evaluated that may augment the supportive care approach or more specific approaches (e.g., Tarpeyo, various complement inhibitors, and therapies targeting B-cell development).

Following biopsy-confirmed diagnosis of IgAN, the guidelines recommend assessment of disease progression.[3] The primary focus of IgAN treatment should include multiple modalities such as renin angiotensin system blockage (maximum dose or maximum tolerated dose), blood pressure control, cardiovascular risk minimization, and adherence to lifestyle advice (i.e., dietary counseling, smoking cessation, weight control, and exercise as appropriate). When proteinuria remains > 0.75 to 1.0 g/day despite ≥ 90 days of optimized supportive care, the patient has a high risk of progressive loss of kidney function and may be considered for a 6-month course of

steroid therapy (recently cited trials include prednisone or methylprednisolone), or preferably the opportunity to take part in a clinical trial.[4] Guidelines point out that the clinical benefit of steroids in IgAN is not established, and should be used with extreme caution or avoided in patients with eGFR < 30 mL/min/1.73 m^2, diabetes, obesity (body mass index > 30 kg/m^2), latent infections (e.g., tuberculosis, viral hepatitis), secondary disease (e.g., cirrhosis), active peptic ulceration, uncontrolled psychiatric illness, and severe osteoporosis. There are no data to support the efficacy or reduced toxicity of alternate day steroid regimens or dose-reduced protocols.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Tarpeyo. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Tarpeyo as well as the monitoring required for adverse events and long-term efficacy, approval requires Tarpeyo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Tarpeyo™ (budesonide delayed-release capsules (Calliditas)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Primary Immunoglobulin A Nephropathy.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 10 months if the patient meets the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The diagnosis has been confirmed by biopsy; AND
     - **iii.** Patient is at high risk of disease progression, defined by meeting the following (a and b):
       - **a)** Patient meets ONE of the following [(1) or (2)]:
         - **(1)** Proteinuria > 0.75 g/day; OR
         - **(2)** Urine protein-to-creatinine ratio ≥ 0.8 g/g; AND
       - **b)** Patient has been receiving the maximum or maximally tolerated dose of ONE of the following for ≥ 90 days [(1) or (2)]:
         - **(1)** Angiotensin converting enzyme inhibitor; OR
         - **(2)** Angiotensin receptor blocker; AND
     - **iv.** According to the prescriber, the patient has received ≥ 90 days of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification; AND
     - **v.** Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2; AND
     - **vi.** Patient has not previously been treated with Tarpeyo; AND

Note: For a patient currently receiving Tarpeyo, review using Criterion 1B.

vii. The medication is prescribed by or on consultation with a nephrologist.

B) Patient is Currently Receiving Tarpeyo. Approve for up to 10 months (total) if the patient meets the following (i, ii, iii, iv, v, and vi):

Note: Approval is not to exceed 10 consecutive months; for example if a patient has received 3 consecutive months approve 7 months to complete 10 consecutive months of therapy.

i. Patient is ≥ 18 years of age; AND

ii. The diagnosis has been confirmed by biopsy; AND

iii. Patient has been receiving the maximum or maximally tolerated dose of ONE of the following for ≥ 90 days (a or b):

a) Angiotensin converting enzyme inhibitor; OR

b) Angiotensin receptor blocker; AND

iv. According to the prescriber, the patient has received ≥ 90 days of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification; AND

v. Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2; AND

vi. The medication is prescribed by or on consultation with a nephrologist.

CONDITIONS NOT COVERED

- **Tarpeyo™ (budesonide delayed-release capsules (Calliditas)**

is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Tarpeyo™ capsules [prescribing information]. Stockholm, Sweden: Calliditas; December 2023.
2. Barratt J, Lafayette R, Kristensen J, et al; for the NefIgArd Trial Investigators. Results from part A of the Multicenter, double-blind, randomized, placebo-controlled NefIgArd trial, which evaluated targeted-release formulation of budesonide for the treatment of primary immunoglobulin A nephropathy. *Kidney International.* 2023;103:391-402.
3. KDIGO 2021 clinical practice guidelines for the management of glomerular diseases. *Kidney International.* 2021;100:S1-S276. Available at: https://www.kidney-international.org/action/showPdf?pii=S0085-2538%2821%2900562-7. Accessed on: January 24, 2024.
4. Lafayette R, Kristensen J, Stone A, et al; on behalf of the NefIgArd trial investigators. Efficacy and safety of a targeted-release formulation of budesonide in patients with primary IgA nephropathy (NefIgArd): 2-year results from a randomized phase 3 trial. *Lancet*. 2023;402(10405):859-870.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/05/2022
Selected Revision	**Primary Immunoglobulin A Nephropathy:** The approval duration was changed to 10 months for initial therapy (previously the approval duration was 9 months) and up to 10 months for continuation therapy (previously the approval duration was up to 9 months).	01/19/2022
Annual Revision	No criteria changes.	01/11/2023
Annual Revision	**Primary Immunoglobulin A Nephropathy:** The criterion requiring that the patient is at high risk of disease progression, defined by ONE of the following: urine-to-protein-creatinine ratio ≥ 1.5 g/g OR proteinuria ≥ 0.75 g/day was revised to require that the patient is at high risk of disease progression, defined by urine-to-protein-creatinine ratio ≥ 0.8 g/g OR proteinuria ≥ 0.75 g/day.	01/31/2024