



## PRIOR AUTHORIZATION POLICY

**POLICY:** Nephrology – Tarpeyo Prior Authorization Policy

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

**REVIEW DATE:** 01/31/2024; selected revision 10/02/2024

### **INSTRUCTIONS FOR USE**

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## **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.<sup>1</sup>

The recommended dose is 16 mg orally once daily (QD) at least 1 hour before a meal for 9 months.<sup>1</sup> 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  $\geq 18$  years of age with IgAN.<sup>1,2,4</sup> Eligible patients had biopsy-proven IgAN, proteinuria (defined as either  $\geq 1$  g/day) or a urinary protein-to-creatinine ratio (UPCR)  $\geq 0.8$  g/g despite optimized supportive care, and estimated glomerular filtration rate (eGFR)  $\geq 35$  mL/min/1.73 m<sup>2</sup> and  $\leq 90$  mL/min/1.73 m<sup>2</sup>.<sup>2,4</sup> 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  $\geq 3$  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.<sup>2</sup>

Following the 9-month randomized, treatment period, patients were followed for 15 months during an observational period in which no study medication was administered.<sup>4</sup> 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<sup>2</sup> vs. -7.52 mL/min/1.73 m<sup>2</sup>, 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<sup>2</sup> and -4.56 mL/min/1.73 m<sup>2</sup>, 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<sup>2</sup> in the Tarpeyo group vs. -12.00 mL/min/1.73 m<sup>2</sup> 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<sup>2</sup>/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 for high-risk IgAN patients by the Kidney Diseases Improving Global Outcomes (KDIGO) guidelines for the management IgAN and immunoglobulin A vasculitis (2024).<sup>3</sup> According to the guidelines, budesonide products are recommended for a 9-month treatment course for patients who are at risk of progressive kidney function loss with IgAN.

Following biopsy-confirmed diagnosis of IgAN, the guidelines recommend assessment of disease progression.<sup>3</sup> 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 ≥ 0.5 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.<sup>4</sup> 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<sup>2</sup>, diabetes, obesity (body mass index > 30 kg/m<sup>2</sup>), 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 ALL of 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 BOTH of the following (a and b):

**a)** Patient meets ONE of the following [(1) or (2)]:

**(1)** Proteinuria ≥ 0.5 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<sup>2</sup>; 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 ALL of 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  $\geq$  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  $\geq$  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  $\geq$  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  $\geq$  30 mL/min/1.73 m<sup>2</sup>; 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) including the following; criteria will be updated as new published data are available**

**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. Kidney Diseases: Improving Global Outcomes (KDIGO) 2024 clinical practice guidelines for the management of immunoglobulin A nephropathy (IgAN) and immunoglobulin A vasculitis (IgAV). *Draft published online ahead of print*. Available at: <https://kdigo.org/wp-content/uploads/2024/08/KDIGO-2024-IgAN-IgAV-Guideline-Public-Review-Draft.pdf>. Accessed on September 23, 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
Annual Revision	No criteria changes.	01/11/2023

Annual Revision	<b>Primary Immunoglobulin A Nephropathy:</b> The criterion requiring that the patient is at high risk of disease progression, defined by ONE of the following: urine-to-protein-creatinine ratio $\geq$ 1.5 g/g OR proteinuria $\geq$ 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 $\geq$ 0.8 g/g OR proteinuria $\geq$ 0.75 g/day.	01/31/2024
Selected Revision	<b>Primary Immunoglobulin A Nephropathy:</b> The criterion requiring that the patient is at high risk of disease progression, defined by ONE of the following: urine-to-protein-creatinine ratio $\geq$ 0.8 g/g OR proteinuria $\geq$ 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 $\geq$ 0.8 g/g OR proteinuria $\geq$ 0.5 g/day.	10/02/2024

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