

PRIOR AUTHORIZATION POLICY

POLICY: Nephrology – Tarpeyo Prior Authorization Policy

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

REVIEW DATE: 01/31/2024

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 m² and ≤ 90 mL/min/1.73 m².^{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 m² vs. -7.52 mL/min/1.73 m², 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 m² and -4.56 mL/min/1.73 m², 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 m² in the Tarpeyo group vs. -12.00 mL/min/1.73 m² in the placebo group corresponding to a difference in the 2-year total eGFR slope (supportive endpoint) of 2.95 mL/min/1.73 m²/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%).

01/31/2024

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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 m², diabetes, obesity (body mass index > 30 kg/m²), 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tarpeyo is recommended in those who meet the following criteria:

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 m²; 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 m²; AND
 - vi. The medication is prescribed by or on consultation with a nephrologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Tarpeyo is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. 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. 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.

