Tarpeyo Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date	Date of Origin
9/1/2022	9/1/2022

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
TARPEYO™ (budesonide) Delayed release capsule	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) greater than or equal to 1.5 g/g		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Immunoglobulin A Nephropathy (2,3)	Immunoglobulin A nephropathy (IgAN), also known as Berger's disease, is a kidney disease that occurs when IgA deposits build up in the kidneys, causing inflammation that damages the glomeruli, in turn causing the kidneys to leak blood and protein into the urine. The damage may lead to scarring of the nephrons that progresses slowly over may years. Eventually, IgAN can lead to end-stage renal disease (ESRD). IgAN cannot be reliably diagnosed with blood or urine tests and kidney biopsy is required to confirm the diagnosis. Biopsy is usually only performed if there are signs suggestive of more severe or progressive disease, such as persistent proteinuria of at least 500 mg per day or an elevated serum creatinine concentration. After a diagnosis has been established, underlying causes of secondary IgAN (e.g., liver cirrhosis, HIV, hepatitis, inflammatory bowel disease) should be considered. The primary focus of IgAN management should be optimized supportive care [e.g., blood pressure management, maximally tolerated angiotensin-converting-enzyme inhibitor (ACEI) or angiotensin II blocker (ARB), lifestyle modification, address cardiovascular risk]. Guidelines recommend that all patients with proteinuria greater than 0.5g/dL be treated with an ACEI or ARB irrespective of whether they have hypertension. Guidelines define high risk of progression in IgAN as proteinuria greater than 0.75 – 1 g/d despite at least 90 days of optimized supportive care. It is suggested that patients who remain at high risk despite maximal supportive care be considered for a 6 month course of glucocorticoid therapy. They stress the importance of discussing treatment-emergent toxicity, particularly those who have an eGFR less than 50 mL/min/1.73 m^2. It is further noted that glucocorticoids should be given with extreme caution or avoided entirely in the following situations: • eGFR less than 30 mL/min/1.73 m^2 • Diabetes • Obesity (BMI greater than 30 kg/m^2) • Latent infections (e.g., viral hepatitis, tuberculosis) • Secondary disease (e.g., cirrhosis) • Active peptic ulceration • Uncontrolled psychiatric illness • Severe osteoporosis
Efficacy (1,2)	The effect of Tarpeyo on proteinuria was assessed in a randomized, double-blind, multicenter study (NEFIGAN, NCT: 03643965) in patients with biopsy-proven IgAN, estimated glomular filtration rate (eGFR) greater than or equal to 35 mL/min/1.73 m^2, and proteinuria (defined as either greater than or equal to 1 g/day or urine protein-to-creatinine ratio (UPCR) greater than or equal to 0.8 g/g) who were on a stable

	dose of maximally-tolerated renin-angiotensin-system (RAS) inhibitor therapy. Patients with other glomerulopathies, nephrotic syndrome, or those who had been treated with systemic immunosuppressive medications were excluded. Patients were randomized 1:1 to either Tarpeyo 16 mg once daily or placebo and treated for nine months followed by a 2-week taper of either Tarpeyo 8 mg once daily or placebo. Of the 199 patients who completed the Month 9 visit, 68% were male, 86% were Caucasian, 12% were Asian, and 16% were from the US. The median age was 44 years (range 23 to 73 years). At baseline, the mean eGFR was approximately 58 mL/min/1.73 m^2, with 62% of patients having an eGFR 3.5 g/24 hours. Approximately 73% of patients had a history of hypertension and 5% had a history of type 2 diabetes mellitus. At baseline, 98% were treated with an ACEI or ARB and less than 1% of patients were on a sodium-glucose cotransporter-2 (SGLT2) inhibitor. The primary outcome assessed all randomized patients who took at least one post-dose of study drug and had at least one post-dose efficacy measurement. The interim analysis included all patients who were randomized at the time the 90th patient had completed 9 months treatment, even if some of these patients had data only up to 1-month, 3-month, or 6-month timepoint. • The mean changes in UPCR at 9 months from baseline were -27.3% for 16 mg/day targeted release formulation (TRF)-budesonide-treated patients and -21.5% for 8 mg/day TRF-budesonide-treated patients versus the placebo-treated patients (95% CI; p=.0092). Patients who received placebo had an increase in mean UPCR of 2.7% • Upon completion of the 3-month follow-up, after cessation of trial medication, the mean reduction was sustained in the 8 mg/day TRF-budesonide group (-22.6% change from baseline) and decreased further in the 16 mg/day group (-32% change from baseline versus an increase of 0.5% for placebo. Compared with placebo, the changes in UPCR at 12 months in both active treatment groups were statistically significant (16 mg/day vs placebo [95% CI, p=.0005]; 8 mg/day vs placebo [95% CI, p=.0101]) The secondary outcomes were mean changes from baseline in UPCR at 12 months and eGFR. • Upon completion of 3-month follow-up, the mean reduction was sustained in the 8 mg/day TRF-budesonide group (-22.6% change from baseline) and decreased further in the 16 mg/day group (-32% change from baseline) versus an increase of 0.5% for placebo. • Mean percentage change from baseline in eGFR at 9 months was -9.8% for placebo, 0.6% for 16 mg/day, and -0.9% for 8 mg/day. Comparisons with placebo achieved statistical significance at 9 months (16 mg/day vs placebo [95% CI, p=.0026; 8 mg/day vs placebo [95% CI, p=.0064]). eGFR levels in the TRF-budesonide 16 mg/day group sustained throughout the trial, the mean percentage change from baseline at 12 months was 0.7% vs -10.9% for placebo; 95% CI, p=.0134
Safety (1)	Tarpeyo is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of Tarpeyo. Serious hypersensitivity reactions, including anaphylaxis have occurred with other budesonide formulations.

REFERENCES

Number	Reference
1	Tarpeyo Prescribing Information. Calliditas Therapeutics AB. December 2021.
2	Fellstrom BC, Barratt J, Cook H, et al. Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomized, placebo-controlled phase 2b trial. Lancet. 2017;389(10084):2117-2127. doi:10.1016/S0140-6736(17)30550-0.
3	KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021 Oct;100(4S):S1-S276. doi:10.1016/j.kint.2021.05.021.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Agent Names	Strength	Targeted MSC	Available MSC	Effective Date
TARPEYO*budesonide delayed release cap	4 MG	M ; N ; O ; Y	N	09-01-2022

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Agent GPI	Agent Names	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
22100012006520	TARPEYO*Budesonide Delayed Release Cap 4 MG	4 MG	120.0	CAPS	30	Days				09-01-2022

CLIENT SUMMARY – PRIOR AUTHORIZATION

Agent Names	Strength	Client Formulary
TARPEYO*budesonide delayed release cap	4 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Agent Names	Strength	Client Formulary
TARPEYO*Budesonide Delayed Release Cap 4 MG	4 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of primary immunoglobulin A nephropathy (IgAN) confirmed by kidney biopsy **AND** 2. ONE of the following: A. The patient has a urine protein-to-creatinine ratio (UPCR) greater than or equal to 1.5 g/g **OR** B. The patient has proteinuria greater than or equal to 1 g/day **AND** 3. The patient's eGFR is greater than or equal to 35 mL/min/1.73 m^2 **AND** 4. ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 5. ONE of the following: A. The patient's medication history includes therapy with a maximally tolerated ACEI or ARB (e.g., benazepril, lisinopril, losartan), or a combination medication containing an ACEI or ARB AND ONE of the following: 1. BOTH of the following: A. The patient has had an inadequate response to a maximally tolerated ACEI or ARB (e.g., benazepril, lisinopril, losartan), or a combination medication containing an ACEI or ARB **AND**

Module	Clinical Criteria for Approval
	B. The patient will be using an ACEI or ARB or a combination medication containing and ACEI or ARB in combination with the requested agent **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over a maximally tolerated ACEI or ARB (e.g., benazepril, lisinopril, losartan), or a combination medication containing an ACEI or ARB **OR** B. The patient has an intolerance or hypersensitivity to an ACEI or ARB, or a combination medication containing an ACE or ARB **OR** C. The patient has an FDA labeled contraindication to ALL ACEI and ARB **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL ACEI and ARBs cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 6. ONE of the following: A. The patient has an intolerance or hypersensitivity to oral generic budesonide that is not expected to occur with the requested agent **OR** B. The patient has an FDA labeled contraindication to the oral generic budesonide that is not expected to occur with the requested agent **OR** C. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** D. BOTH of the following: 1. The patient's medication history includesoral generic budesonide as indicated by ONE of the following: A. Evidence of a paid claim(s) within the past 999 days **OR** B. The presciber has stated that the patient has tried oral generic budesonide in the past 999 days **AND** 2. ONE of the following: A. Oral generic budesonide was discontinued due to lack of effectiveness or an adverse event **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over oral generic budesonide **OR** E. The prescriber has provided documentation that oral generic budesonide cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 7. ONE of the following: A. The patient has not previously been treated with a course of therapy (9 months) with the requested agent **OR** B. The patient has previously been treated with a course of therapy with the requested agent AND the provider has provided information in support of an additional course or therapy with the requested agent **AND** 8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**

Module	Clinical Criteria for Approval
	9. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 10 months NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit **OR** B. ALL of the following: 1. The requested quantity (dose) is greater than the program quantity limit AND ONE of the following: **AND** 2. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 3. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **Length of Approval:** 10 months

The BCBS MN Step Therapy Supplement applies to this program for Medicaid.