budesonide (Tarpeyo™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO258

Description

Budesonide (Tarpeyo) is an orally administered corticosteroid indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression.

Length of Authorization

- N/A

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
budesonide (Tarpeyo)	Primary Immunoglobulin A Nephropathy (IgAN)	4 mg capsules	120 capsules/30 days

Initial Evaluation

I. **Budesonide (Tarpeyo)** is considered not medically necessary when used for all conditions, including but not limited to primary immunoglobulin A nephropathy (IgAN).

II. Budesonide (Tarpeyo) is considered investigational when used for all other conditions, including but not limited to:
   A. IgAN in members less than 18 years of age
   B. Secondary IgA Nephropathy

Renewal Evaluation

I. N/A – Product not eligible for renewal

Supporting Evidence

I. Budesonide (Tarpeyo) is the first therapy FDA approved for the treatment of patients with primary immunoglobulin A (IgA) nephropathy at risk of rapid disease progression (UPCR ≥ 1.5 g/g). IgA nephropathy, also known as Berger's disease, is a rare kidney disease that occurs when IgA antibody deposits build up in the kidneys, causing inflammation that damages kidney tissues. The deposits can cause the kidneys to leak blood and protein into the urine. IgA

nephropathy complications can include high blood pressure and chronic kidney disease, which can sometimes progress to kidney failure. FDA approval of budesonide (Tarpeyo) was granted under accelerated approval. Confirmation studies to assess whether budesonide (Tarpeyo) slows kidney function decline in patients with IgA nephropathy and to describe the clinical benefit of budesonide (Tarpeyo) are expected to conclude in late 2023.

II. Clinical studies NEFIGAN and NefigArd were conducted in adult patient populations (18 years of age and older). The efficacy and safety of budesonide (Tarpeyo) in pediatric populations is unknown at this time. Additionally, guidelines indicate there is insufficient data currently available to recommend that pediatric IgAN populations be managed as adults.

III. KDIGO guidelines indicate IgAN can only be diagnosed with a kidney biopsy. While there are several prognostic scoring tools that have been developed to assist in predicting kidney outcomes of IgAN patients (i.e., MEST-C, International IgAN Prediction Tool, etc.) there are currently are no validated diagnostic serum or urine biomarkers.

IV. Reduced glomerular filtration rates can be a marker of kidney disease; specifically, those under 35mL/min/1.73 m^2 which can indicate moderate-to-severe kidney disease (stage 3b). Guidelines recommend supportive care for these patients with moderate-to-severe kidney disease as opposed to therapy with corticosteroids.

V. The primary focus of IgAN management is optimized supportive care (i.e., blood pressure management, maximally tolerated ACEi/ARBs, lifestyle modification, and reduction of cardiovascular risks). Proteinuria and eGFR are the only validated prognostic serum or urine biomarkers in IgAN. In all types of proteinuric glomerular diseases, including IgAN, higher levels of proteinuria are associated with worse kidney outcomes (acute kidney injury, chronic kidney disease, end stage renal disease, etc.). Reduction in proteinuria, independent of blood pressure control, is associated with improved kidney outcomes. KDIGO guidelines recommend that all patients with proteinuria >0.5 g/d, irrespective of whether they have hypertension, be treated with either an ACEi or ARB to further protect renal function.

VI. Patients with IgAN who are at high risk of progressive chronic kidney disease (CKD) despite maximal supportive care are defined as those with proteinuria greater than 0.75 to 1 g/day despite treatment with a maximally tolerated or allowed daily dose of RAS blockade (ACEi/ARB) for ≥ 3 months. Guideline recommendations indicate proteinuria reduction to under 1 g/day as a surrogate marker of improved kidney outcomes in IgAN. Furthermore, a reduction to under 1 g/day is a reasonable treatment target.

VII. Incremental levels of sustained proteinuria above 1 g/d are associated with marked changes in the risk of loss of kidney function. Reduction of proteinuria, ideally to under 1 g/d, is associated with favorable outcomes. The urinary protein-creatinine ratio (UPCR) has relatively poor correlation with 24-hour urine protein excretion, particularly when proteinuria is over 1 g/d. This makes distinguishing smaller changes in proteinuria (e.g., 1.5 vs 2 g/d) challenging. UPCR cannot be directly compared with a 24-h proteinuria level; however, UPCR gives the ability to

overcome possible collection errors and deviations from normal creatinine excretion (e.g., physically active and muscular men). Due to this reason both can be used to assess proteinuria.

VIII. Budesonide (Tarpeyo) has not been included in KDIGO guidelines. Currently guidelines recommend enrollment into clinical trials prior to use of corticosteroids or other immunosuppressants. If the benefit outweighs the risk, treatment with prednisone or methylprednisolone is recommended based on limited clinical trial experience. No corticosteroid, including budesonide (Tarpeyo), has been found to slow kidney function decline (reduce eGFR decline or progression to ESRD) in IgAN patients. Of the other alternative agents, mycophenolate Mofetil (MMF) is the preferred option. There is limited clinical data to support the use of other immunosuppressive agents.

IX. Endpoints from corticosteroid studies followed patients for up to 10 years. Safety and efficacy of treatment with subsequent courses of budesonide (Tarpeyo) have not been established at this time. Similarly designed trials with long-term safety data have limited total glucocorticoid exposure to six months due to increased risks of treatment-related adverse events (infection risk, impaired glucose tolerance, weight gain, etc.).

Investigational or Not Medically Necessary Uses

I. Primary immunoglobulin A nephropathy (IgAN)
   A. Budesonide (Tarpeyo) for the treatment of primary IgAN adjunct to supportive therapy with ACE inhibitors and ARBs has been evaluated in clinical trials. Results showed reduction in proteinuria; however, available data do not support clinically meaningful long term renal outcomes (reduction of eGFR decline or progression to ESRD). Other glucocorticoid therapies (prednisone, methylprednisolone, and IV methylprednisolone) have demonstrated similar reductions in proteinuria and have comparable safety profiles to budesonide (Tarpeyo). At this time it is unproven if budesonide (Tarpeyo) is more likely to produce similar therapeutic results or is superior to other glucocorticoid therapies that could be utilized. Additionally, budesonide (Tarpeyo) is significantly more costly than other glucocorticoid therapies that could be utilized. Given these factors, budesonide (Tarpeyo) is not medically necessary.

II. Budesonide (Tarpeyo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. IgAN in members less than 18 years of age
      i. The use of budesonide (Tarpeyo) has not been evaluated in children. Additionally, while guidelines acknowledge use of immunosuppressants, specifically corticosteroids, are more widespread in children there is a lack of randomized controlled trials and consensus-driven indications for use in pediatric populations. As in adults, children with rapidly progressive IgAN have a poor outcome, and

despite limited evidence, this subgroup should be offered treatment with glucocorticoids (usually as methylprednisolone pulses) and cyclophosphamide.

B. Secondary IgA Nephropathy
    i. Secondary IgAN can be attributed to a variety of other disorders including but not limited to cirrhosis and other severe forms of liver disease, celiac disease, HIV infection, monoclonal gammopathy of renal significance (MGRS), seronegative arthritis, etc. While there is no standard of care treatment for IgAN in these patients, therapy should be directed at the underlying primary disease.

References

1. Tarpeyo [Prescribing Information]. Stockholm, Sweden: Calliditas Therapeutics AB. December 2021.
2. 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. doi:10.1016/S0140-6736(17)30550-0
3. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021;100(4S):S1-S276. doi:10.1016/j.kint.2021.05.021
4. UpToDate, Inc. IgA nephropathy: Clinical features and diagnosis. UpToDate [database online]. Waltham, MA. Last updated February 9, 2022. Available at: http://www.uptodate.com/home/index.html.
5. UpToDate, Inc. IgA nephropathy: Treatment and prognosis. UpToDate [database online]. Waltham, MA. Last updated January 3, 2022. Available at: http://www.uptodate.com/home/index.html.
6. Pattrapornpisut, P., Avila-Casado, C., & Reich, H. N. (2021). Iga nephropathy: Core curriculum 2021. American Journal of Kidney Diseases, 78(3), 429–441. https://doi.org/10.1053/j.ajkd.2021.01.024

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created.	04/2022