VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Kygevvi Prior Authorization Policy
- Kygevvi™ (doxecitine and doxribtimine powder for oral solution – UCB)

REVIEW DATE: 12/17/2025

OVERVIEW

Kygevvi is a combination of doxecitine and doxribtimine, both pyrimidine nucleosides, indicated for the treatment of thymidine kinase 2 deficiency (TK2d) in adults and pediatric patients with an age of symptom onset on or before 12 years.[1]

Disease Overview

TK2d is an ultra-rare, progressive, and often life-threatening mitochondrial myopathy caused by autosomal recessive mutations in the *TK2* gene, resulting in impaired mitochondrial DNA maintenance and energy production.[2,3] TK2d presents with progressive proximal muscle weakness and respiratory insufficiency, frequently leading to loss of ambulation, feeding difficulties, and dependence on ventilatory support. The disease can manifest in early childhood or later in life, with earlier onset associated with more rapid progression and higher mortality risk. TK2d is diagnosed based on symptoms, clinical exam, laboratory, and genetic tests. Genetic testing for biallelic pathogenic (or likely pathogenic) variants in the *TK2* gene confirms the diagnosis.

Clinical Efficacy

The efficacy of Kygevvi for the treatment of patients with TK2d, with an age of symptom onset on or before 12 years of age, was established based on data from one Phase 2 clinical study, two retrospective chart review studies, and an expanded access program.[1] Patients included in a survival analysis had confirmed biallelic pathogenic TK2 variants, and the median age of TK2d symptom onset was 1.5 years.[1,4] Treatment reduced the overall risk of death from treatment start by approximately 86% (95% confidence interval [CI]: 61%, 96%).[1]

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Thymidine Kinase 2 Deficiency (TK2d).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient has had a genetic test confirming the diagnosis of TK2d with biallelic pathogenic or likely pathogenic variants in the *TK2* gene; AND
   - **B)** According to the prescriber, the patient had onset of symptoms consistent with TK2d at ≤ 12 years of age; AND
     Note: Examples of symptoms consistent with TK2d include progressive muscle weakness, hypotonia (i.e., low muscle tone), respiratory insufficiency, loss of motor skills, feeding and/or swallowing difficulties, facial weakness/paralysis, ptosis (i.e., drooping eyelid[s]), ophthalmoparesis (i.e., difficulty moving the eyes), developmental delay and regression, hearing loss, and seizures.
   - **C)** The medication is prescribed by or in consultation with a neurologist, geneticist, or physician who specializes in metabolic and/or neuromuscular disorders.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Kygevvi 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. Kygevvi™ powder for oral solution [prescribing information]. Smyrna, GA: UCB; November 2025.
2. National Organization for Rare Disorders. Thymidine kinase 2 deficiency. Available at: https://rarediseases.org/rare-diseases/thymidine-kinase-2-deficiency/. Updated March 4, 2025. Accessed on December 1, 2025.
3. Wang J, El-Hattab AW, Wong LJC. TK2-Related Mitochondrial DNA Maintenance Defect, Myopathic Form. 2012 Dec 6 [Updated 2018 Jul 26]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025.
4. Hirano M, Garone C, Haas R, et al. Survival analyses in patients with thymidine kinase 2 deficiency aged ≤12 years at symptom onset who received pyrimidine nucleos(t)ide therapy. Presented at: Muscular Dystrophy Association (MDA) Clinical & Scientific Conference; 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/17/2025