Drug Coverage Policy

Effective Date.....6/1/2026
Coverage Policy Number.....IP0780
Policy Title.....Kygevvi

Kygevvi for Individual and Family Plans

- Kygevvi™ (doxecitine and doxribtimine powder for oral solution - UCB)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for 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.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, prescription receipts and/or other information. All documentation must include patient-specific identifying information.

Kygevvi is considered medically necessary when the following are met:

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 **[documentation required]**; 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 Covered

Kygevvi for any other use is considered not medically necessary. 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.

Revision Details

Summary of Changes	Review Date	Effective Date
New policy.	4/23/2026	6/1/2026

The policy effective date is in force until updated or retired.