

Clinical Policy: Doxecitine and Doxribtimine (Kygevvi)

Reference Number: PA.CP.PHAR.738

Effective Date: 02/2026

Last Review Date: 01/2026

Description

Doxecitine and doxribtimine (Kygevvi[®]) is a combination pyrimidine nucleoside therapy.

FDA Approved Indication(s)

Kygevvi is 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness[®] that Kygevvi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Thymidine Kinase 2 Deficiency (must meet all):

1. Diagnosis of TK2d as evidenced by a mutation in the thymidine kinase 2 (TK2) gene;
2. Prescribed by or in consultation with a neurologist or metabolic disease specialist;
3. Age of symptom onset \leq 12 years (e.g., proximal muscle weakness, respiratory weakness, facial diplegia; *see Appendix D*);
4. Documentation of member's current weight in kg;
5. Dose does not exceed doxecitine 400 mg/kg and doxribtimine 400 mg/kg per day (*see Appendix E for the recommended number of packets per day based on total daily dose*).

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Thymidine Kinase 2 Deficiency (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. Documentation of member's current weight in kg;
4. If request is for a dose increase, new dose does not exceed doxecitine 400 mg/kg and doxribtimine 400 mg/kg per day (*see Appendix E for the recommended number of packets per day based on total daily dose*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

TK2d: thymidine kinase 2 deficiency

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Clinical symptoms of TK2d:
 - Proximal muscle weakness (muscle weakness affecting the muscles of the trunk, shoulders, and thighs)
 - Respiratory weakness (including mechanical ventilation or continuous non-invasive ventilation)
 - Loss in motor functions (holding head upright, sitting, standing, walking, climbing, running)
 - Facial diplegia
 - Ptosis (droopy eyelids)
 - Seizures
 - Encephalopathy
 - Dysphagia
 - Cognitive dysfunction or decline
 - Multiple bone fractures

Appendix E: Number of Packets Based on Total Daily Dose per Prescribing Information

Total Daily Dose (mg/day)	Total Number of Kygevvi Packets for Reconstitution
750 – 4,049	1
4,050 – 8,249	2
8,250 – 12,749	3

Total Daily Dose (mg/day)	Total Number of Kygevvi Packets for Reconstitution
12,750 – 17,249	4
17,250 – 21,749	5
21,750 – 24,749	6
24,750 – 29,249	7
29,250 – 33,749	8
33,750 – 38,249	9
38,250 – 42,749	10
42,750 – 47,249	11
47,250 – 51,749	12
51,750 – 54,749	13
54,750 – 59,249	14
59,250 – 63,749	15
63,750 – 68,249	16

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
TK2d	<p>Kygevvi is administered PO in 3 equally divided doses:</p> <ul style="list-style-type: none"> Starting: 260 mg/kg/day (consisting of 130 mg doxecitine and 130 mg doxribtamine) Intermediate: 520 mg/kg/day (consisting of 260 mg doxecitine and 260 mg doxribtamine) Maintenance: 800 mg/kg/day (consisting of 400 mg doxecitine and 400 mg doxribtamine) <p>Titrate to the next dosage level based on tolerability after a minimum of 2 weeks at the current dosage level</p>	800 mg/kg/day

VI. Product Availability

Powder for oral solution: 2 g doxecitine and 2 g doxribtamine

VII. References

1. Kygevvi Prescribing Information. Smyrna, GA: UCB, Inc.; November 2025. Available at: <https://www.ucb-usa.com/kygevvi-prescribing-information.pdf>. Accessed November 5, 2025.
2. ClinicalTrials.gov. An open-label study of continuation treatment with combination pyrimidine nucleosides in patients with TK2 deficiency (Continuation). Available at: <https://www.clinicaltrials.gov/study/NCT03845712>. Accessed November 5, 2025.
3. ClinicalTrials.gov. A retrospective study of subjects with thymidine kinase 2 deficiency. Available at: <https://clinicaltrials.gov/study/NCT05017818>. Accessed November 5, 2025.
4. ClinicalTrials.gov. A RETROspective study of patients with TK2d (RETRO). Available at: <https://clinicaltrials.gov/study/NCT03701568>. Accessed November 5, 2025.
5. Berardo A, Domínguez-González C, Engelstad K, et al. Advances in thymidine kinase 2 deficiency: Clinical aspects, translational progress, and emerging therapies. *J Neuromuscul Dis.* 2022;9(2):225-235. doi: 10.3233/JND-210786. PMID: 35094997; PMCID: PMC9028656.

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6. Garone C, Taylor RW, Nascimento A, et al. Retrospective natural history of thymidine kinase 2 deficiency. *J Med Genet.* 2018 Aug;55(8):515-521. doi: 10.1136/jmedgenet-2017-105012.

Reviews, Revisions, and Approvals	Date
Policy created	01/2026