kygevvi™
(doxecitine and doxribtimine)
Powder for Oral Solution
2 g/2 g per packet

Guide to Writing a Letter of Medical Necessity*

A health plan may request a letter of medical necessity to support coverage of KYGEVVI. A letter of medical necessity can help explain your rationale and clinical decision-making in choosing therapy for the specific patient and may include supporting documentation (e.g., medical records, peer-reviewed literature, and Prescribing Information). The letter may be submitted as part of the prior authorization (PA) process, with the claim form, or in response to a health plan's request for additional documentation.

This resource provides information on the process of drafting a letter of medical necessity. Included below is a checklist that can be followed when creating a letter of medical necessity. In addition, attached to this document is a sample letter with information that health plans often require.

Preparing an Effective Letter of Medical Necessity

- **When requesting treatment for your patient, follow the patient's plan requirements, which may require specific forms for documenting a letter of medical necessity; otherwise, treatment may be delayed**
- **Provide complete, comprehensive information regarding your patient's condition and the clinical rationale for treatment. Information recommended for a letter of medical necessity typically includes:**
  - Patient information
    - Full name
    - Date of birth
    - Case ID number (if available)
    - Insurance ID/group number
    - Diagnosis, including ICD-10-CM code(s)
  - Current condition and severity
    - Current symptoms
    - Functional status
    - Required medical devices
  - Laboratory findings
    - Genetic testing (confirmed *TK2* mutation[s])
    - Investigative biomarkers (e.g., mtDNA)
    - Neuroimaging
  - Clinical rationale for treatment
    - Medical history
    - Physical examination
    - Trial data
    - Dosing and administration
  - Summary of your recommendations
- **Attach documentation that supports your recommendations, including patient information and current treatment data (as applicable)**
  - Additional rationale for treatment
    - Prescribing Information
    - Clinical trial data
    - Peer-reviewed literature
    - FDA approval letter
  - Additional patient information
    - Patient medical records
    - Clinical notes
    - Lab results
    - Genetic testing

***Use of the information in this letter does not guarantee that the health plan will provide reimbursement for KYGEVVI. The information in this letter is not intended to be a substitute for, or an influence on, your independent medical judgment.** It is presented for informational purposes only and is not intended to provide reimbursement or legal advice. HCPs are encouraged to contact third-party payers for specific information on their current coverage policies. For other questions, please call ONWARD® at 1-844-ONWARD-1 (1-844-669-2731).

FDA=US Food and Drug Administration; HCP=healthcare professional; ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification; ID=identification; mtDNA=mitochondrial deoxyribonucleic acid; *TK2*=thymidine kinase 2 gene; TK2d=thymidine kinase 2 deficiency.

INDICATION

KYGEVVI is indicated for the treatment of thymidine kinase 2 deficiency (TK2d) in adult and pediatric patients with an age of symptom onset on or before 12 years.

IMPORTANT SAFETY INFORMATION

Increase in Liver Transaminases

Elevated liver transaminase [alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)] levels were reported in patients treated with KYGEVVI. Obtain baseline liver transaminase (ALT, AST) and total bilirubin levels in patients prior to treatment initiation with KYGEVVI. If signs or symptoms consistent with liver injury are observed, interrupt treatment with KYGEVVI until liver transaminase (ALT, AST) and total bilirubin levels have either returned to baseline or stabilized at a new baseline value. Consider permanently discontinuing KYGEVVI if signs or symptoms consistent with liver injury persist or worsen. Monitor liver transaminases and total bilirubin levels yearly and as clinically indicated.

Please see additional Important Safety Information on page 4 and the full Prescribing Information.

Guide to Writing a Letter of Medical Necessity* (cont'd)

Sample Letter of Medical Necessity

Below is a sample letter of medical necessity that may be used as a starting point to describe your reasoning for why KYGEVVI is medically necessary for your patient. The content of the letter of medical necessity should be personalized based on your patient's medical information. Always exercise your independent medical judgment and discretion when providing a diagnosis and characterization of the patient's medical condition. It is recommended you use your institution's letterhead for the final draft that you submit to the health plan unless the health plan requires you to use their specific letter of medical necessity form.

SAMPLE LETTER OF MEDICAL NECESSITY
UPDATE AND PLACE ON YOUR LETTERHEAD

[Date]

[Contact Name]
[Title]
[Name of Health Insurance Company or Pharmacy Benefit Manager]
[Address]
[City, State ZIP Code]
Insured: [Full Name of Patient]; Date of Birth [MM-DD-YYYY]; Policy Number: [Number]; Group Number: [Number]
Date(s) of service: [Date(s)]

Re: Coverage for KYGEVVI® (doxecitine and doxribtimine) for [Full Name of Patient]

Dear [Name of Contact]:

I am writing on behalf of my patient, [Full Name of Patient], to provide information supporting medical necessity for treatment with KYGEVVI. This letter of medical necessity provides information regarding my patient's medical history and diagnosis, and my treatment rationale for the use of KYGEVVI.

Patient Information and Medical History
[Full Name of Patient] is a[n] [age]-year-old [male/female] born [MM-DD-YYYY] who has been diagnosed with thymidine kinase 2 deficiency (TK2d).

[Please provide a summary of rationale for treatment with KYGEVVI for this patient based on your independent clinical assessment and medical opinion. Include a description of the patient's relevant TK2d clinical signs and symptoms, including age at onset, disease progression, history of prior treatments, as well as any specific clinical presentations and relevant patient-specific clinical scenarios demonstrating medical necessity.]

Potential Consequences of Not Receiving the Treatment
Without this medically necessary treatment, [Patient Name] is at risk of [list potential negative outcomes, based on patient's current condition and your independent assessment of potential disease progression].

Summary
Considering the patient's medical information provided and the supporting documentation enclosed, as well as the fact that KYGEVVI is the only US Food and Drug Administration (FDA)-approved treatment for TK2d in adult and pediatric patients with an age of symptom onset on or before 12 years. I believe KYGEVVI is indicated and medically necessary for [Patient Name]. If you have any further questions, please feel free to call me at [physician's phone number] to discuss. Thank you kindly for your prompt attention to this request.

Sincerely,
[Physician's Name, Credentials]
[Physician's Identification Number]
[Physician's Practice Name]
[Physician's Phone Number]
[Physician's Fax Number]
[Physician's Email]

Enclosures: [clinical documentation, Prescribing Information, clinical notes and medical records, FDA approval letter for KYGEVVI, etc.]

To avoid a delay, consider submitting a letter of medical necessity even if not requested.

See the next page for specific examples of patient medical history you may consider including here.

If you are unsure, confirm with the payer what specific documentation needs to be submitted with your letter.

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HCP=healthcare professional.

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Guide to Writing a Letter of Medical Necessity* (cont'd)

Examples of Medical History for a Letter of Medical Necessity

- Documented diagnosis of TK2d
  - Genetic testing results confirming biallelic *TK2* mutations[1]
  - Muscle biopsy and skeletal muscle magnetic resonance imaging (MRI) can also support TK2d diagnosis[1,2]
- Record the patient's symptoms and functional status, including any case notes and clinical impressions
  - TK2d can present as progressive myopathy and respiratory insufficiency[3]
  - Myopathic symptoms of TK2d can include proximal muscle weakness, hypotonia, and dysphagia[3]
- Laboratory findings and skeletal muscle pathology features,[1] such as
  - Raised creatine kinase
  - Reduced mtDNA content
  - Multiple mtDNA deletions or mtDNA depletion along with ragged red fibers and/or COX-deficient fibers in skeletal muscle
- Relevant histopathology, investigative biomarkers, and/or neuroimaging, if available

NOTE: This is not an all-inclusive list of the parameters of a medical history of a patient with TK2d. Please always use your independent clinical judgment when deciding what to include for review

Potential Reasons for Denial

Listed below are some of the most common reasons why a health plan may initially deny coverage of KYGEVVI that can be addressed in a letter of appeal, using the patient's medical history and your clinical judgment.

- Unclear understanding of KYGEVVI indication
- Lack of information regarding symptoms, lab results, or histopathology
- Missing clinical information to support initiation of KYGEVVI
- Confusion regarding patient's participation in the KYGEVVI clinical trial (if applicable)

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COX=cytochrome-C oxidase; HCP=healthcare professional; mtDNA=mitochondrial deoxyribonucleic acid; *TK2*=thymidine kinase 2 gene; TK2d=thymidine kinase 2 deficiency.

Guide to Writing a Letter of Medical Necessity* (cont'd)

ONWARD

Patient Support

If you have questions about enrolling your patients who are receiving KYGEVVI in the ONWARD® Patient Support Program, please visit ucbONWARD.com to access resources for healthcare professionals.

ONWARD is provided as a service of UCB and is intended to support the appropriate use of UCB medicines. ONWARD may be amended or canceled at any time without notice. Some program and eligibility restrictions may apply.

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Gastrointestinal Adverse Reactions

Diarrhea and vomiting leading to hospitalization, dose reduction, and permanent discontinuation were reported in patients treated with KYGEVVI. Based on the severity of the diarrhea and/or vomiting, reduce the dosage of KYGEVVI or interrupt treatment until diarrhea and/or vomiting improves or returns to baseline. Consider restarting KYGEVVI at the last tolerated dose, and increase the dose as tolerated. For persistent or recurring diarrhea and/or vomiting, consider discontinuing KYGEVVI permanently and provide supportive care with electrolyte repletion as clinically indicated.

Adverse Reactions

The most common adverse reactions (incidence ≥5%) are diarrhea, abdominal pain (including abdominal pain upper), vomiting, alanine aminotransferase increased (ALT), and aspartate aminotransferase increased (AST).

Please see the full Prescribing Information.

For more information about KYGEVVI, visit KYGEVVIhcp.com.

For additional information, contact UCBCares® at 1-844-599-CARE (2273).

References: 1. Wang J, El-Hattab AW, Wong LJC. *TK2*-related mitochondrial DNA maintenance defect, myopathic form. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 2012, updated 2018. PMID: 23230576. **2.** de Barcelos IP, Emmanuele V, Hirano M. Advances in primary mitochondrial myopathies. *Curr Opin Neurol*. 2019;32(5):715-721. **3.** Garone C, Taylor RW, Nascimento A, et al. Retrospective natural history of thymidine kinase 2 deficiency. *J Med Genet*. 2018;55(8):515-521.

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