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

Guide to Writing a Letter of Appeal*

When a patient's health plan denies a prior authorization (PA) request for KYGEVVI, you can submit a letter of appeal in response to the official denial letter. In the letter of appeal, you can explain your clinical rationale for prescribing KYGEVVI, provide supporting documentation that addresses the reason(s) for the denial, and request approval.

This resource provides information on the process and a checklist to follow when drafting a letter of appeal. In addition, this document includes a sample letter with information that health plans often require.

Preparing an Effective Letter of Appeal

Refer to the health plan's specific appeals process, as there may be varying processes

- Some health plans may require you to use their specific appeal form; if not, draft the letter on your letterhead

Confirm the health plan's time frame for submitting an appeal

- If appropriate, mark the appeal request "urgent" based on the patient's needs and the health plan's timelines

Understand the reason for denial and include why you believe the decision should be reconsidered

- If the denial was for inaccurate or incomplete information, correct or update the discrepancies
- Include specific and relevant medical information that, in your independent clinical judgment, supports the use of KYGEVVI for your patient in accordance with the health plan's criteria
- Directly address any specific rationale cited by the health plan for the denial

Include all required information. Information recommended for a letter of appeal typically includes:

- Patient's full name, plan identification number, gender, date of birth, and case identification number (if available)
- Patient's medical history, diagnosis (including ICD-10-CM code), and any other patient characteristics and/or clinical considerations relevant to KYGEVVI therapy
- Summary of your treatment recommendations
- Any additional enclosures to be submitted at the same time as the letter of appeal and in the correct order indicated in the health plan's appeal instructions. Additional enclosures typically include:
  - Letter of Medical Necessity
  - A copy of the health plan's denial letter
  - Relevant patient documentation, such as physician notes, lab results, and medical records
  - Clinical support, including trial data or relevant peer-reviewed articles (as applicable)

***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).

HCP=healthcare professional; ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification.

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 Appeal* (cont'd)

Sample Letter of Appeal

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

SAMPLE LETTER OF APPEAL
UPDATE AND PLACE ON YOUR LETTERHEAD

[Date]

[Contact Name]
[Title]
[Name of Health Insurance Company or Pharmacy Benefit Manager]
[Address]
[City, State ZIP Code]
Date(s) of service: [Date(s)]

Re: [First/Second]-Level Appeal for Coverage Denial of KYGEVVI® (doxecitine and doxribtimine): [Request for Expedited Review Due to Medical Urgency]

Date of Denial Letter: [MM-DD-YYYY]
Denial Reference Number: [Denial Reference Number]
Insured: [Full Name of Patient]; Date of Birth: [MM-DD-YYYY]; Policy Number: [Number]; Group Number: [Number]

Dear [Name of Contact]:

I am writing on behalf of my patient, [Full Name of Patient], to appeal the coverage denial for treatment with KYGEVVI for thymidine kinase 2 deficiency (TK2d). The aforementioned letter of denial stated [list reasons for denial] as the reason for coverage denial. This appeal letter 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 TK2d.

[Please provide a summary of rationale for treatment with KYGEVVI for this patient based on your independent clinical assessment and medical opinion. Address the reason for denial directly. 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], and, as such, the coverage decision should be reversed. 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, Letter of Medical Necessity, copy of health plan's denial letter, etc.]

Download a copy of the full Prescribing Information.

Directly address the reason for denial and include relevant medical information that, in your clinical judgment, supports your patient's appropriate use in accordance with the health plan's criteria. See next page for specific examples of patient medical history to consider including.

Confirm that the documents are listed and attached in the order specified by the health plan.

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

Examples of Medical History for a Letter of Appeal

- 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.

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Guide to Writing a Letter of Appeal* (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.

IMPORTANT SAFETY INFORMATION

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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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