kygevvi™

(doxecitine and doxribtimine)

Powder for Oral Solution

2 g/2 g per packet

The first and only FDA-approved treatment for people with early-onset TK2d

KYGEVVI is used for the treatment of **thymidine kinase 2 deficiency (TK2d)** **in adults and children** with a symptom onset on or before 12 years of age.

INDICATION

KYGEVVI is a prescription medicine used for the treatment of thymidine kinase 2 deficiency (TK2d) in adults and children with a symptom onset on or before 12 years of age.

IMPORTANT SAFETY INFORMATION

KYGEVVI may cause serious side effects including elevated liver enzyme levels. Increased liver enzyme levels in your blood are common with KYGEVVI. Your healthcare provider will do blood tests to check your liver enzyme levels before starting treatment and during treatment with KYGEVVI. Tell your healthcare provider right away if you develop any signs or symptoms of liver problems, including loss of appetite, pain on the right side of your stomach area, dark or amber-colored urine, yellowing of your skin or the white part of your eyes, nausea and vomiting, or itching.

Please see the full Important Safety Information on page 7 and the Patient Information Leaflet.

WHAT IS THYMIDINE KINASE 2 DEFICIENCY (TK2d)?

TK2d is a **mitochondrial disease**

Mitochondrial diseases are the result of genetic mutations that impact the mitochondria.

Mitochondria are responsible for making energy that the body's organs need to function properly.

Some mitochondrial diseases are called mitochondrial myopathies, which means that they mainly affect the muscles. TK2d is a mitochondrial myopathy, and muscle weakness is the main symptom. It can show up as fatigue, trouble eating or breathing, and difficulty with motor skills like walking.

TK2d SYMPTOMS MAY VARY, AND NOT EVERY PERSON WILL EXPERIENCE EVERY SYMPTOM. POSSIBLE SYMPTOMS INCLUDE:

Low muscle tone (called floppy baby syndrome in infants), **delay or loss of milestones** like sitting up and walking, facial weakness, and eyelid drooping

Trouble breathing that can be severe

Trouble chewing and **swallowing**

Some people experience **seizures and other neurological symptoms**

TK2d is caused by a **genetic mutation**

This mutation stops an enzyme called TK2 from working properly. This prevents the mitochondria from producing enough energy to power the body.

The result is weakness that gets worse over time in the muscles, including those needed to walk, eat, and breathe.

TK2d SYMPTOMS CAN START AT ANY POINT IN LIFE

Symptom onset at 12 years old or younger is considered early-onset TK2d.

It is possible that you or your loved one developed symptoms as an infant or child but didn't get diagnosed until after age 12.

This is still early-onset TK2d.

If you or a family member has been diagnosed with TK2d, then direct relatives (like siblings) may also carry the mutated gene or have TK2d. **Genetic testing can detect these mutations**.

Genetic testing that includes the *TK2* gene is the **only way** to confirm a diagnosis.

KYGEVVI is **intended to support mitochondrial DNA (mtDNA)** production in muscles

KYGEVVI is intended to provide building blocks called pyrimidine nucleosides that are added into muscle mtDNA. In studies with mice with TK2d, this restored mtDNA levels.

Based on preclinical data.

IMPORTANT SAFETY INFORMATION (CONT'D)

KYGEVVI may cause stomach and intestinal (gastrointestinal) problems. Diarrhea and vomiting are common with KYGEVVI, but may also be severe and lead to hospitalization. Tell your healthcare provider right away if you have diarrhea or vomiting during treatment with KYGEVVI that lasts longer than a few days.

The most common side effects of KYGEVVI include diarrhea, stomach area (abdominal) pain including pain in the upper stomach area, vomiting, and increased liver enzyme levels in your blood.

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78 treated patients with TK2d symptom onset ≤12 years of age were compared to a control group of 78 untreated patients

Clinical trials usually include two groups—one given the drug being studied and one given a placebo.

KYGEVVI data were collected differently. Researchers conducted a clinical trial where patients received KYGEVVI. Researchers also reviewed past health records of patients who had taken pyrimidine nucleosides. An expanded access program allowed other patients to receive KYGEVVI. Results from patients who received KYGEVVI were compared to results for patients who did not receive any treatment.

TO STUDY KYGEVVI, RESEARCHERS COMPARED 2 GROUPS:

Treated patients (n=78)

Health record review

+

Open-label clinical trial

+

Expanded access program

Patients were treated for 1 day to 12 years, with a median of 4 years.

Control group of untreated patients (n=78)

Health record review

+

Medical literature review

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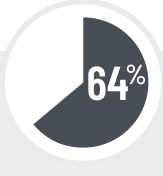
Studies found that KYGEVVI may help people with early-onset TK2d **live longer**

To see if KYGEVVI can help patients with early-onset TK2d live longer, researchers matched and compared patients who received treatment to untreated patients to determine improvement in survival time after starting treatment.

KYGEVVI was found to **reduce the overall risk of death by approximately 86%** once treatment was started compared to untreated patients.

96% (n=75/78) of treated patients with TK2d were alive at the end of the study



64% (n=50/78) of untreated patients with TK2d were alive at the end of the study

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Important Safety Information

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Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with KYGEVVI if you develop certain side effects.

Before taking or giving KYGEVVI, tell your healthcare provider about all of your medical conditions, including if you have or have had liver problems. In addition, tell your healthcare provider if you are pregnant or plan to become pregnant. It is not known if KYGEVVI will harm your unborn baby. Also, tell your healthcare provider if you are breastfeeding or plan to breastfeed. It is not known if KYGEVVI passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take KYGEVVI. **Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.

These are not all of the possible side effects of KYGEVVI. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to UCB, Inc. at UCBCares® (1-844-599-CARE [2273]).

Please see additional information in the Patient Information Leaflet.

Please see the Instructions for Use for full preparation and administration information.

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KYGEVVI is taken **3 times a day** orally or by feeding tube

You'll receive an **administration kit** to prepare and give or take KYGEVVI.

In the morning, **prepare the full one-day supply** of KYGEVVI solution.

Between doses, the prepared KYGEVVI solution can be stored at **room temperature** or in the **fridge**.

KYGEVVI is taken **3 times a day about 6 hours apart** (plus or minus 2 hours) with food.

WHAT TO EXPECT WITH KYGEVVI DOSING

- Take or give KYGEVVI exactly as your healthcare provider tells you. Your healthcare provider should tell you when and how much KYGEVVI to take or give
- Your healthcare provider may change your or your child's dose of KYGEVVI depending on how you or your child respond to treatment and based on your or your child's weight
- See the detailed Instructions for Use that comes with KYGEVVI for important information about the correct way to prepare and take or give a dose of KYGEVVI

WHAT TO DO IF YOU MISS A DOSE

If you miss a dose of KYGEVVI, take the missed dose as soon as possible. If it is within 2 hours of your next scheduled dose, do not take the missed dose. Take your next dose at your next scheduled time. Do not take 2 doses to make up for the missed dose.

Always take KYGEVVI as prescribed.

Please see the full Important Safety Information on page 7 and the Patient Information Leaflet.

ONWARD® was created with the help of people with rare diseases and healthcare providers

ONWARD
RARE DISEASE SUPPORT DESIGNED TO MOVE YOU FORWARD

- Personalized support from a dedicated **Care Coordinator*** throughout the treatment journey
- Provides updated information and support to work with our specialty pharmacy, PANTHERx Rare
- Help with reviewing insurance coverage and potential financial assistance options
- Preparation and administration support from PANTHERx Rare
- **Tools** and **resources** to get started and ongoing treatment support

JOIN ONWARD: There are three ways to get started.

ASK
your doctor
to sign you up.

OR

VISIT
ucbONWARD.com/KYGEVVI
to download an ONWARD
start form and take it
to your doctor.

OR

CALL
1-844-ONWARD-1
(1-844-669-2731)
Monday–Friday,
8 AM–8 PM ET.

*ONWARD Care Coordinators do not provide medical advice and will refer you to your healthcare professional for any questions related to your treatment plan.

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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Support is available on your rare disease journey

Find resources and **community**

There are resources that can help you navigate life with TK2d and treatment with KYGEVVI.

There is also a small but mighty TK2d community with strong supportive networks around the world, such as:

United Mitochondrial Disease Foundation (UMDF) and MitoAction

Visit **KYGEVVI.com** to explore resources, support, and more.

Helpful terms to better understand TK2d and KYGEVVI

Genetic testing: a type of diagnostic testing that typically uses a blood or saliva sample to find mutations in DNA. In the case of TK2d, genetic testing looks for changes in the *TK2* gene.

Mitochondrial DNA (mtDNA): DNA that is found in the mitochondria of cells and not the nucleus. This DNA is very important to the mitochondria's job, which is to create energy to power the body.

Mitochondrial myopathy: a type of disease caused by genetic mutations that impact the mitochondria. The most prominent symptom is muscle weakness.

Myopathy: weakness in the muscles connected to bones, also called skeletal muscles.

Placebo: a treatment that looks like and is given the same way as the drug being studied in a clinical trial. Researchers use the response to the placebo drug to evaluate how the study drug performs. A well-known example is the sugar pill.

Survival time: the length of time patients are alive during a study. It is a common endpoint in cancer clinical trials to measure how well a treatment works.

The first and only FDA-approved treatment for people with early-onset **TK2d**

KYGEVVI is a prescription medicine used for the treatment of thymidine kinase 2 deficiency (TK2d) in adults and children with a symptom onset on or before 12 years of age.

Studies found KYGEVVI treatment **improved survival time**, lowering the overall risk of death by **approximately 86%** from treatment start compared to untreated patients.

The most common side effects of KYGEVVI are diarrhea, stomach area pain, vomiting, and increased liver enzyme levels in your blood

KYGEVVI is taken **3x every day** by mouth or feeding tube

Support is available for eligible patients through ONWARD®

Visit **KYGEVVI.com** to learn more.

IMPORTANT SAFETY INFORMATION (CONT'D)

KYGEVVI may cause serious side effects including elevated liver enzyme levels. Increased liver enzyme levels in your blood are common with KYGEVVI. Your healthcare provider will do blood tests to check your liver enzyme levels before starting treatment and during treatment with KYGEVVI. Tell your healthcare provider right away if you develop any signs or symptoms of liver problems, including loss of appetite, pain on the right side of your stomach area, dark or amber-colored urine, yellowing of your skin or the white part of your eyes, nausea and vomiting, or itching.

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