KEVEYIS (pronounced keh-VAY-iss) (dichlorphenamide) is the first and only FDA-approved treatment for Primary Periodic Paralysis.[1] It is a prescription drug used to treat primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and other similar diseases. Keveyis has been shown to reduce the number, severity, and duration of Primary Periodic Paralysis attacks.[1,2]

Primary Periodic Paralysis (PPP) is a rare genetic condition that affects muscles and causes episodes of muscle weakness and/or temporary paralysis, that can be progressive and debilitating.[3,4]

PPP episodes (muscle weakness or temporary paralysis) can vary in how often they occur, how severe they are, and in how long they last. A study found that most episodes range from 30 minutes to several hours. For some patients, episodes can last for days.[5]

Episodes of weakness or paralysis usually start happening in childhood before age 20. Some people begin having attacks as early as age 2 or even younger.[5] PPP is usually inherited, meaning that it is passed down from a parent to a child. However, not having the genetic abnormality does not mean you don't have PPP if you have the signs and symptoms of the condition.[4,5]

There are several subtypes of PPP with varying prevalence:
Hyperkalemic (~1 in 200,000)[3]
Common symptoms include attacks of weakness in the limbs and elevated serum levels of potassium as the potassium shifts from the muscle to the extracellular space. Sometimes serum potassium levels can remain normal.[3,8]

Hypokalemic (~1 in 100,000)[3]
Typically manifests as flaccid muscle weakness that can last for at least several hours. Serum levels of potassium usually decrease as the potassium shifts from the extracellular space to skeletal muscle.[8]

Paramyotonia congenita (PMC) (<1 in 100,000)[6]
Patients may present with sustained muscle tensing that prevents muscles from relaxing. PMC can present with elevated or normal serum potassium levels. [3,6]

Andersen-Tawil syndrome (ATS) (1 in 1 million)[3]*
Serum potassium levels can be low, high, or normal.[3] Other characteristics include abnormal skeletal features and cardiac abnormalities such as ventricular arrhythmias, prolonged QT interval, and prominent U waves. [7,8]
*Patients with ATS were not included in clinical trials for KEVEYIS.

Important Safety Information

Contraindications

- Hypersensitivity to dichlorphenamide or other sulfonamides
- Concomitant use of KEVEYIS and high-dose aspirin
- Severe pulmonary disease, limiting compensation to metabolic acidosis caused by KEVEYIS
- Hepatic insufficiency: KEVEYIS may aggravate hepatic encephalopathy

Warnings and Precautions

Hypersensitivity and Other Life-Threatening Reactions

- Fatalities associated with the administration of sulfonamides have occurred because of adverse reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias.
- Pulmonary involvement can occur in isolation or as part of a systemic reaction.
- Discontinue KEVEYIS at the first appearance of skin rash or any sign of immune-mediated or other life-threatening adverse reaction.

Concomitant Use of Aspirin or Other Salicylates

- Carbonic anhydrous inhibitors, including KEVEYIS, can cause metabolic acidosis, which can increase the risk of salicylate toxicity.
- Anorexia, tachypnea, lethargy, and coma have been reported with concomitant use of dichlorphenamide and high-dose aspirin.
- Concomitant use of KEVEYIS and high-dose aspirin is contraindicated. Use with caution and carefully monitor in patients receiving low-dose aspirin.

Hypokalemia

- KEVEYIS increases potassium excretion and can cause hypokalemia.
- The risk of hypokalemia is greater when KEVEYIS is used in patients with conditions associated with hypokalemia (e.g., adrenocortical excess, renal tubular acidosis type 1 and 2), and in patients receiving other drugs that may cause hypokalemia (e.g., loop diuretics, thiazide diuretics, laxatives, antifungals, penicillin, and theophylline).
- Baseline and periodic measurements of serum potassium are recommended.
- If hypokalemia develops or persists, consider reducing the dose or discontinuing KEVEYIS and correction of potassium levels.

Metabolic Acidosis

- KEVEYIS can cause hyperchloremic non-anion gap metabolic acidosis.
- Concomitant use of KEVEYIS with other drugs that cause metabolic acidosis may increase the severity of acidosis.
- Concomitant use of KEVEYIS in compensated patients with respiratory acidosis, such as in advanced lung diseases, may lead to respiratory decompensation.
- Baseline and periodic measurements of serum bicarbonate during KEVEYIS treatment are recommended.
- If metabolic acidosis develops or persists, consider reducing the dose or discontinuing KEVEYIS.

Falls

- KEVEYIS increases the risk of falls; risk is greater in the elderly and with higher doses.
- Consider dose reduction or discontinuation of KEVEYIS in patients who experience falls while treated with KEVEYIS.

Pregnancy and Lactation

Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known in humans whether dichlorphenamide is excreted in human milk; exercise caution when administered to a nursing woman.

Adverse Reactions

The most common adverse reactions seen in clinical trials (incidence ≥ 10% and greater than placebo) include paresthesias, cognitive disorder, dysgeusia, and confusional state.

Please see Full Prescribing Information

1. KEVEYIS [package insert]. Feasterville-Trevose, PA: Strongbridge Biopharma; 2019.
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3. Statland JM, Fontaine B, Hanna MG, et al. Review of the diagnosis and treatment of periodic paralysis. *Muscle Nerve*. 2018;57:522-530.
4. Cavel-Greant D, Lehmann-Horn F, Jurkat-Rott K. The impact of permanent muscle weakness on quality of life in periodic paralysis: a survey of 66 patients. *Acta Myol*. 2012;31:126-133.
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8. Weber F, Jurkat-Rott K, Lehmann-Horn F. Hyperkalemic Periodic Paralysis. GeneReviews®. NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. 2016.