HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DICLOFENAC POTASSIUM FOR ORAL SOLUTION safely and effectively. See full prescribing information for DICLOFENAC POTASSIUM FOR ORAL SOLUTION.

DICLOFENAC POTASSIUM for oral solution
Initial U.S. Approval: 1988

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

See full prescribing information for complete boxed warning

- **Non-steroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use (5.1)**
- **Diclofenac potassium for oral solution is contraindicated in the setting of coronary artery bypass graft (CABG) surgery (4, 5.1)**
- **NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events (5.2)**

----------------------INDICATIONS AND USAGE----------------------

Diclofenac potassium for oral solution is a non-steroidal anti-inflammatory drug (NSAID) indicated for the acute treatment of migraine attacks with or without aura in adults 18 years of age or older (1)

Limitations of Use (1):

- Diclofenac potassium for oral solution is not indicated for the prophylactic therapy of migraine
- Safety and effectiveness of diclofenac potassium for oral solution not established for cluster headache, which is present in an older, predominantly male population

-------------------DOSAGE AND ADMINISTRATION-------------------

Single 50 mg dose; mix single packet contents with 1 to 2 ounces or 2 to 4 tablespoons (30 to 60 mL) of water prior to administration

- Use the lowest effective dose for shortest duration consistent with individual patient treatment goals (2.1)

-----------------DOSAGE FORMS AND STRENGTHS-----------------

Packets: Each containing buffered diclofenac potassium 50 mg in a soluble powder (3)

-------------------------CONTRAINDICATIONS-------------------------

- Known hypersensitivity to diclofenac or NSAIDs or any components of the drug product (4)
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs (4)
- In the setting of (CABG) surgery (4)

-------------------WARNINGS AND PRECAUTIONS-------------------

- Hepatotoxicity: Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop (5.3, 8.6, 12.3)
- Hypertension: Patients taking some antihypertensive medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure (5.4, 7)
- Heart Failure and Edema: Avoid use of diclofenac potassium for oral solution in patients with severe heart failure unless benefits are expected to outweigh risk of worsening heart failure (5.5)
- Renal Toxicity: Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia. Avoid use of diclofenac potassium for oral solution in patients with advanced renal disease unless benefits are expected to outweigh risk of worsening renal function (5.6)
- Anaphylactic Reactions: Seek emergency help if an anaphylactic reaction occurs (5.7)
- Exacerbation of Asthma Related to Aspirin Sensitivity: Diclofenac potassium for oral solution is contraindicated in patients with aspirin-sensitive asthma. Monitor patients with preexisting asthma (without aspirin sensitivity) (5.8)
- Serious Skin Reactions: Discontinue diclofenac potassium for oral solution at first appearance of skin rash or other signs of hypersensitivity (5.9).
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): Discontinue and evaluate clinically (5.10)
- Medication Overuse Headache: Detoxification may be necessary. (5.11)
- Fetal Toxicity: Limit use of NSAIDs, including diclofenac potassium for oral solution, between about 20 to 30 weeks in pregnancy due to the risk of oligohydramnios/fetal renal dysfunction. Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/fetal dysfunction and premature closure of the fetal ductus arteriosus (5.12, 8.1)
- Hematologic Toxicity: Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia (5.13, 7)

-----------------------ADVERSE REACTIONS-----------------------

Most common adverse reactions (≥1% and >placebo) were nausea and dizziness (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Taro Pharmaceuticals U.S.A., Inc. at 1-866-923-4914 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

------------------------DRUG INTERACTIONS------------------------

- Drugs that Interfere with Hemostasis (e.g. warfarin, aspirin, SSRIs/SNRIs): Monitor patients for bleeding who are concomitantly taking diclofenac potassium for oral solution with drugs that interfere with hemostasis. Concomitant use of diclofenac potassium for oral solution and analgesic doses of aspirin is not generally recommended (7)
- ACE Inhibitors and ARBs: Concomitant use with diclofenac potassium for oral solution in elderly, volume depleted, or those with renal impairment may result in deterioration of renal function. In such high risk patients, monitor for signs of worsening renal function (7)
- Diuretics: NSAIDs can reduce natriuretic effect of loop and thiazide diuretics. Monitor patients to assure diuretic efficacy including antihypertensive effects (7)
- Digoxin: Concomitant use with diclofenac potassium for oral solution can increase serum concentration and prolong half-life of digoxin. Monitor serum digoxin levels (7)

-----------------USE IN SPECIFIC POPULATIONS-----------------

- Infertility: NSAIDs are associated with reversible infertility. Consider withdrawal of diclofenac potassium for oral solution in women who have difficulties conceiving (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 6/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Thrombotic Events

- **Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use *[see Warnings and Precautions (5.1)]*.**
- **Diclofenac potassium for oral solution is contraindicated in the setting of coronary artery bypass graft (CABG) surgery *[see Contraindications (4) and Warnings and Precautions (5.1)]*.**

Gastrointestinal Bleeding, Ulceration, and Perforation

- **NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events *[see Warnings and Precautions (5.2)]*.**

1 INDICATIONS AND USAGE

Diclofenac potassium for oral solution is indicated for the acute treatment of migraine attacks with or without aura in adults (18 years of age or older).

Limitations of Use

- Diclofenac potassium for oral solution is not indicated for the prophylactic therapy of migraine.
- The safety and effectiveness of diclofenac potassium for oral solution have not been established for cluster headache, which is present in an older, predominantly male population.

2 DOSAGE AND ADMINISTRATION

2.1 Acute Treatment of Migraine

Administer one packet (50 mg) of diclofenac potassium for oral solution for the acute treatment of migraine. Empty the contents of one packet into a cup containing 1 to 2 ounces (30 to 60 mL) of water, mix well and drink immediately.

Do not use liquids other than water.

Taking diclofenac potassium for oral solution with food may cause a reduction in effectiveness compared to taking diclofenac potassium for oral solution on an empty stomach *[see Clinical Pharmacology (12.3)]*.

Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. The safety and effectiveness of a second dose have not been established.

2.2 Non-Interchangeability with Other Formulations of Diclofenac

Different formulations of oral diclofenac (e.g., diclofenac potassium for oral solution, diclofenac sodium enteric-coated tablets, diclofenac sodium extended-release tablets, or diclofenac potassium immediate-release tablets) may not be bioequivalent even if the milligram strength is the same. Therefore, it is not possible to convert dosing from any other formulation of diclofenac to diclofenac potassium for oral solution.

3 DOSAGE FORMS AND STRENGTHS

Diclofenac potassium for oral solution, USP is available in individual packets each designed to deliver a 50 mg dose when mixed in water.

4 CONTRAINDICATIONS

Diclofenac potassium for oral solution is contraindicated in the following patients:

- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to diclofenac or any components of the drug product *[see Warnings and Precautions (5.7, 5.9)]*
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients *[see Warnings and Precautions (5.7, 5.8)]*
- In the setting of coronary artery bypass graft (CABG) surgery *[see Warnings and Precautions (5.1)]*

5 WARNINGS AND PRECAUTIONS

5.1 Cardiovascular Thrombotic Events

Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. Based on available data, it is unclear that the risk for CV thrombotic events is similar for all NSAIDs. The relative increase in serious CV thrombotic events over baseline conferred by NSAID use appears to be similar in those with and without known CV disease or risk factors for CV disease. However, patients with known CV disease or risk factors had a higher absolute incidence of excess serious CV thrombotic events, due to their increased baseline rate. Some observational studies found that this increased risk of serious CV thrombotic events began as early as the first weeks of treatment. The increase in CV thrombotic risk has been observed most consistently at higher doses.

To minimize the potential risk for an adverse CV event in NSAID-treated patients, use the lowest effective dose for the shortest duration possible. Physicians and patients should remain alert for the development of such events, throughout the entire treatment course, even in the absence of previous CV symptoms. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur. There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID, such as diclofenac, increases the risk of serious gastrointestinal (GI) events *[see Warnings and Precautions (5.2)]*.

Status Post Coronary Artery Bypass Graft (CABG) Surgery

Two large, controlled clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10 to 14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG *[see Contraindications (4)]*.

Post-MI Patients

Observational studies conducted in the Danish National Registry have demonstrated that patients treated with NSAIDs in the post-MI period were at increased risk of reinfarction, CV-related death, and all-cause mortality beginning in the first week of treatment. In this same cohort, the incidence of death in the first year post-MI was 20 per 100 person years in NSAID-treated patients compared to 12 per 100 person years in non-NSAID exposed patients. Although the absolute rate of death declined somewhat after the first year post-MI, the increased relative risk of death in NSAID users persisted over at least the next four years of follow-up.

Avoid the use of diclofenac potassium for oral solution in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If diclofenac potassium for oral solution is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

5.2 Gastrointestinal Bleeding, Ulceration, and Perforation

NSAIDs, including diclofenac, cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occurred in approximately 1% of patients treated for 3 to 6 months, and in about 2% to 4% of patients treated for one year. However, even short-term NSAID therapy is not without risk.

Risk Factors for GI Bleeding, Ulceration, and Perforation

Patients with a prior history of peptic ulcer disease and/or GI bleeding who used NSAIDs had a greater than 10-fold increased risk for developing a GI bleed compared to patients without these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy; concomitant use of oral corticosteroids, aspirin, anticoagulants, or selective serotonin reuptake inhibitors (SSRI); smoking; use of alcohol; older age; and poor general health status. Most postmarketing reports of fatal GI events occurred in elderly or debilitated patients. Additionally, patients with advanced liver disease and/or coagulopathy are at increased risk for GI bleeding.

Strategies to Minimize the GI Risk in NSAID-treated patients:

- Use the lowest effective dosage for the shortest possible duration.
- Avoid administration of more than one NSAID at a time.
- Avoid use in patients at higher risk unless benefits are expected to outweigh the increased risk of bleeding. For high risk patients, as well as those with active GI bleeding, consider alternate therapies other than NSAIDs.
- Remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy.
- If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue diclofenac potassium for oral solution until a serious GI adverse event is ruled out.
- In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding *[see Drug Interactions (7)]*.

5.3 Hepatotoxicity

Elevations of one or more liver tests may occur during therapy with diclofenac potassium for oral solution. These laboratory abnormalities may progress, may persist, or may only be transient with continued therapy. Borderline elevations (less than 3 times the upper limit of the normal [ULN] range) or greater elevations of transaminases occurred in about 15% of diclofenac-treated patients. Of the markers of hepatic function, ALT (SGPT) is recommended for the monitoring of liver injury.

In clinical trials, meaningful elevations (i.e., more than 3 times the ULN) of AST (SGOT) occurred in about 2% of approximately 5,700 patients at some time during treatment (ALT was not measured in all studies). In an open-label, controlled trial of 3,700 patients treated for 2 to 6 months, patients were monitored at 8 weeks and 1,200 patients were monitored again at 24 weeks. Meaningful elevations of ALT and/or AST occurred in about 4% of the 3,700 patients and included marked elevations (>8 times the ULN) in about 1% of the 3,700 patients. In this open-label study, a higher incidence of borderline (less than 3 times the ULN), moderate (3 to 8 times the ULN), and marked (>8 times the ULN) elevations of ALT or AST was observed in patients receiving diclofenac when compared to other NSAIDs. Almost all meaningful elevations in transaminases were detected before patients became symptomatic *[see Warnings and Precautions (5.15)]*.

Abnormal tests occurred during the first 2 months of therapy with diclofenac in 42 of the 51 patients in all trials who developed marked transaminase elevations. In postmarketing reports, cases of drug-induced hepatotoxicity have been reported in the first month, and in some cases, the first 2 months of NSAID therapy, but can occur at any time during treatment with diclofenac. Postmarketing surveillance has reported cases of severe hepatic reactions, including liver necrosis, jaundice, fulminant hepatitis with and without jaundice, and liver failure. Some of these reported cases resulted in fatalities or liver transplantation.

Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue diclofenac potassium for oral solution immediately, and perform a clinical evaluation of the patient.

To minimize the potential risk for an adverse liver-related event in patients treated with diclofenac potassium for oral solution, use the lowest effective dose for the shortest duration possible. Exercise caution when prescribing diclofenac potassium for oral solution with concomitant drugs that are known to be potentially hepatotoxic (e.g., acetaminophen, certain antibiotics, antiepileptics). Caution patients to avoid taking nonprescription acetaminophen-containing products while using diclofenac potassium for oral solution.

5.4 Hypertension

NSAIDs, including diclofenac potassium for oral solution, can lead to new onset of hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Use NSAIDs, including diclofenac potassium for oral solution, with caution in patients with hypertension. Monitor blood pressure closely during the initiation of NSAID treatment and throughout the course of therapy.

Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazides, or loop diuretics may have impaired response to these therapies when taking NSAIDs *[see Drug Interactions (7)]*.

5.5 Heart Failure and Edema

The Coxib and traditional NSAID Trialists' Collaboration meta-analysis of randomized controlled trials demonstrated an approximately two-fold increase in hospitalizations for heart failure in COX-2 selective-treated patients and nonselective NSAID-treated patients compared to placebo-treated patients. In a Danish National Registry study of patients with heart failure, NSAID use increased the risk of MI, hospitalization for heart failure, and death.

Additionally, fluid retention and edema have been observed in some patients treated with NSAIDs. Use of diclofenac may blunt the CV effects of several therapeutic agents used to treat these medical conditions (e.g., diuretics, ACE inhibitors, or angiotensin receptor blockers [ARBs]) *[see Drug Interactions (7)]*.

Avoid the use of diclofenac potassium for oral solution in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If diclofenac potassium for oral solution is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

5.6 Renal Toxicity and Hyperkalemia

Renal Toxicity

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, dehydration, hypovolemia, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors or ARBs, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

No information is available from controlled clinical studies regarding the use of diclofenac potassium for oral solution in patients with advanced renal disease. The renal effects of diclofenac potassium for oral solution may hasten the progression of renal dysfunction in patients with pre-existing renal disease.

Correct volume status in dehydrated or hypovolemic patients prior to initiating diclofenac potassium for oral solution. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia during use of diclofenac potassium for oral solution *[see Drug Interactions (7)]*. Avoid the use of diclofenac potassium for oral solution in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If diclofenac potassium for oral solution is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Hyperkalemia

Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state.

5.7 Anaphylactic Reactions

Diclofenac has been associated with anaphylactic reactions in patients with and without known hypersensitivity to diclofenac and in patients with aspirin-sensitive asthma *[see Contraindications (4) and Warnings and Precautions (5.8)]*.

Seek emergency help if an anaphylactic reaction occurs.

5.8 Exacerbation of Asthma Related to Aspirin Sensitivity

A subpopulation of patients with asthma may have aspirin-sensitive asthma which may include chronic rhinosinusitis complicated by nasal polyps; severe, potentially fatal bronchospasm; and/or intolerance to aspirin and other NSAIDs. Because cross-reactivity between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, diclofenac potassium for oral solution is contraindicated in patients with this form of aspirin sensitivity *[see Contraindications (4)]*. When diclofenac potassium for oral solution is used in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

5.9 Serious Skin Reactions

NSAIDs, including diclofenac, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin reactions, and to discontinue the use of diclofenac potassium for oral solution at the first appearance of skin rash or any other sign of hypersensitivity.

Diclofenac potassium for oral solution is contraindicated in patients with previous serious skin reactions to NSAIDs *[see Contraindications (4)]*.

5.10 Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as diclofenac potassium for oral solution. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue diclofenac potassium for oral solution and evaluate the patient immediately.

5.11 Medication Overuse Headache

Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, nonsteroidal anti-inflammatory drugs or combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in frequency of migraine attacks. Detoxification of patients, including withdrawal of the overused drugs and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary.

5.12 Fetal Toxicity

Premature Closure of Fetal Ductus Arteriosus

Avoid use of NSAIDs, including diclofenac potassium for oral solution, in pregnant women at about 30 weeks gestation and later. NSAIDs, including diclofenac potassium for oral solution, increase the risk of premature closure of the fetal ductus arteriosus at approximately this gestational age.

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs, including diclofenac potassium for oral solution, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation.

Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit diclofenac potassium for oral solution use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if diclofenac potassium for oral solution treatment extends beyond 48 hours. Discontinue diclofenac potassium for oral solution if oligohydramnios occurs and follow up according to clinical practice *[see Use in Specific Populations (8.1)]*.

5.13 Hematologic Toxicity

Anemia has occurred in NSAID-treated patients. This may be due to occult or gross blood loss, fluid retention, or an incompletely described effect upon erythropoiesis. If a patient treated with diclofenac potassium for oral solution has any signs or symptoms of anemia, monitor hemoglobin or hematocrit.

NSAIDs, including diclofenac potassium for oral solution, may increase the risk of bleeding events. Concomitant use of warfarin and other anticoagulants, antiplatelet agents (e.g., aspirin), and serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) may increase this risk. Monitor these patients and any patient who may be adversely affected by alterations in platelet function for signs of bleeding *[see Drug Interactions (7)]*.

5.14 Masking of Inflammation and Fever

The pharmacological activity of diclofenac potassium for oral solution in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

5.15 Laboratory Monitoring

Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs, consider monitoring patients on long-term NSAID treatment with a CBC and a chemistry profile periodically *[see Warnings and Precautions (5.2, 5.3, 5.6)]*.

Discontinue diclofenac potassium for oral solution if abnormal liver tests or renal tests persist or worsen.

5.16 Phenylketonurics

Diclofenac potassium for oral solution contains phenylalanine 25 mg per each 50 mg packet.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Cardiovascular Thrombotic Events *[see Warnings and Precautions (5.1)]*
- GI Bleeding, Ulceration and Perforation *[see Warnings and Precautions (5.2)]*
- Hepatotoxicity *[see Warnings and Precautions (5.3)]*
- Hypertension *[see Warnings and Precautions (5.4)]*
- Heart Failure and Edema *[see Warnings and Precautions (5.5)]*
- Renal Toxicity and Hyperkalemia *[see Warnings and Precautions (5.6)]*
- Anaphylactic Reactions *[see Warnings and Precautions (5.7)]*
- Serious Skin Reactions *[see Warnings and Precautions (5.9)]*
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) *[see Warnings and Precautions (5.10)]*
- Medication Overuse Headache *[see Warnings and Precautions (5.11)]*
- Hematologic Toxicity *[see Warnings and Precautions (5.13)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of a single dose of diclofenac potassium for oral solution was evaluated in 2 placebo-controlled trials with a total of 634 migraine patients treated with diclofenac potassium for oral solution for a single migraine headache. Following treatment with diclofenac potassium (either diclofenac potassium for oral solution or diclofenac potassium immediate-release tablets [as a control]), 5 subjects (0.8%) withdrew from the studies; following placebo exposure, 1 subject (0.2%) withdrew.

The most common adverse reactions (i.e., that occurred in 1% or more of diclofenac potassium for oral solution-treated patients) and more frequent with diclofenac potassium for oral solution than with placebo were nausea and dizziness (see Table 1).

Table 1: Adverse Reactions with Incidence >1% and Greater Than Placebo in Studies 1 and 2 Combined

Adverse Reactions	Diclofenac Potassium for Oral Solution n=634	Placebo n=646
Gastrointestinal		
Nausea	3%	2%
Nervous System		
Dizziness	1%	0.5%

The most common adverse events resulting in discontinuation of patients following diclofenac potassium for oral solution dosing in controlled clinical trials were urticaria (0.2%) and flushing (0.2%). No withdrawals were due to a serious reaction.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of diclofenac or other NSAIDs. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Adverse Reactions Reported With Diclofenac and Other NSAIDs

In patients taking diclofenac or other NSAIDs, the most frequently reported adverse reactions occurring in approximately 1% to 10% of patients are: GI reactions (including abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers [gastric/duodenal], and vomiting), abnormal renal function, anemia, dizziness, edema, elevated liver enzymes, headaches, increased bleeding time, pruritus, rashes, and tinnitus.

Additional adverse reactions reported in patients taking NSAIDs include occasionally:

Body as a Whole: Fever, infection, sepsis
Cardiovascular System: Congestive heart failure, hypertension, tachycardia, syncope
Digestive System: Dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice
Hemic and Lymphatic System: Ecchymosis, eosinophilia, leukopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia
Metabolic and Nutritional: Weight changes
Nervous System: Anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo
Respiratory System: Asthma, dyspnea
Skin and Appendages: Alopecia, photosensitivity, sweating increased
Special Senses: Blurred vision
Urogenital System: Cystitis, dysuria, hematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure

Other adverse reactions in patients taking NSAIDs, which occur rarely, are:

Body as a Whole: Anaphylactic reactions, appetite changes, death
Cardiovascular System: Arrhythmia, hypotension, myocardial infarction, palpitations, vasculitis
Digestive System: Colitis, eructation, liver failure, pancreatitis
Hemic and Lymphatic System: Agranulocytosis, hemolytic anemia, aplastic anemia, lymphadenopathy, pancytopenia
Metabolic and Nutritional: Hyperglycemia
Nervous System: Convulsions, coma, hallucinations, meningitis
Respiratory System: Respiratory depression, pneumonia
Skin and Appendages: Angioedema, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, urticaria
Special Senses: Conjunctivitis, hearing impairment

7 DRUG INTERACTIONS

See Table 2 for clinically significant drug interactions with diclofenac.

Table 2: Clinically Significant Drug Interactions with Diclofenac

Drugs That Interfere with Hemostasis	
Clinical Impact:	• Diclofenac and anticoagulants such as warfarin have a synergistic effect on bleeding. The concomitant use of diclofenac and anticoagulants have an increased risk of serious bleeding compared to the use of either drug alone. • Serotonin release by platelets plays an important role in hemostasis. Case-control and cohort epidemiological studies showed that concomitant use of drugs that interfere with serotonin reuptake and an NSAID may potentiate the risk of bleeding more than an NSAID alone.
Intervention:	Monitor patients with concomitant use of diclofenac potassium for oral solution with anticoagulants (e.g., warfarin), antiplatelet agents (e.g., aspirin), selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs) for signs of bleeding *[see Warnings and Precautions (5.13)]*.
Aspirin	
Clinical Impact:	Controlled clinical studies showed that the concomitant use of NSAIDs and analgesic doses of aspirin does not produce any greater therapeutic effect than the use of NSAIDs alone. In a clinical study, the concomitant use of an NSAID and aspirin was associated with a significantly increased incidence of GI adverse reactions as compared to use of the NSAID alone *[see Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)]*.
Intervention:	Concomitant use of diclofenac potassium for oral solution and analgesic doses of aspirin is not generally recommended because of the increased risk of bleeding *[see Warnings and Precautions (5.13)]*.
ACE Inhibitors, Angiotensin Receptor Blockers, and Beta-Blockers	
Clinical Impact:	• NSAIDs may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or beta-blockers (including propranolol). • In patients who are elderly, volume-depleted (including those on diuretic therapy), or have renal impairment, co-administration of an NSAID with ACE inhibitors or ARBs may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible.
Intervention:	• During concomitant use of diclofenac potassium for oral solution and ACE-inhibitors, ARBs, or beta-blockers, monitor blood pressure to ensure that the desired blood pressure is obtained. • During concomitant use of diclofenac potassium for oral solution and ACE-inhibitors or ARBs in patients who are elderly, volume-depleted, or have impaired renal function, monitor for signs of worsening renal function *[see Warnings and Precautions (5.6)]*.
Diuretics	
Clinical Impact:	Clinical studies, as well as post-marketing observations, showed that NSAIDs reduced the natriuretic effect of loop diuretics (e.g., furosemide) and thiazide diuretics in some patients. This effect has been attributed to the NSAID inhibition of renal prostaglandin synthesis.
Intervention:	During concomitant use of diclofenac potassium for oral solution with diuretics, observe patients for signs of worsening renal function, in addition to assuring diuretic efficacy including antihypertensive effects *[see Warnings and Precautions (5.6)]*.

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Medication Guide
Diclofenac Potassium (dye-KLOE-fen-ak poe-TAS-ee-um) for Oral Solution, USP

What is the most important information I should know about diclofenac potassium for oral solution?

Diclofenac potassium for oral solution contains diclofenac (a non-steroidal anti-inflammatory drug or NSAID).

NSAIDs, including diclofenac potassium for oral solution, can cause serious side effects, including:

- **Increased risk of a heart attack or stroke that can lead to death.** This risk may happen early in treatment and may increase:
  - with increasing doses of NSAIDs
  - with longer use of NSAIDs

Do not take NSAIDs, including diclofenac potassium for oral solution, right before or after a heart surgery called a "coronary artery bypass graft (CABG)."

Avoid taking NSAIDs, including diclofenac potassium for oral solution, after a recent heart attack, unless your healthcare provider tells you to. You may have an increased risk of another heart attack if you take NSAIDs after a recent heart attack.

- **Increased risk of bleeding, ulcers, and tears (perforation) of the esophagus (tube leading from the mouth to the stomach), stomach and intestines:**
  - anytime during use
  - without warning symptoms
  - that may cause death

The risk of getting an ulcer or bleeding increases with:

- past history of stomach ulcers, or stomach or intestinal bleeding with use of NSAIDs
- taking medicines called "corticosteroids", "anticoagulants", "SSRIs", or "SNRIs"
- increasing doses of NSAIDs
- longer use of NSAIDs
- smoking
- drinking alcohol
- older age
- poor health
- advanced liver disease
- bleeding problems

Diclofenac potassium for oral solution should only be used:

- exactly as prescribed
- at the lowest dose possible for your treatment
- for the shortest time needed

What is diclofenac potassium for oral solution?

Diclofenac potassium for oral solution is a prescription medicine used to treat migraine attacks in adults. It does not prevent or lessen the number of migraines you have, and it is not for other types of headaches. Diclofenac potassium for oral solution contains diclofenac potassium (a non-steroidal anti-inflammatory drug or NSAID).

How should I take diclofenac potassium for oral solution?

Take diclofenac potassium for oral solution exactly as your healthcare provider tells you to take it.

Take 1 dose of diclofenac potassium for oral solution to treat your migraine headache:

- open packet only when you are ready to use it
- empty contents of packet into 1 to 2 ounces (30 to 60 mL) of water
- mix well and drink the water and powder mixture
- throw away empty packet in a safe place and out of the reach of children.
- taking diclofenac potassium for oral solution with food may cause a reduction in effectiveness compared to taking diclofenac potassium for oral solution on an empty stomach
- do not take more diclofenac potassium for oral solution than directed by your healthcare provider. In case of overdose, get medical help or contact a Poison Control Center right away

Who should not take diclofenac potassium for oral solution?

Do not take diclofenac potassium for oral solution:

- if you have had an asthma attack, hives, or other allergic reaction with aspirin, diclofenac, or any other NSAIDs.
- right before or after heart bypass surgery.

Before taking diclofenac potassium for oral solution, tell your healthcare provider about all of your medical conditions, including if you:

- have liver or kidney problems
- have a history of stomach ulcer or bleeding in your stomach or intestines
- have any allergies to any medicines
- have chest pain, shortness of breath, irregular heartbeats
- have high blood pressure
- have asthma
- are pregnant, think you might be pregnant, or are trying to become pregnant. Taking NSAIDs, including diclofenac potassium for oral solution, at about 20 weeks of pregnancy or later may harm your unborn baby. If you need to take NSAIDs for more than 2 days when you are between 20 and 30 weeks of pregnancy, your healthcare provider may need to monitor the amount of fluid in your womb around your baby. **You should not take NSAIDs after about 30 weeks of pregnancy.**
- are breastfeeding or plan to breastfeed.
- have a headache that is different from your usual migraine

Tell your healthcare provider about all of the medicines you take, including prescription or over-the-counter medicines, vitamins or herbal supplements. NSAIDs, like diclofenac potassium for oral solution, and some other medicines can interact with each other and cause serious side effects. **Do not start taking any new medicine without talking to your healthcare provider first.**

Especially tell your doctor if you take:

- aspirin
- any anticoagulant medicines (warfarin, Coumadin, Jantoven)

Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.

What are the possible side effects of diclofenac potassium for oral solution?

Diclofenac potassium for oral solution can cause serious side effects, including:

See "What is the most important information I should know about diclofenac potassium for oral solution?"

- new or worse high blood pressure
- heart failure
- liver problems including liver failure
- kidney problems including kidney failure
- bleeding and ulcers in the stomach and intestine
- low red blood cells (anemia)
- life-threatening skin reactions
- life-threatening allergic reactions
- asthma attacks in people who have asthma
- medication overuse headaches. Some people who use too much diclofenac potassium for oral solution may have worse headaches (medication overuse headache). If your headaches get worse, your healthcare provider may decide to stop your treatment with diclofenac potassium for oral solution.
- **Other side effects of NSAIDs include:** stomach pain, constipation, diarrhea, gas, heartburn, nausea, vomiting, and dizziness.

Get emergency help right away if you get any of the following symptoms:

- shortness of breath or trouble breathing
- chest pain
- weakness in one part or side of your body
- slurred speech
- swelling of the face or throat

Stop taking diclofenac potassium for oral solution and call your healthcare provider right away if you get any of the following symptoms

- nausea that seems out of proportion to your migraine
- sudden or severe pain in your belly
- more tired or weaker than usual
- diarrhea
- itching
- your skin or eyes look yellow
- indigestion or stomach pain
- vomit blood
- there is blood in your bowel movement or it is black and sticky like tar
- unusual weight gain
- more tired or weaker than usual
- skin rash or blisters with fever
- swelling of the arms, legs, hands and feet
- flu-like symptoms

If you take too much of your NSAID, call your healthcare provider or get medical help right away.

These are not all the possible side effects of NSAIDs. For more information, ask your healthcare provider or pharmacist about NSAIDs. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Other information about NSAIDs

- Aspirin is an NSAID but it does not increase the chance of a heart attack. Aspirin can cause bleeding in the brain, stomach, and intestines. Aspirin can also cause ulcers in the stomach and intestines.
- Some NSAIDs are sold in lower doses without a prescription (over-the-counter). Talk to your healthcare provider before using over-the-counter NSAIDs for more than 10 days.

General information about the safe and effective use of NSAIDs

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use NSAIDs for a condition for which it was not prescribed. Do not give NSAIDs to other people, even if they have the same symptoms that you have. It may harm them.

If you would like more information about NSAIDs, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about NSAIDs that is written for health professionals.

For more information, call Taro Pharmaceuticals U.S.A., Inc. at 1-866-923-4914 or visit ww.taro.com

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