Nevertheless, plasma concentrations as high as 10 mcg/mL will only occupy approximately 5 % of the albumin binding sites. Thus, the unbound fraction for each enantiomer will be constant over the therapeutic range. A decrease in serum albumin، however، will result in increased free drug concentrations.

- Ketorolac tromethamine is excreted in human milk.

Metabolism:

Ketorolac tromethamine is largely metabolized in the liver. The metabolic products are hydroxylated and conjugated forms of the parent drug. The products of metabolism, and some unchanged drug, are excreted in the urine.

Excretion:

- The principal route of elimination of ketorolac and its metabolites is renal. About 92% of a given dose is found in the urine, approximately 40% as metabolites and 60% as unchanged ketorolac. Approximately 6% of a dose is excreted in the feces. A single-dose study with 10 mg ketorolac tromethamine demonstrated that the S-enantiomer is cleared approximately two times faster than the R-enantiomer and that the clearance was independent of the route of administration. This means that the ratio of S/R plasma concentrations decreases with time after each dose. There is little or no inversion of the R- to S- form in humans.
- The half-life of the ketorolac tromethamine S-enantiomer was approximately 2.5 hours compared with 5 hours for the R-enantiomer. In other studies, the half-life for the racemate has been reported to lie within the range of 5 to 6 hours.

Accumulation:

- Ketorolac tromethamine administered as an IV bolus every 6 hours for 5 days to healthy subjects, showed no significant difference in Cmax on Day 1 and Day 5. Trough levels averaged 0.29 mcg/mL on Day 1 and 0.55 mcg/mL on Day 6.Steady state was approached after the fourth dose .
- Accumulation of ketorolac tromethamine has not been studied in special populations (geriatric, pediatric, renal failure or hepatic disease patients).

Kinetics in Special Populations:

Geriatric Patient:

Based on single-dose data only, the half-life of the ketorolac tromethamine racemate increased from 5 to 7 hours in the elderly (65 to 78 years) compared with young healthy volunteers (24 to 35 years) .There was little difference in the Cmax for the two groups (elderly, 2.52 mcg/mL ± 0.77; young, 2.99 mcg/mL ± 1.03).

Pediatric Patients:

Limited information is available regarding the pharmacokinetics of dosing of ketorolac tromethamine in the pediatric population. Following a single intravenous bolus dose of 0.5 mg/kg in 10 children 4 to 8 years old, the half-life was 5.8 ± 1.6 hours, the average clearance was 0.042 ± 0.01 L/hr/kg, the volume of distribution during the terminal phase (Vß) was 0.34 ± 0.12 L/kg and the volume of distribution at steady state (Vss) was 0.26 ± 0.08 L/kg. The volume of distribution and clearance of ketorolac in pediatric patients was higher than those observed in adult subjects. There are no pharmacokinetic data available for administration of ketorolac tromethamine by the IM route in pediatric patients.

Renal Insufficiency:

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D.Azza
Alaa

Ketorolin Ampoules

composition :

each 2 ml ampoule contains :

active ingredients :

ketorolac tromethamine 30 mg

inactive ingredients :

propylene glycol , sodium chloride , sodium hydroxide / Hydrochloric acid , water for injection .

PHARMACEUTICAL FORM

Solution in Ampoule for I.M. / I.V. Injection

Clinical Pharmacology:

Pharmacodynamics:

- Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits analgesic activity. The mechanism of action of ketorolac, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition. The biological activity of ketorolac tromethamine is associated with the S-form. Ketorolac tromethamine possesses no sedative or anxiolytic properties.
- The peak analgesic effect of ketorolac tromethamine occurs within 2 to 3 hours and is not statistically significantly different over the recommended dosage range of ketorolac tromethamine. The greatest difference between large and small doses of ketorolac tromethamine by either route is in the duration of analgesia.

Pharmacokinetics:

Ketorolac tromethamine is a racemic mixture of [-]S- and [+]R-enantiomeric forms, with the S-form having analgesic activity.

Comparison of IV, IM and Oral Pharmacokinetics:

The pharmacokinetics of ketorolac tromethamine, following IV and IM doses of ketorolac tromethamine and oral doses of ketorolac tromethamine, are compared. In adults, the extent of bioavailability following administration of the oral form of ketorolac tromethamine and the IM form of ketorolac tromethamine was equal to that following an IV bolus.

Linear Kinetics:

In adults, following administration of single oral doses of ketorolac tromethamine or IM or IV doses of ketorolac tromethamine in the recommended dosage ranges, the clearance of the racemate does not change. This implies that the pharmacokinetics of ketorolac tromethamine in adults, following single or multiple IM or IV doses of ketorolac tromethamine or recommended oral doses of ketorolac tromethamine, are linear. At the higher recommended doses, there is a proportional increase in the concentrations of free and bound racemate.

Absorption:

Ketorolac tromethamine is 100% absorbed after oral administration. Oral administration of Ketorolac tromethamine after a high-fat meal resulted in decreased peak and delayed time-to-peak concentrations of ketorolac tromethamine by about 1 hour. Antacids did not affect the extent of absorption.

Distribution:

- The mean apparent volume (Vß) of ketorolac tromethamine following complete distribution was approximately 13 liters. This parameter was determined from single dose data. The ketorolac tromethamine racemate has been shown to be highly protein bound (99%)

- Ketorolac tromethamine is contraindicated in patients with active peptic ulcer disease, in patients with recent gastrointestinal bleeding or perforation and in patients with a history of peptic ulcer disease or gastrointestinal bleeding.
- Ketorolac tromethamine should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.
- Ketorolac tromethamine is contraindicated as prophylactic analgesic before any major surgery.
- Ketorolac tromethamine is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.
- Ketorolac tromethamine is contraindicated in patients with advanced renal impairment or in patients at risk for renal failure due to volume depletion.
- Ketorolac Tromethamine is contraindicated in labor and delivery because, through its prostaglandin synthesis inhibitory effect, it may adversely affect fetal circulation and inhibit uterine contractions, thus increasing the risk of uterine hemorrhage.
- Ketorolac tromethamine inhibits platelet function and is, therefore, contraindicated in patients with suspected or confirmed cerebrovascular bleeding.
- Ketorolac Tromethamine is contraindicated in patients currently receiving aspirin or NSAIDs because of the cumulative risks of inducing serious NSAID-related adverse events.
- The concomitant use of ketorolac tromethamine and probenecid is contraindicated.
- The concomitant use of ketorolac tromethamine and pentoxifylline is contraindicated.

Warnings:

Cardiovascular Risk :

NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction (MI), and stroke, which can be fatal.This risk may increase with duration of use.Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. NSAIDs is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk :

NSAIDs cause an increased risk of serious gastrointestinal adverse events including inflammation, 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 are at greater risk for serious gastrointestinal (GI) events.

The total combined duration of use of oral ketorolac tromethamine and IV or IM dosing of ketorolac tromethamine is not to exceed 5 days in adults. Ketorolac tromethamine is not indicated for use in pediatric patients.

Special warnings and precautions for use of ketorolin Solution in Ampoule for I.M. / I.V. Injection:

As this product contains propylene glycol It may cause alcohol – like symptoms when exceeding

- 200 mg/kg/day for children

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- Based on single-dose data only, the mean half-life of ketorolac tromethamine in renally impaired patients is between 6 and 19 hours and is dependent on the extent of the impairment. There is poor correlation between creatinine clearance and total ketorolac tromethamine clearance in the elderly and populations with renal impairment (r=0.5).
- In patients with renal disease, the AUC∞ of each enantiomer increased by approximately 100% compared with healthy volunteers. The volume of distribution doubles for the S-enantiomer and increases by 1/5th for the R-enantiomer. The increase in volume of distribution of ketorolac tromethamine implies an increase in unbound fraction .
- The AUC∞-ratio of the ketorolac tromethamine enantiomers in healthy subjects and patients remained similar, indicating there was no selective excretion of either enantiomer in patients compared to healthy subjects.

Hepatic Insufficiency:

There was no significant difference in estimates of half-life, AUC∞ and Cmax in 7 patients with liver disease compared to healthy volunteers.

Race:

Pharmacokinetic differences due to race have not been identified.

IV Administration:

In normal adult subjects, the total clearance of 30 mg IV-administered ketorolac tromethamine was 0.030 (0.017-0.051) L/h/kg. The terminal half-life was 5.6 (4.0-7.9) hours.

Indications and Usage:

Carefully consider the potential benefits and risks of ketorolac tromethamine and other treatment options before deciding to use ketorolac. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Acute Pain in Adult Patients:

- Ketorolac tromethamine is indicated for the short-term (≤5 days) management of moderately severe acute pain that requires analgesia at the opioid level, usually in a postoperative setting. Therapy should always be initiated with IV or IM dosing of ketorolac tromethamine, and oral ketorolac tromethamine is to be used only as continuation treatment, if necessary.
- The total combined duration of use of ketorolac tromethamine injection and oral ketorolac tromethamine is not to exceed 5 days of use because of the potential of increasing the frequency and severity of adverse reactions associated with the recommended doses. Patients should be switched to alternative analgesics as soon as possible, but ketorolac tromethamine therapy is not to exceed 5 days.
- Ketorolac tromethamine injection has been used concomitantly with morphine and meperidine and has shown an opioid-sparing effect. For breakthrough pain, it is recommended to supplement the lower end of the ketorolac tromethamine injection dosage range with low doses of narcotics prn, unless otherwise contraindicated. Ketorolac tromethamine injection and narcotics should not be administered in the same syringe.

Contraindications:

- Ketorolac tromethamine is contraindicated in patients with previously demonstrated hypersensitivity to ketorolac tromethamine .

ketorolac tromethamine. Therefore, peri- operative use of ketorolac tromethamine should be avoided and postoperative use be undertaken with caution when hemostasis is critical.

Renal Effects:

- 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 a 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، heart failure، liver dysfunction، those taking diuretics and ACE inhibitors، and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.
- Ketorolac tromethamine and its metabolites are eliminated primarily by the kidneys، which، in patients with reduced creatinine clearance، will result in diminished clearance of the drug Therefore، ketorolac tromethamine should be used with caution in patients with impaired renal function and such patients should be followed closely.With the use of ketorolac tromethamine، there have been reports of acute renal failure، interstitial nephritis and nephrotic syndrome.

Impaired Renal Function:

Ketorolac tromethamine is contraindicated in patients with serum creatinine concentrations indicating advanced renal impairment .Ketorolac tromethamine should be used with caution in patients with impaired renal function or a history of kidney disease because it is a potent inhibitor of prostaglandin synthesis. Because patients with underlying renal insufficiency are at increased risk of developing acute renal decompensation or failure, the risks and benefits should be assessed prior to giving ketorolac tromethamine to these patients.

Anaphylactoid Reactions:

As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to ketorolac tromethamine. Ketorolac tromethamine should not be given to patients with the aspirin triad.This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Cardiovascular Effects:

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.

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- 400 mg/kg/day for adults

The most serious risks associated with ketorolac tromethamine are:

Gas trointes tinal Effects – Ris k of Ulceration, Bleeding and Perforation:

- Ketorolac tromethamine is contraindicated in patients with previously documented peptic ulcers and/or gastrointestinal (GI) bleeding. Ketorolac tromethamine can cause serious (GI) adverse events including bleeding, ulceration and perforation, of the 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 ketorolac tromethamine.
  - Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Minor upper gastrointestinal problems, such as dyspepsia, are common and may also occur at any time during NSAID therapy. The incidence and severity of gastrointestinal complications increases with increasing dose of, and duration of treatment with ketorolac tromethamine. Do not use ketorolac tromethamine for more than five days. However, even short-term therapy is not without risk. In addition to past history of ulcer disease, other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids, or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population.
  - To minimize the potential risk for an adverse GI event, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of ketorolac tromethamine until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.
  - NSAIDs should be given with care to patients with a history of inflammatory bowel disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated.

Hemorrhage:

Because prostaglandins play an important role in hemostasis and NSAIDs affect platelet aggregation as well, use of ketorolac tromethamine in patients who have coagulation disorders should be undertaken very cautiously, and those patients should be carefully monitored. Patients on therapeutic doses of anticoagulants (e.g., heparin or dicumarol derivatives) have an increased risk of bleeding complications if given ketorolac tromethamine concurrently; therefore, physicians should administer such concomitant therapy only extremely cautiously. The concurrent use of ketorolac tromethamine and therapy that affects hemostasis, including prophylactic low-dose heparin (2500 to 5000 units q12h), warfarin and dextrans have not been studied extensively, but may also be associated with an increased risk of bleeding. Until data from such studies are available, physicians should carefully weigh the benefits against the risks and use such concomitant therapy in these patients only extremely cautiously. Patients receiving therapy that affects hemostasis should be monitored closely .In postmarketing experience, postoperative hematomas and other signs of wound bleeding have been reported in association with the peri-operative use of IV or IM dosing of

Precautions:

General:

- Ketorolac tromethamine cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
- The pharmacological activity of ketorolac tromethamine in reducing inflammation may diminish the utility of this diagnostic sign in detecting complications of presumed noninfectious, painful conditions.

Hepatic Effects:

- Ketorolac tromethamine should be used with caution in patients with impaired hepatic function or a history of liver disease. Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including ketorolac tromethamine. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported .
- A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with ketorolac tromethamine. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), ketorolac tromethamine should be discontinued.

Hematologic Effects:

Anemia is sometimes seen in patients receiving NSAIDs, including ketorolac tromethamine. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including ketorolac tromethamine, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible.Patients receiving ketorolac tromethamine who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants should be carefully monitored.

Pre-existing Asthma:

Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, ketorolac tromethamine should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with pre-existing asthma.

Information for Patients:

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- 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 ketorolac tromethamine, increases the risk of serious gastrointestinal (GI) events

Status Post Coronary Artery Bypass Graft (CABG) Surgery:

NSAIDs are contraindicated in the setting of CABG.

Post-MI Patients:

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

Hypertension:

NSAIDs, including ketorolac tromethamine, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events.Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including ketorolac tromethamine, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Heart Failure and Edema:

- 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 ketorolac tromethamine 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).
- Avoid the use of ketorolac tromethamine in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If ketorolac tromethamine is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

Skin Reactions:

NSAIDs, including ketorolac tromethamine, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Pregnancy:

In late pregnancy, as with other NSAIDs, ketorolac tromethamine should be avoided because it ma cause premature closure of the ductus arteriosus.

Laboratory Tests:
Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. Patients on long-term treatment with NSAIDs should have their CBC and a chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g., eosinophilia, rash etc.) Or if abnormal liver tests persist or worsen, ketorolac tromethamine should be discontinued.

Drug Interactions:
Ketorolac is highly bound to human plasma protein (mean 99.2%). There is no evidence in animal or human studies that ketorolac tromethamine induces or inhibits hepatic enzymes capable of metabolizing itself or other drugs.

Warfarin, Digoxin, Salicylate, and Heparin:

- The in vitro binding of warfarin to plasma proteins is only slightly reduced by ketorolac tromethamine (99.5% control vs 99.3%) when ketorolac plasma concentrations reach 5 to 10 mcg/mL. Ketorolac does not alter digoxin protein binding. In vitro studies indicate that, at therapeutic concentrations of salicylate (300 mcg/mL), the binding of ketorolac was reduced from approximately 99.2% to 97.5%, representing a potential two fold increase in unbound ketorolac plasma levels. Therapeutic concentrations of digoxin، warfarin, ibuprofen, naproxen, piroxicam, acetaminophen, phenytoin andtolbutamide did not alter ketorolac tromethamine protein binding.
- The administration of ketorolac tromethamine to patients taking anticoagulants should be done extremely cautiously and patients should be closely monitored .
- The effects of warfarin and NSAIDs, in general, on GI bleeding are synergistic, such that the users of both drugs together have a risk of serious GI bleeding higher than the users of either drug alone.

Aspirin:
When ketorolac tromethamine is administered with aspirin, its protein binding is reduced, although the clearance of free ketorolac tromethamine is not altered. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of ketorolac tromethamine and aspirin is not generally recommended because of the potential of increased adverse effects.

Diuretics:
Clinical studies, as well as postmarketing observations, have shown that ketorolac tromethamine can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure, as well as to assure diuretic efficacy.

Probenecid:
Concomitant administration of oral ketorolac tromethamine and probenecid resulted in decreased clearance and volume of distribution of ketorolac and significant increases in ketorolac plasma levels (total AUC increased approximately threefold from 5.4 to 17.8 mcg/h/mL) and terminal half-life increased approximately twofold from 6.6 to 15.1 hours. Therefore, concomitant use of ketorolac tromethamine and probenecid is contraindicated.

Lithium:

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- Ketorolac tromethamine is a potent NSAID and may cause serious side effects such as gastrointestinal bleeding or kidney failure, which may result in hospitalization and even fatal outcome.
- Physicians, when prescribing ketorolac tromethamine, should inform their patients or their guardians of the potential risks of ketorolac tromethamine treatment , instruct patients to seek medical advice if they develop treatment-related adverse events, and advise patients not to give oral ketorolac tromethamine to other family members and to discard any unused drug.
- Remember that the total combined duration of use of oral ketorolac tromethamine and IV or IM dosing of ketorolac tromethamine is not to exceed 5 days in adults. Ketorolac tromethamine is not indicated for use in pediatric patients.
- Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.

1- **Cardiovas cular Thrombotic Events:** Advise patients to be alert for the symptoms of cardiovascular thrombotic events, including chest pain، shortness of breath, weakness, or slurring of speech, and to report any of these symptoms to their health care provider immediately.

2- Ketorolac tromethamine, like other NSAIDs, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization and even death. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative sign or symptoms including epigastric pain, dyspepsia, melena, and hematemesis. Patients should be apprised of the importance of this follow-up.

3- Ketorolac tromethamine, like other NSAIDs, can cause serious skin side effects such as exfoliative dermatitis, SJS, and TEN, which may result in hospitalizations and even death. Although serious skin reactions may occur without warning, patients should be alert for the signs and symptoms of skin rash and blisters, fever, or other signs of hypersensitivity such as itching, and should ask for medical advice when observing any indicative signs or symptoms. Patients should be advised to stop the drug immediately if they develop any type of rash and contact their physicians as soon as possible.

4- **Heart Failure and Edema:** Advise patients to be alert for the symptoms of congestive heart failure including shortness of breath، unexplained weight gain, or edema and to contact their healthcare provider if such symptoms occur.

5- Patients should promptly report signs or symptoms of un explained weight gain, or edema and to contact their physicians.

6- Patients should be informed of the warning signs and symptoms of hepatotoxicity (e.g., nausea، fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy.

7- Patients should be informed of the signs of an anaphylactoid reaction (e.g., difficulty breathing، swelling of the face or throat). If these occur, patients should be instructed to seek immediate emergency help.

8- In late pregnancy, as with other NSAIDs, ketorolac tromethamine should be avoided because it will cause premature closure of the ductus arteriosus.

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The use of ketorolac tromethamine, as with any drug known to inhibit cyclooxygenase/ prostaglandin synthesis, may impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of ketorolac tromethamine should be considered.

Nursing Mothers:

Exercise caution when ketorolac is administered to a nursing woman. Available information has not shown any specific adverse events in nursing infants؛ however، instruct patients to contact their infant's healthcare provider if they note any adverse events.

Pediatric Use:

Ketorolac tromethamine is not indicated for use in pediatric patients. The safety and effectiveness of ketorolac tromethamine in pediatric patients below the age of 17 have not been established.

Geriatric Use (≥65 Years of Age):

Because ketorolac tromethamine may be cleared more slowly by the elderly who are also more sensitive to the dose-related adverse effects of NSAIDs extreme caution and reduced dosages, and careful clinical monitoring must be used when treating the elderly with ketorolac tromethamine.

Adverse Reactions:

- Adverse reaction rates increase with higher doses of ketorolac tromethamine. Practitioners should be alert for the severe complications of treatment with ketorolac tromethamine, such as G.I. ulceration، bleeding and perforation, postoperative bleeding, acute renal failure, anaphylactic and anaphylactoid reactions and liver failure.These NSAID-related complications can be serious in certain patients for whom ketorolac tromethamine is indicated, especially when the drug is used inappropriately.
- In patients taking ketorolac tromethamine or other NSAIDs in clinical trials, the most frequently reported adverse experiences in approximately 1% to 10% of patients are:

Gastrointestinal (GI) experiences including:

abdominal pain*	constipation/diarrhea	dyspepsia*
flatulence	GI fullness	GI ulcers (gastric/duodenal)
gross bleeding/perforation	heartburn	nausea*
stomatitis	vomiting	

Other experiences:

abnormal renal function	anemia	dizziness
drowsiness	edema	elevated liver enzymes
headaches*	hypertension	increased bleeding time
injection site pain	pruritus	purpura
rashes	tinnitus	sweating

*Incidence greater than 10%.

Additional adverse experiences reported occasionally (<1% in patients taking ketorolac tromethamine or other NSAIDs in clinical trials) include:

Body as a Whole: fever, infections, sepsis.

Cardiovas cular: congestive heart failure, palpitation, pallor, tachycardia, syncope.

Dermatologic: alopecia, photosensitivity, urticaria.

Gastrointestinal: anorexia, dry mouth, eructation, esophagitis, excessive thirst, gastritis, glossitis، hematemesis, hepatitis, increased appetite, jaundice, melena, rectal bleeding.

NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Methotrexate:

NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

ACE Inhibitors /Angiotens in II Receptor Antagonists:

- Concomitant use of ACE inhibitors and/or angiotens in II receptor antagonists may increase the risk of renal impairment, particularly in volume-depleted patients.
- Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE inhibitors and/or angiotensin II receptor antagonists. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors and/or angiotensin II receptor antagonists.

Antiepileptic Drugs:

Sporadic cases of seizures have been reported during concomitant use of ketorolac tromethamine and antiepileptic drugs (phenytoin, carbamazepine).

Psychoactive Drugs:

Hallucinations have been reported when ketorolac tromethamine was used in patients taking psychoactive drugs (fluoxetine, thiothixene, alprazolam).

Pentoxifylline:

When ketorolac tromethamine is administered concurrently with pentoxifylline, there is an increased tendency to bleeding.

Nondepolarizing Mus cle Relaxants:

In postmarketing experience there have been reports of a possible interaction between ketorolac tromethamine IV/IM and nondepolarizing muscle relaxants that resulted in apnea. The concurrent use of ketorolac tromethamine with muscle relaxants has not been formally studied.

Selective Serotonin Reuptake Inhibitors (SSRIs):

There is an increased risk of gastrointestinal bleeding when s elective s erotonin reuptake inhibitors (SSRIs) are combined with NSAIDs. Caution should be used when NSAIDs are administered concomitantly with SSRIs.

Pregnancy:

Pregnancy Category C:

There are no adequate and well-controlled studies of ketorolac tromethamine in pregnant women. Ketorolac tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery:

The use of ketorolac tromethamine is contraindicated in labor and delivery because, through its prostaglandin synthesis inhibitory effect, it may adversely affect fetal circulation and inhibit uterine contractions, thus increasing the risk of uterine hemorrhage.

Effects on Fertility:

Dosage and Administration:
Carefully consider the potential benefits and risks of ketorolac tromethamine and other treatment options before deciding to us e ketorolac tromethamine. Use the lowest effective dos e for the shortest duration consistent with individual patient treatment goals. In adults, the combined duration of us e of IV or IM dosing of ketorolac tromethamine and oral ketorolac tromethamine is not to exceed 5 days. In adults, the use of oral ketorolac tromethamine is only indicated as continuation therapy to IV or IM dosing of ketorolac tromethamine.
Transition from IV or IM dosing of ketorolac tromethamine (single- or multipledose) to multiple-dose ketorolac tromethamine:
Patients age 17 to 64: 20 mg PO once followed by 10 mg q4-6 hours prn not >40 mg/day.
Patients age ≥ 65, renally impaired, and/or weight <50 kg (110 lbs): 10 mg PO once followed by 10 mg q4-6 hours prn not >40 mg/day.
Note:
- Oral formulation should not be given as an initial dose.
- Use minimum effective dose for the individual patient.
- Do not shorten dosing interval of 4 to 6 hours

Total duration of treatment in adult patients: the combined duration of use of IV or IM dosing of ketorolac tromethamine and ketorolac tromethamine tablets is not to exceed 5 days .
The following table summarizes Ketorolac tromathamine tablet dosing instructions in terms of age group :

Summary of Dosing Instructions

Patient Population	Ketorolac Tromethamine Tablets (Following IV or IM dosing of ketorolac tromethamine)
Age < 17 years	Oral not approved.
Adult Age 17 to 64 years	20 mg once, then 10 mg q4 to 6 hours prn not > 40 mg / day.
Adult Age ≥ 65 years, renally impaired, and / or weight < 50 kg.	10 mg once, then 10 mg q4 to 6 hours prn not > 40 mg / day.

Storage Conditions:
Store at temperature not exceeding 30°C in outer carton in order to protect from light.
Keep out of reach of children.
Pack :
- Carton box containing 5 brown (type I) glass ampoules each contains 2 ml solution in a plastic tray and insert leaflet.(local)
- Carton box containing 10 brown (type I) glass ampoules each contains 2 ml solution in a plastic tray and insert leaflet.(for export only)

Reporting side effects:
If you find any side effects even if not found in this Pamphlet Please report to www.EPVC.gov.eg
Shelf life:
Three years
Manufacturer:
Pharaonia Pharmaceuticals (Pharo Pharma) New Burg El Arab city – 3rd Industrial zone – block no. 16 – Alexandria – Egypt

Human drug Registration Directorate Approval Date:21/9/2020 Revised by: DR/AZZA
Pharmacology Department According to : FAM INSERT sec rev:DR/ALAA

Hemic and Lymphatic: ecchymosis, eosinophilia, epistaxis, leukopenia, thrombocytopenia.
Metabolic and Nutritional: weight change.
Nervous System: abnormal dreams, abnormal thinking, anxiety, asthenia, confusion, depression, euphoria, extrapyramidal symptoms, hallucinations, hyperkinesis, inability to concentrate, insomnia, nervousness, paresthesia, somnolence, stupor, tremors, vertigo, malaise.
Reproductive, female: infertility.
Respiratory: asthma, cough, dyspnea, pulmonary edema, rhinitis.
Special Senses: abnormal taste, abnormal vision, blurred vision, hearing loss.
Urogenital: cystitis, dysuria, hematuria, increased urinary frequency, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure, urinary retention.
Other rarely observed reactions (reported from postmarketing experience in patients taking ketorolac tromethamine or other NSAIDs) are:
Body as a Whole: angioedema, death, hypersensitivity reactions such as anaphylaxis, anaphylactoid reaction, laryngeal edema, tongue edema, myalgia.
Cardiovascular: arrhythmia, bradycardia, chest pain, flushing, hypotension, myocardial infarction, vasculitis.
Dermatologic: exfoliative dermatitis, erythema multiforme, Lyell's syndrome, bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis.
Gastrointestinal: acute pancreatitis, liver failure, ulcerative stomatitis, exacerbation of inflammatory bowel disease (ulcerative colitis, Crohn's disease).
Hemic and Lymphatic: agranulocytosis, aplastic anemia, hemolytic anemia, lymphadenopathy, pancytopenia, postoperative wound hemorrhage (rarely requiring blood transfusion.
Metabolic and Nutritional: hyperglycemia, hyperkalemia, hyponatremia.
Nervous System: aseptic meningitis, convulsions, coma, psychosis.
Respiratory: bronchospasm, respiratory depression, pneumonia.
Special Senses: conjunctivitis.
Urogenital: flank pain with or without hematuria and/or azotemia, hemolytic uremic syndrome.
Overdosage:
Symptoms and Signs:
Symptoms following acute NSAIDs overdoses are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.
Treatment:
- Patients should be managed by symptomatic and supportive care following a NSAIDs overdose. There are no specific antidotes. Emesis and/or activated charcoal (60 g to 100 g in adults, 1 g/kg to 2 g/kg in children) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large oral overdose (5 to 10 times the usual dose). Forced diuresis, alkalization of urine, hemodialysis or hemoperfusion may not be useful due to high protein binding.
- Single overdoses of ketorolac tromethamine have been variously associated with abdominal pain, nausea, vomiting, hyperventilation, peptic ulcers and/or erosive gastritis and renal dysfunction which have resolved after discontinuation of dosing.

كيتورولين أمبول
محلول للحقن العضلى أو الوريدى

بيان التركيب:
مواد فعالة
تحتوى كل٢مللى أمبول على :
كيتورولاك ترومیثامین ٣٠ مجم
مواد غير فعالة : بروبيلين جليكول ، كلوريد الصوديوم ، صوديوم هيدروكسيد / حمض الهيدروكلوريك و ماء نقى

ما هي المعلومات الأكثر أهمية التي يجب معرفتها عن الأدوية الغير إستيرودية المضادة للالتهاب؟
- زيادة خطر الإصابة بالأزمة القلبية أو السكتة الدماغية و يمكن أن يحدث هذا الخطر في بداية العلاج و يمكن أن يزيد :
- مع زيادة الجرعة من الأدوية الغير إستيرودية المضادة للالتهاب.
- مع الاستخدام الطويل من الأدوية الغير إستيرودية المضادة للالتهاب.

لا تستخدم الأدوية الغير إستيرودية المضادة للالتهاب قبل أو بعد إجراء عملية جراحية في القلب "و التي تسمى عمليات تحويل مسار الشريان التاجى الجراحية ".
تجنب استخدام الأدوية الغير إستيرودية المضادة للالتهاب بعد الإصابة بأزمات قلبية حديثة ، إلا إذا نصحك طبيبك بهذا . حيث يمكن أن يزداد لديك خطر الإصابة بأزمة قلبية أخرى إذا تناولت الأدوية الغير إستيرودية المضادة للالتهاب بعد الإصابة بأزمة قلبية حديثة.
- زيادة خطر الإصابة بنزيف، قرح، ثقوب المرئ (الأنبوبة المؤدية من الفم إلى المعدة) ،المعدة و الأمعاء و ذلك
- في أي وقت خلال الاستخدام.
- بدون أعراض تحذيرية.
- يمكن أن يسبب الوفاة.

يزداد خطر القرحة أو النزيف في حالة وجود :
- تاريخ قديم من الإصابة بقرح المعدة ، أو نزيف المعدة أو الأمعاء مع استخدام الأدوية الغير إستيرودية المضادة للالتهاب.
- تقدم السن.
- استخدام الأدوية التي تسمى بالكورتيكوستيرويدات ، مضادات التجلط ، مثبطات استرجاع السيروتونين الانتقائية ، أو مثبطات استرجاع السيروتونين و النورأدرينالين الانتقائية.
- ضعف الصحة بشكل عام .
- زيادة جرعات الأدوية الغير إستيرودية المضادة الاتهاب.
- الاستخدام الطويل للأدوية الغير إستيرودية المضادة الاتهاب.
- أمراض الكبد المتقدمة.
- مشاكل النزيف .
- التدخين.
- تناول الكحول

يجب استخدام الأدوية الغير إستيرودية المضادة للالتهاب:
- بالضبط كما تم وصفه لك
- أقل جرعة ممكنة للعلاج
- لأقل وقت ممكن

معلومات هامة عن بعض المكونات في كيتورولين أمبول :
تحتوى هذا المستحضر على بروبيلين جليكول فمن الممكن أن يسبب آثار مشابهة للكحول عند :
- تخطى ٢٠٠ مجم/كجم/يوم بالنسبة للأطفال

- تخطى ٤٠٠ مجم/كجم/يوم بالنسبة للكبار

ما هي الأدوية الغير إستيرودية المضادة للالتهاب وما هو استخدامها:
- تستخدم الأدوية الغير إستيرودية المضادة للالتهاب في علاج الألم و الاحمرار ، التورم ، و الحرارة (الالتهاب) الناتجين عن مشاكل صحية مثل أنواع مختلفة من التهاب المفاصل ، تقلصات الحيض كما تستخدم كمسكنات قوية للآلام على المدى القصير.

من يجب عليه ألا يستخدم الأدوية الغير إستيرودية المضادة للالتهاب؟
لا تستخدم الأدوية الغير إستيرودية المضادة للالتهاب:
- إذا حدث لك نوبة ربو ، طفح جلدى ، أو أي تفاعلات حساسية أخرى مع الأسبرين أو أي أدوية أخرى من الأدوية الغير إستيرويدية المضادة للالتهاب
- قبل أو بعد عمليات جراحة القلب التحويلية.

قبل أن تستخدم الأدوية الغير إستيرودية المضادة للالتهاب أخبر طبيبك عن كل المشاكل الصحية التي تعانى منها و تشمل :
- مشاكل بالكبد أو الكلى
- ارتفاع ضغط الدم
- الربو
- إذا كنت حاملا أو تخططين للحمل، تحدثى مع طبيبك إذا كنت تستخدمين الأدوية الغير إستيرويدية المضادة للالتهاب أثناء الحمل.

لا يجب أن تستخدمى الأدوية الغير إستيرودية المضادة للالتهاب بعد ٢٩ أسبوع من الحمل.
- إذا كنت في فترة الرضاعة الطبيعية أو تخططين للقيام بالرضاعة الطبيعية
- أخبر طبيبك عن كل الأدوية التي تستخدمها ، بما في ذلك الادوية التي تصرف بروشتة و التي تصرف بدون .
- الفيتامينات أو المكملات العشبية. الأدوية الغير إستيرودية المضادة للالتهاب و الادوية الأخرى يمكن أن تتفاعل مع بعضها البعض و تسبب آثار جانبية خطيرة . لا تبدأ باستخدام أي دواء جديد بدون التحدث مع طبيبك أولا

الآثار الجانبية المحتملة:
يمكن أن تسبب الأدوية الغير إستيرودية المضادة للالتهاب آثار جانبية خطيرة تشمل :
(انظر : ما هي المعلومات الأكثر أهمية التي يجب معرفتها عن الأدوية الغير إستيرودية المضادة للالتهاب؟)
- ارتفاع ضغط الدم أو زيادته سوءا
- قصور عضلة القلب
- مشاكل بالكلى و تشمل الفشل الكلوى
- انخفاض عدد كرات الدم الحمراء (الأنيميا)
- تفاعلات جلدية مهددة للحياة
- مشاكل بالكبد و تشمل الفشل الكبدى

آثار جانبية أخرى الأدوية الغير إستيرودية المضادة للالتهاب تشمل : ألم بالمعدة ، الإمساك ، الإسهال ، الغازات ، حموضة ، غثيان ، قئ و دوخة .
عليك أن تحصل على المساعدة الطبية العاجلة إذا حدث لك أي من الاعراض التالية :
- قصر النفس أو مشاكل بالتنفس
- آلام الصدر
- ضعف في جزء واحد او جانب واحد من الجسم
- اضطراب في الكلام
- تورم الوجه او الحلق

توقف عن استخدام الأدوية الغير إستيرودية المضادة للالتهاب و اتصل بطبيبك على الفور إذا حدث لك أي من الأعراض التالية :
- الغثيان
- قئ به دم
- الإصابة بالإعياء أو الضعف بشكل أكثر من الطبيعي
- إذا كان يوجد دم في البراز أو إذا كان لونه أسود و لزج مثل القطران
- الإسهال

- زيادة في الوزن غير طبيعية
- الحكة
- الطفح الجلدى أو البثور مع الحمى
- تلون الجلد أو العين باللون الأصفر
- تورم الذراعين ، الأرجل ، الأيدى و القدمين
- عسر الهضم او آلام بالمعدة
- أعراض تشبه البرد.

إذا استخدمت الكثير من الأدوية الغير إستيرودية المضادة للالتهاب ، اتصل بطبيبك أو احصل على المساعدة الطبية على الفور.
هذه ليست كل الآثار الجانبية الممكنة للأدوية الغير إستيرودية المضادة للالتهاب، لمعرفة معلومات أكثر ، اسأل طبيبك أو الصيدلى عن الادوية الغير إستيرودية المضادة للالتهاب.

معلومات أخرى عن الادوية الغير إستيرودية المضادة للالتهاب.

- يعد الأسبرين من الادوية الغير إستيرودية المضادة للالتهاب و لكن لا يزيد من خطر حدوث الأزمة القلبية.

يمكن ان يسبب الأسبرين نزيف في المخ ، المعدة أو الأمعاء . و يمكن أن يسبب أيضا قرح في المعدة و الأمعاء .
تباع بعض الادوية الغير إستيرودية المضادة للالتهاب بجرعات أقل و ذلك بدون وصفة طبية . تحدث إلى طبيبك قبل استخدام الادوية الغير إستيرودية المضادة للالتهاب التي تتصرف بدون روشتة طبية لمدة أكثر من ١٠ أيام.

التحذيرات

الخطر القلبى الوعائى
قد تترافق الأدوية مثل كيتورولين مع زيادة متوسطة في خطر حدوث حالات التخثر القلبى الوعائى،احتشاء عضلة القلب أو السكتات الدماغية التي قد تكون مميتة. من المرجح أن يحدث هذا الخطر عند استخدام جرعات عالية ومدة علاج طويلة . لا تتجاوز الجرعة الموصى بها أو مدة العلاج.
إذا كنت تعاني من مشاكل في القلب ، أو لديك تاريخ مرضى من السكتات الدماغية ، أو تعتقد أنك قد تكون معرضًا لخطر الإصابة بهذه الحالات (على سبيل المثال ، لديك ارتفاع في ضغط الدم ، أو مرض السكري ، أو مستوى الكوليسترول لديك عالى ، أو كنت مدخنًا) يجب عليك استشارة طبيبك أو الصيدلي فيما يخص هذا العلاج
وبالمثل ، يمكن أن يتسبب هذا النوع من الأدوية في احتباس السوائل ، خاصة في المرضى الذين يعانون من قصور القلب و / أو ارتفاع ضغط الدم .يمنع استخدام الادوية الغير إستيرودية المضادة للالتهاب في علاج الالام المصاحبة لعمليات تحويل مسار الشريان التاجى الجراحية.

الخطر الخاص بالمعدة و الأمعاء :
مضادات الالتهاب غير الستيرويدية تتسبب في زيادة خطر حدوث أحداث ضارة في المعدة و الأمعاء خطيرة بما في ذلك الالتهاب والنزيف والتقرح وانثقاب المعدة والأمعاء التي قد تكون قاتلة. يمكن أن تحدث هذه الأحداث في أي وقت أثناء الاستخدام وبدون أعراض تحذيرية. المرضى المسنون معرضون أكثر لهذه الأحداث الخطيرة.

معلومات عامة عن أمان و فعالية الادوية الغير إستيرودية المضادة للالتهاب :

- في بعض الأحيان ، يتم وصف الأدوية لأعراض أخرى غير المذكورة في النشرة . لا تستخدم الأدوية الغير إستيرويدية المضادة للالتهاب لغرض آخر غير الموصوفة له ز لا تقم بإعطاء الادوية الغير إستيرودية المضادة للالتهاب لمرضى آخرين ، حتى و إن كان لديهم نفس الأعراض التي لديك . حيث يمكن أن يضر هم.
- إذا كنت تريد معرفة معلومات أكثر عن الادوية الغير إستيرودية المضادة للالتهاب ، تحدث مع طبيبك ، يمكنك أن تسأل الصيدلى أو الطبيب عن معلومات أكثر عن الادوية الغير إستيرودية المضادة للالتهاب المذكورة في النشرة الخاصة بالفريق الطبى

العبوة :
علبة كرتون تحتوى على ٥ أمبولة زجاجية بنية تحتوي كل منها على ٢ مللي من المحلول في علبة بلاستيكية و معها نشرة داخلية.(محلى)

علبة كرتون تحتوى على ١٠ أمبولات زجاجية بنية تحتوي كل منها على ٢ مللي من المحلول في علبة بلاستيكية و معها نشرة داخلية. (للتصدير فقط)

الإبلاغ عن الآثار الجانبية
إذا تعرضت لإية آثار جانبية ، استشر طبيبك أو الصيدلي أو الممرضة. يتضمن ذلك أي آثار جانبية محتملة غير مدرجة في هذه النشرة. يمكنك أيضًا الإبلاغ عن الآثار الجانبية مباشرةً علىwww.EPVC.gov.eg .

مدة الصلاحية : ثلاثة سنوات

التخزين

- قم بحفظ الدواء في درجة حرارة لا تتجاوز ٣٠°م في العبوة الخارجية لتحفظ الدواء من الضوء.
- لا تقم بالتخلص من هذا الدواء من خلال مياه الصرف الصحي أو النفايات المنزلية و لكن قم بسؤال الصيدلي علي الطريقة الصحيحة للتخلص منه من اجل حماية البيئة.
- قم بحفظ الدواء بعيدا عن متناول الأطفال.

الإنتاج:
الشركة الفرعونية للأدوية (فارو فارما) المنطقة الصناعية الثالثة- بلوك ١٦ قطعة رقم ١- مدينة برج العرب الجديدة.