

PRESCRIBING INFORMATION

Pr KENALOG*-10 INJECTION
(Triamcinolone Acetonide Injectable Suspension, U.S.P); 10 mg/mL

THERAPEUTIC CLASSIFICATION

Corticosteroid

NOTE: KENALOG-10 INJECTION is triamcinolone acetonide, a synthetic glucocorticoid corticosteroid with marked anti-inflammatory action, in a sterile aqueous suspension suitable for intradermal, intra-articular, and intra-bursal injection and for injection into tendon sheaths. **This formulation is not for intravenous, intramuscular, intraocular, epidural or intrathecal injection.**

ACTION AND CLINICAL PHARMACOLOGY

Naturally occurring glucocorticoids (e.g., hydrocortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Synthetic analogs such as triamcinolone are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND CLINICAL USE

Intra-articular: For intra-articular or intrabursal administration, and for injections into tendon sheaths, as adjunctive therapy for short-term administration in the following conditions: synovitis of osteoarthritis, rheumatoid arthritis, acute and subacute bursitis, acute gouty arthritis, epicondylitis, acute nonspecific tenosynovitis, and post-traumatic osteoarthritis.

Intradermal: Intralesional administration is indicated for the treatment of keloids, discoid lupus erythematosus, necrobiosis lipoidica diabetorum, alopecia areata, and localized hypertrophic, infiltrated, inflammatory lesions of lichen planus, psoriatic plaques, granuloma annulare, and lichen simplex chronicus (neurodermatitis).

CONTRAINDICATIONS

Corticosteroids are generally contraindicated in patients with systemic infections. KENALOG-10 is also contraindicated in patients with a sensitivity to the medicinal or nonmedicinal ingredients (see Warnings).

The preparation should not be injected into infected areas.

WARNINGS

Because KENALOG-10 is a suspension, it should **not** be administered i.v.

Epidural and intrathecal administration of this product should not be used. Reports of serious medical events have been associated with epidural and intrathecal routes of administration.

Cases of serious anaphylactic reactions and anaphylactic shock, including death, have been reported in individuals receiving triamcinolone acetonide injection, regardless of the route of administration.

KENALOG-10 is a long-acting preparation, and is **not** suitable for use in acute situations.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts or glaucoma with possible damage to the optic nerve. Prolonged use may also enhance the likelihood of secondary ocular infections.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when they are used in large doses; dietary salt restriction and potassium supplementation may be necessary (see Precautions). All corticosteroids increase calcium excretion, which may be associated with osteoporosis or aggravate preexisting osteoporosis.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used. In addition, patients who are on immunosuppressant drugs including corticosteroids are more susceptible to infections than those not taking these drugs. Moreover, chickenpox and measles can have a more serious or even fatal course in patients on corticosteroids. In such children, or adults receiving corticosteroids who have not had these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin (VZIG) or pooled i.v. immunoglobulin (IVIG), as appropriate, may be indicated. If chickenpox or herpes zoster develops, treatment with antiviral agents may be considered. Similarly, corticosteroids should be used with great caution in patients with *Strongyloides* (threadworm) infestation because corticosteroid-induced immunosuppression may lead to *Strongyloides* hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal Gram-negative septicemia.

Patients should not be vaccinated or immunized while on corticosteroid therapy, especially on high doses, because of a lack of antibody response predisposing to medical complications, particularly neurological ones.

The use of triamcinolone acetonide in patients with active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. Chemoprophylaxis should be used in patients with latent tuberculosis or tuberculin reactivity who are taking corticosteroids.

Rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy. Appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

Adequate studies to demonstrate the safety of KENALOG-10 use by intratubal, subconjunctival, sub-tenons, retrobulbar and intraocular (intravitreal) injections have not been performed.

Endophthalmitis, eye inflammation, increased intraocular pressure and visual disturbances including vision loss have been reported with intravitreal administration. Several instances of blindness have been reported following injection of corticosteroid suspensions into the nasal turbinates and intralesional injection about the head. Administration of KENALOG-10 (Triamcinolone Acetonide Injectable Suspension) by any of these routes is not recommended.

This product contains benzyl alcohol as a preservative. Benzyl alcohol has been associated with serious adverse events and death, particularly in pediatric patients. The "gasping syndrome" has been associated with benzyl alcohol. Although normal therapeutic doses of this product deliver amounts of benzyl alcohol that are substantially lower than those reported in

association with the "gasping syndrome", the minimum amount of benzyl alcohol at which toxicity may occur is not known. Premature and low-birth-weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity.

Pregnancy and Lactation: Many corticosteroids have been shown to be teratogenic in laboratory animals at low doses. Since adequate human reproduction studies have not been performed with corticosteroids, the use of these drugs in pregnancy, nursing mothers, or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and the embryo, fetus, or breast-fed infant. Other systemic corticosteroids have been shown to appear in breast milk and to slightly elevate (by 1%) the risk of cleft palate in human fetuses. Infants born to mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of adrenal suppression.

Children: Because corticosteroids can suppress growth, the development of infants and children on prolonged corticosteroid therapy should be carefully observed. Caution should be used in the event of exposure to chickenpox, measles or other communicable diseases. Children should not be vaccinated or immunized while on corticosteroid therapy (see Warnings). Corticosteroids may also affect endogenous steroid production.

Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, metabolic acidosis), particularly in neonates, and an increased incidence of kernicterus, particularly in small preterm infants. There have been rare reports of deaths, primarily in preterm infants, associated with exposure to excessive amounts of benzyl alcohol (see WARNINGS).

PRECAUTIONS

Drug induced adrenocortical insufficiency may occur with corticosteroids and persist for months after discontinuation of therapy; therefore, in any situation of stress such as trauma, surgery or severe illness occurring during that period, hormone therapy should be reinstated. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced corticosteroid effect in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Psychiatric disturbances may appear when corticosteroids are used. These can include insomnia, depression (sometimes severe), euphoria, mood swings, psychotic symptoms and personality changes. Pre-existing emotional instability or psychosis may also be aggravated by corticosteroids. The use of antidepressant drugs does not relieve and may exacerbate adrenocorticoid-induced mental disturbances.

Corticosteroids should be used with caution in the following conditions: Nonspecific ulcerative colitis (if there is a probability of perforation, abscess, or other pyogenic infection); diverticulitis; recent intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; acute glomerulonephritis; chronic nephritis; hypertension; congestive heart failure; thrombophlebitis; thromboembolism; osteoporosis; exanthema; Cushing's syndrome; diabetes mellitus; convulsive disorders; metastatic carcinoma; myasthenia gravis.

Although therapy with KENALOG-10 may ameliorate symptoms of inflammation, it does not obviate the need to treat the cause.

Intra-articular injection of a corticosteroid may produce systemic as well as local effects. The

inadvertent injection of the suspension into the soft tissues surrounding a joint may lead to the occurrence of systemic effects and is the most common cause of failure to achieve the desired local results.

Following intra-articular steroid therapy, patients should be specifically warned to avoid overuse of joints in which symptomatic benefit has been obtained. Otherwise an increase in joint deterioration can occur.

Overdistention of the joint capsule and deposition of steroid along the needle track should be avoided in intra-articular injection, since this may lead to s.c. atrophy.

Corticosteroids should not be injected into unstable joints. Repeated intra-articular injection may in some cases itself result in instability of the joint. In selected cases, particularly where repeated injections are given, x-ray follow-up is suggested.

An increase in joint discomfort has seldom occurred. A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of a septic arthritis. If these complications should appear, and the diagnosis of septic arthritis is confirmed, administration of triamcinolone acetonide should be stopped, and antimicrobial therapy should be instituted immediately and continued for 7 to 10 days after all evidence of infection has disappeared. Appropriate examination of any joint fluid present is necessary to exclude a septic process. Injection of a steroid into a previously infected joint should therefore be avoided. Repeated injection into inflamed tendons has been followed by tendon rupture. Therefore, it should also be avoided.

Like other potent corticosteroids, triamcinolone acetonide should be used under close clinical supervision. Triamcinolone acetonide can cause elevation of blood pressure, salt and water retention, and increased potassium and calcium excretion necessitating dietary salt restriction and potassium supplementation. Edema may occur in the presence of renal disease with a fixed or decreased glomerular filtration rate.

During prolonged therapy, **an adequate protein intake is essential** to counteract the tendency to gradual weight loss sometimes associated with negative nitrogen balance, wasting and weakness of skeletal muscles.

Menstrual irregularities may also occur with corticosteroid treatment.

In peptic ulcer, recurrence may be asymptomatic until perforation or hemorrhage occurs. Long-term adrenocortical therapy may itself produce hyperacidity or peptic ulcer. Therefore, anti-ulcer therapy is recommended.

Continued supervision of the patient after termination of triamcinolone acetonide therapy is essential, since there may be a sudden reappearance of severe manifestations of the disease for which the patient was treated.

Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

Geriatrics: The common adverse effects of systemic corticosteroids such as osteoporosis or hypertension may be associated with more serious consequences in old age. Close clinical supervision is recommended.

Occupational Hazards: The effects of corticosteroid therapy on the ability to drive or operate machinery have not been studied.

Drug Interactions

Amphotericin B injection and potassium-depleting agents: Patients should be observed for hypokalemia.

Anticholinesterases: Effects of the anticholinesterase agent may be antagonized.

Anticoagulants, oral: Corticosteroids may potentiate or decrease anticoagulant action. Patients receiving oral anticoagulants and corticosteroids should therefore be closely monitored.

Antidiabetics: Corticosteroids may increase blood glucose; diabetic control should be monitored, especially when corticosteroids are initiated, discontinued, or changed in dosage.

Antitubercular drugs: Isoniazid serum concentrations may be decreased.

Cyclosporine: Monitor for evidence of increased toxicity of cyclosporine when the two are used concurrently.

Digitalis glycosides: Coadministration may enhance the possibility of digitalis toxicity.

Estrogens, including oral contraceptives: Corticosteroid half-life and concentration may be increased and clearance decreased.

Hepatic enzyme inducers (e.g., barbiturates, phenytoin, carbamazepine, rifampin): There may be increased metabolic clearance of KENALOG-10 injection. Patients should be carefully observed for possible diminished effect of steroid, and the dosage of KENALOG-10 injection should be adjusted accordingly.

Human growth hormone (e.g., somatrem): The growth-promotion effect of somatrem may be inhibited.

Ketoconazole: Corticosteroid clearance may be decreased, resulting in increased effects.

Nondepolarizing muscle relaxants: Corticosteroids may decrease or enhance the neuromuscular blocking action.

Nonsteroidal anti-inflammatory agents (NSAIDs): Corticosteroids may increase the incidence and/or severity of gastrointestinal bleeding and ulceration associated with NSAIDs. Also, corticosteroids can reduce serum salicylate levels and therefore decrease their effectiveness. Conversely, discontinuing corticosteroids during high-dose salicylate therapy may result in salicylate toxicity. Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinemia.

Thyroid drugs: Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in adrenocorticoid dosage.

Vaccines: Neurological complications and lack of antibody response may occur when patients taking corticosteroids are vaccinated (see WARNINGS).

Laboratory test interactions

Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection, producing false negative results.

ADVERSE REACTIONS

Undesirable reactions following intra-articular administration of the preparation have included post-injection flare, transient pain, irritation at the injection site, sterile abscesses, hyper- or hypopigmentation, Charcot-like arthropathy, and occasional increase in joint discomfort; following intradermal administration, rare instances of blindness associated with intralesional therapy around the face and head, transient local discomfort, sterile abscesses, hyper- or hypopigmentation, cutaneous and s.c. atrophy (which usually disappears, unless the basic disease process is itself atrophic) have occurred.

Since systemic absorption may occasionally occur with intra-articular or other local administration, patients should be watched closely for the following adverse reactions which may be associated with any corticosteroid therapy:

General: anaphylactoid reactions; anaphylactic reactions, anaphylactic shock, aggravation or masking of infections.

Cardiovascular: hypertension, syncope, congestive heart failure, arrhythmias, necrotizing angiitis, thromboembolism, thrombophlebitis.

Fluid and Electrolyte Disturbances: sodium retention, fluid retention associated with hypertension or congestive heart failure, potassium loss which may lead to cardiac arrhythmias or ECG changes, and hypokalemic alkalosis.

Musculoskeletal: muscle weakness, fatigue, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, delayed healing of fractures, aseptic necrosis of femoral and humeral heads, pathologic fractures of long bones, and spontaneous fractures.

Gastrointestinal: peptic ulcer with possible subsequent perforation and hemorrhage, pancreatitis, abdominal distention, ulcerative esophagitis.

Dermatologic: impaired wound healing, thin fragile skin, petechiae and ecchymoses, facial erythema, increased sweating, purpura, striae, hirsutism, acneiform eruptions, lupus erythematosus-like lesions, hives, rash, suppressed reactions to skin tests.

Neuropsychiatric: convulsions, increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment, vertigo, headache, insomnia, neuritis, parasthesias, and aggravation of pre-existing psychiatric conditions, depression (sometimes severe), euphoria, mood swings, psychotic symptoms and personality changes.

Endocrine: menstrual irregularities; development of the cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress (e.g., trauma, surgery, or illness); decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; and increased requirements for insulin or oral hypoglycemic agents in diabetics.

Ophthalmic: posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, and exophthalmos, corneal perforation.

Metabolic: hyperglycemia, glycosuria, and negative nitrogen balance due to protein catabolism.

SYMPTOMS AND TREATMENT OF OVERDOSE

Chronic

The symptoms of glucocorticoid overdose may include confusion, anxiety, depression, gastrointestinal cramping or bleeding, ecchymosis, moon face and hypertension. After long-term use, rapid withdrawal can result in acute adrenal insufficiency (which also may occur in times of stress); Cushingoid changes can result from continued use of large doses.

Acute

There is no specific treatment for overdose, but supportive therapy should be instituted and, if gastrointestinal bleeding occurs, it should be treated as peptic ulcer.

DOSAGE AND ADMINISTRATION

This preparation contains benzyl alcohol. Not for use in newborn or premature infants (see WARNINGS: Children).

Intra-articular or intrabursal and tendon sheaths: The initial dose of KENALOG-10 for intra-articular or intrabursal administration and for injection into tendon sheaths may vary from 2.5 to 5 mg (0.25 to 0.5 mL) for smaller joints and from 5 to 15 mg (0.5 to 1.5 mL) for larger joints, depending on the specific disease entity being treated. Single injections into several joints, up to a total of 20 mg (2 mL) or more, have been given without incident.

Intradermal: The initial dose of triamcinolone acetonide will vary depending upon the specific disease entity being treated but should be limited to 1 mg (0.1 mL) per injection site, since larger volumes are more likely to produce cutaneous atrophy.

Multiple sites separated by 1 cm or more may be injected, keeping in mind that the greater the total volume employed the more corticosteroid becomes available for systemic absorption and systemic effects. Such injections may be repeated, if necessary, at weekly or less frequent intervals.

Localization of Dose: The lower dosages in the initial dosage range of triamcinolone may produce the desired effect when the corticosteroid is administered to provide a localized concentration. The site and volume of the injection should be carefully considered when triamcinolone is administered for this purpose.

General: The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, KENALOG-10 should be gradually discontinued and the patient transferred to other appropriate therapy.

Dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient. Dosage adjustments may be necessary in accordance with changes in clinical status.

ADMINISTRATION

Strict aseptic technique is mandatory. The vial should be shaken before use to ensure a uniform suspension. Prior to withdrawal, the suspension should be inspected for clumping or granular appearance (agglomeration). An agglomerated product results from exposure to freezing temperatures and should not be used. After withdrawal, inject without delay to prevent settling in the syringe. Careful technique should be employed to avoid the possibility of entering a blood vessel or introducing infection.

Injection Technique: For treatment of joints, the usual intra-articular injection techniques should be followed. If an excessive amount of synovial fluid is present in the joint, some, but not all, should be aspirated to aid in the relief of pain and to prevent undue dilution of the steroid.

With intra-articular or intrabursal administration, and with injection of KENALOG-10 into tendon sheaths or ganglia, prior use of a local anesthetic may often be desirable. Care should be taken with this kind of injection, particularly in the deltoid region, to avoid injecting the suspension into the tissues surrounding the site, since this may lead to tissue atrophy.

For treatment of ganglia, KENALOG-10 injection is injected directly into the cyst cavity.

In treating acute tenosynovitis, care should be taken to ensure that the injection of KENALOG-10 is made into the tendon sheath rather than the tendon substance. Epicondylitis may be treated by infiltrating the preparation into the area of greatest tenderness.

Intralesional: For treatment of dermal lesions, KENALOG-10 should be injected directly into the lesion, i.e., intradermally or s.c. For accuracy of dosage measurement and ease of administration, it is preferable to employ a tuberculin syringe and a small bore needle (23 to 25 gauge). Ethyl chloride spray may be used to alleviate the discomfort of the injection.

Safety in Handling

Due to the high potency of this drug and its potential for absorption through the skin, persons who handle KENALOG-10 should avoid skin and eye contact, as well as inhalation of airborne drug.

AVAILABILITY OF DOSAGE FORMS

Each mL of sterile, aqueous suspension contains: triamcinolone acetonide 10 mg.

Nonmedicinal ingredients: benzyl alcohol, carboxymethylcellulose sodium, hydrochloric acid, polysorbate, sodium chloride, sodium hydroxide and water. pH between 5.0 and 7.5. At the time of manufacture, the air in the container is replaced by nitrogen. Vials of 5 mL. Store at controlled room temperature (15 to 30°C). Do not freeze or refrigerate. Protect from light.

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