

PRESCRIBING INFORMATION

Pr **KENALOG*-40 INJECTION**
(Triamcinolone Acetonide Injectable Suspension, U.S.P); 40 mg/mL

THERAPEUTIC CLASSIFICATION

Corticosteroid

NOTE: KENALOG-40 INJECTION (triamcinolone acetonide) is a synthetic glucocorticoid corticosteroid with marked anti-inflammatory action, in a sterile aqueous suspension suitable for intramuscular, Intra-articular and intrabursal injection. **This formulation is not suitable for intravenous, intradermal, 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.

KENALOG-40 has an extended duration of effect which may be permanent, or sustained over a period of several weeks. Studies indicate that following a single i.m. dose of 60 to 100 mg of triamcinolone acetonide, adrenal suppression occurs within 24 to 48 hours and then gradually returns to normal, usually in 30 to 40 days. This finding correlates closely with the extended duration of therapeutic action achieved with the drug.

INDICATIONS AND CLINICAL USE

Intramuscular (I.M.): The i.m. administration is indicated for systemic corticosteroid therapy in such conditions as dermatoses, or generalized rheumatoid arthritis and other connective tissue disorders. It is also indicated for allergic diseases; however, for acute allergic reactions, epinephrine is the drug of choice, steroid therapy being adjunctive.

I.M. administration is particularly valuable in such conditions when oral corticosteroid therapy is not feasible. Triamcinolone acetonide is not an agent of choice in the treatment of adrenocortical insufficiency or the salt-losing form of the adrenogenital syndrome.

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.

CONTRAINDICATIONS

Corticosteroids are contraindicated in patients with systemic infections. I.M. corticosteroid preparations are contraindicated for idiopathic thrombocytopenic purpura. KENALOG-40 is also contraindicated in patients with a sensitivity to the medicinal or non-medicinal ingredients (see Warnings).

WARNINGS

Because KENALOG-40 is a suspension, it should **not** be administered i.v. The s.c. route of administration must not be used, due to the possibility of local atrophy.

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.

Adequate studies to demonstrate the safety of KENALOG-40 use by intratubinal, subconjunctival, sub-tenons, retrobulbar injection and intraocular (intravitreal) 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-40 (Triamcinolone Acetonide Injectable Suspension) by any of these routes is not recommended.

KENALOG-40 is a long-acting preparation and is not suitable for use in acute situations. To avoid drug-induced adrenal insufficiency, supportive dosage may be required in times of stress (such as trauma, surgery or severe illness) both during treatment with KENALOG-40 and for a year afterwards.

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 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.

Unless a **deep** i.m. injection is given, local atrophy is likely to occur. (For recommendations on injection techniques, see DOSAGE AND ADMINISTRATION). Due to the significantly higher incidence of local atrophy when the material is injected into the deltoid area, this injection site should be avoided in favor of the gluteal area.

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 child-bearing 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: This preparation is not recommended for children under 6 years of age. Because corticosteroids can suppress growth, the development of 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-40 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 also 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 is 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 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, antiulcer therapy is recommended.

Continued supervision of the patient after termination of triamcinolone 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: Increased activity of both cyclosporine and corticosteroids may occur 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-40 injection. Patients should be carefully observed for possible diminished effect of steroid, and the dosage of KENALOG-40 injection should be adjusted accordingly.

Human growth hormone (e.g., somatrem): The growth-promoting 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. ASA 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

General: Following administration by any route, anaphylactoid reactions; anaphylactic reactions, anaphylactic shock, aggravation or masking of infections.

Cardiovascular: hypertension, syncope, congestive heart failure, arrhythmias, necrotizing angitis, 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,

hypokalemic alkalosis.

Musculoskeletal: muscle weakness, fatigue, 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, 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, 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.

Following I.M. administration: Severe pain has been reported following i.m. administration. Sterile abscesses, cutaneous and s.c. atrophy, hyperpigmentation, hypopigmentation and Charcot-like arthropathy have also occurred.

Intra-articular administration: Undesirable reactions have included postinjection flare, transient irritation at the injection site, sterile abscesses, cutaneous and subcutaneous atrophy, hyper- or hypopigmentation, Charcot-like arthropathy and occasional increase in joint discomfort (see Precautions).

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 acute overdose, but supportive therapy should be instituted and, if gastrointestinal bleeding occurs, it should be managed.

DOSAGE AND ADMINISTRATION

General

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

The initial dose of KENALOG-40 may vary from 2.5 to 60 mg/day depending on the specific disease entity being treated (see below). In less severe conditions, lower doses generally suffice, while in other patients, higher initial doses may be required. Usually the parenteral dosage range is one-third to one-half the oral dose, given every 12 hours. In life-threatening situations, administration of higher dosages may be justified.

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-40 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. The lowest possible dose of corticosteroid should be used to control the condition being treated. After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals down to the lowest dosage which will maintain the desired clinical response. Constant monitoring of drug dosage is necessary. Dose adjustments may be necessary in accordance with changes in clinical status. Patient exposure to stressful situations not directly related to the disease may necessitate increasing the dosage. After long-term therapy, it is recommended that KENALOG-40 be withdrawn gradually.

DOSAGE

Systemic

Adults and children over 12 years of age: The suggested initial dose is 60 mg (1.5 mL), **injected deeply into the gluteal muscle**. Atrophy of s.c. fat may occur if the injection is not properly given. Dosage is usually adjusted within the range of 40 to 80 mg, depending upon patient response and duration of relief. However, some patients may be well controlled on doses as low as 20 mg or less.

Hay fever or pollen asthma: Patients with hay fever or pollen asthma who are not responding to pollen administration and other conventional therapy may obtain a remission of symptoms lasting throughout the pollen season after a single injection of 40 to 100 mg (1 to 2.5 mL).

Children 6 to 12 years: The suggested initial dose is 40 mg (1 mL), although dosage depends more on the severity of symptoms than on age or weight. There is insufficient clinical experience with KENALOG-40 to recommend its use in children under 6 years of age.

Local

Intra-articular or intrabursal administration and for injection into tendon sheaths: A single local injection of triamcinolone acetonide is frequently sufficient, but several injections may be needed for adequate relief of symptoms.

Initial Dose: 2.5 to 5 mg (0.063 to 0.125 mL) for smaller joints and from 5 to 15 mg (0.125 to 0.375 mL) for larger joints, depending on the specific disease entity being treated. For adults, doses up to 10 mg (0.25 mL) for smaller areas and up to 40 mg (1 mL) for larger areas have usually been sufficient. Single injections into several joints, up to a total of 80 mg (2 mL), have been given without undue reactions.

ADMINISTRATION

General

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, KENALOG-40 should be injected 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.

Systemic

For systemic therapy, injection should be made **deeply into the gluteal muscle** (see Warnings). For adults, a minimum needle length of 4 cm is recommended. In obese patients, a longer needle may be required. Use alternative sites for subsequent injections.

Local

For treatment of joints, 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 into tendon sheaths, prior use of a local anesthetic may often be desirable. Care should be taken with this kind of injection, particularly in the deltoid region, and with injection into tendon sheaths to avoid injecting the suspension into the tissues surrounding the site, since this may lead to tissue atrophy.

In treating acute nonspecific tenosynovitis, care should be taken to ensure that the injection of the corticosteroid 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.

Safety in Handling

Due to the high potency of this drug and its potential for absorption through the skin, persons who handle KENALOG-40 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 40 mg.

Nonmedicinal ingredients: benzyl alcohol, carboxymethylcellulose sodium, hydrochloric acid, polysorbate, sodium chloride, sodium hydroxide and water. pH is between 5.0 and 7.5. At the time of manufacture, the air in the container is replaced by nitrogen. Vials of 1 and 5 mL. Store at controlled room temperature (15 to 30°C). Do not freeze or refrigerate. Protect from light.

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