

PRODUCT MONOGRAPH

Pr Triamcinolone Hexacetonide Injectable Suspension

Suspension, 20 mg/mL, Intra-Articular/Periarticular/Intrasynovial Injection

Manufacturer's Standard

Glucocorticoid/Anti-inflammatory

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Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION.....3
SUMMARY PRODUCT INFORMATION3
INDICATIONS AND CLINICAL USE.....3
CONTRAINDICATIONS3
WARNINGS AND PRECAUTIONS.....4
ADVERSE REACTIONS.....8
DRUG INTERACTIONS9
DOSAGE AND ADMINISTRATION11
OVERDOSAGE13
DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING13
ACTION AND CLINICAL PHARMACOLOGY14
STORAGE AND STABILITY.....14

PART II: SCIENTIFIC INFORMATION.....15
PHARMACEUTICAL INFORMATION.....15
NON-CLINICAL TOXICOLOGY.....16

PATIENT MEDICATION INFORMATION17

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Nonmedicinal Ingredients
Intra-Articular/ Periarticular/ Intrasynovial Injection	Suspension, 20 mg/mL	benzyl alcohol, polysorbate 80, sorbitol liquid and water for injection <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

INDICATIONS AND CLINICAL USE

Triamcinolone Hexacetonide Injectable Suspension is indicated for intra-articular, intrasynovial, or periarticular use in adults and adolescents for the symptomatic treatment of subacute and chronic inflammatory joint diseases including:

- Rheumatoid arthritis
- Juvenile Idiopathic Arthritis (JIA)
- Osteoarthritis and post-traumatic arthritis
- Synovitis, tendinitis, bursitis and epicondylitis

Triamcinolone Hexacetonide Injectable Suspension has low solubility, delayed onset of action, and prolonged duration of action. If a more rapid therapeutic effect is desired, then a more soluble corticosteroid should be administered (locally or systemically).

Geriatrics (over 65 years of age):

No overall differences in safety or effectiveness were observed between elderly subjects and younger subjects. Reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Pediatrics (3 - 12 years of age):

Triamcinolone Hexacetonide Injectable Suspension may be used as an intra-articular injection in children aged 3-12 years with Juvenile Idiopathic Arthritis (see WARNINGS AND PRECAUTIONS – Special Populations, and DOSAGE AND ADMINISTRATION).

CONTRAINDICATIONS

Triamcinolone Hexacetonide Injectable Suspension is contraindicated in:

- Patients with acute psychoses, active tuberculosis, herpes simplex keratitis, and

systemic mycoses and parasitoses (strongyloides infections).

- Infants and children up to 3 years of age. Triamcinolone Hexacetonide Injectable Suspension contains benzyl alcohol, which may provoke toxic reactions in children under 3 years of age.
- Patients who are hypersensitive to this drug or to any ingredient in the formulation (including benzyl alcohol and any other non-medicinal ingredients), or to any component of the container (For a complete listing, see the DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING section).
- Use for epidural and intrathecal administration. Reports of serious medical events, including death, have been associated with epidural and intrathecal routes of corticosteroid administration. Appropriate measures must be taken to avoid intravascular injection.

WARNINGS AND PRECAUTIONS

General

Triamcinolone Hexacetonide Injectable Suspension must not be administered intravenously, intraocularly, epidurally or intrathecally.

Triamcinolone Hexacetonide Injectable Suspension should not be used to alleviate joint pain arising from infectious states such as gonococcal or tubercular arthritis.

Warning and precautions relating to potential systemic glucocorticoid effects.

This product contains a potent glucocorticoid, and even though systemic adverse effects are unusual when glucocorticoids are given as an intra-articular injection triamcinolone hexacetonide should be used with caution in patients suffering from the following conditions:

- cardiac insufficiency, acute coronary artery disease,
- hypertension,
- thrombophlebitis, thromboembolism
- myasthenia gravis,
- osteoporosis,
- gastric ulcer, diverticulitis, ulcerative colitis, recent intestinal anastomosis,
- exanthematous diseases,
- psychosis,
- Cushing's syndrome,
- diabetes mellitus (transient increase in blood glucose levels can occur),
- hypothyroidism,
- renal insufficiency, acute glomerulonephritis, chronic nephritis,
- cirrhosis,
- infections that cannot be treated with antibiotics,

- metastatic carcinoma
- active tuberculosis
- herpes simplex keratitis,
- systemic mycoses and parasitoses (strongyloides infections).

Inadvertent injection into the soft tissues around the joint may lead to an increased incidence of systemic effects, as may peri-articular injections. As with all local injections, care should be taken to avoid entering a blood vessel. Adverse reactions may be minimised by using the lowest effective dose for a minimum duration of time. Frequent patient review is required to titrate the dose appropriately against disease activity (refer to DOSAGE AND ADMINISTRATION).

Carcinogenesis, Mutagenesis, Impairment of Fertility

No adequate studies have been conducted in animals to determine whether corticosteroids have a potential for carcinogenesis or mutagenesis.

Cardiovascular

Glucocorticoids may increase the risk for thromboembolic events.

Endocrine and Metabolism

Adrenal cortical atrophy develops during prolonged corticosteroid therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must, therefore, always be gradual to avoid acute adrenal insufficiency and should be tapered off over weeks or months according to the dose and duration of treatment. During prolonged therapy any intercurrent illness, trauma, or surgical procedure may require a temporary increase in dosage. If corticosteroids have been stopped following prolonged therapy they may need to be reintroduced temporarily.

Immune

Patients should not be vaccinated or immunized with live vaccines while they are under treatment with moderate or high dose corticosteroids for longer than 2 weeks treatment, since a possible lack of an antibody response may predispose to medical, and particularly neurological, complications. Intraarticular and periarticular corticosteroid use, or steroids given for less than 2 weeks, or in a long-term regular dosage of 10 mg daily, are not considered a contraindication to use of live vaccines.

Caution should be used in the event of exposure to chickenpox, measles or other communicable diseases, since the course of specific viral diseases such as chickenpox and measles may be particularly severe in patients treated with glucocorticoids. At particular risk are immunocompromised (immunosuppressed) children and individuals with no history of chickenpox or measles infection. If such individuals should come into contact with people infected with chickenpox or measles during treatment with Triamcinolone Hexacetonide Injectable Suspension, prophylactic treatment should be considered as appropriate.

Musculoskeletal

Triamcinolone Hexacetonide Injectable Suspension is a corticosteroid product which may increase calcium excretion, and predispose patients to osteoporosis.

The prolonged and repeated use of glucocorticoids in weight-bearing joints may result in further joint degeneration. This may be related to increased use of still-diseased joints following relief of pain and other symptoms, or it may be due to inhibition by corticosteroids of protein synthesis in articular cartilage. It is inadvisable to inject unstable joints. Repeated injections may, in some cases, result in instability of the joint. Severe joint destruction with necrosis of bone may occur if repeated intra-articular injections are given over a long period of time.

Sterile technique is necessary to prevent infections or contamination. Appropriate examination of any joint fluid present is necessary to exclude a septic process. A marked increase in pain, accompanied by local swelling, further restriction of joint motion, fever and malaise occurring after intra-articular injection is suggestive of septic arthritis. If this complication appears and the diagnosis of sepsis is confirmed, antimicrobial therapy should be instituted immediately.

Patients should be advised not to overuse treated joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

Ophthalmologic

Ophthalmic complications during prolonged corticosteroid therapy have been observed. These include posterior subcapsular cataract, central serous chorioretinopathy, glaucoma and possible damage to optic nerves, and enhancement of secondary ocular infections due to fungi or virus.

Psychiatric Disorders

Psychiatric disorders may be seen with corticosteroid treatment, including sleep disorders, depression, euphoria, mood swings, psychotic disorders and personality disorders. Existing emotional instability or psychotic disorder may be aggravated by corticosteroids.

Sensitivity/Intolerance

Triamcinolone Hexacetonide Injectable Suspension contains sorbitol. Patients with very rare hereditary problems of fructose intolerance should not take this medicine.

Sexual Health

Corticosteroid therapy may cause menstrual disorders and amenorrhea in premenopausal women, and vaginal bleeding in postmenopausal women.

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Special Populations

Pregnant Women:

Triamcinolone crosses the placenta. Corticosteroids have been shown to be teratogenic in many species when given at doses equivalent to the human dose. Animal studies in which corticosteroids have been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. Long-term use of corticosteroids in humans and animals has led to a decrease in weight of the placenta and the newborn.

There are no adequate and well-controlled studies in pregnant women. Triamcinolone hexacetonide should be used during pregnancy only if the potential benefit to the mother clearly outweighs the risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Women:

Triamcinolone hexacetonide is excreted in human milk, but is not likely to have any effect on the child at therapeutic doses. Caution must be observed with the long-term use of large doses.

Pediatrics (< 18 years of age):

Children on prolonged corticosteroid therapy should have their growth and development monitored.

This product contains benzyl alcohol as a preservative. Benzyl alcohol has been linked to severe adverse reactions and death, especially in very young pediatric patients. Exposure to excessive quantities of benzyl alcohol has been linked to toxicity (hypotension, metabolic acidosis, respiratory distress – “Gasping Syndrome”), especially in neonates, and to an increased incidence of kernicterus, mainly in premature infants. Although normal therapeutic doses of Triamcinolone Hexacetonide Injectable Suspension release substantially lower quantities of benzyl alcohol than those associated with “Gasping Syndrome,” the minimum quantity of benzyl alcohol capable of producing toxicity is not known. Premature and low-birth-weight infants, as well as patients taking high doses, are more likely to develop toxicity.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse reactions depend on the dose and the duration of treatment. Systemic adverse reactions are rare, but may occur as a result of repeated periarticular injection. As with other intra-articular steroid treatments, transient adrenocortical suppression has been observed during the first week after injection. This effect is enhanced if corticotropin or oral steroids are used concomitantly.

Administration site conditions: local reactions include sterile abscesses, post-injection erythema, pain, swelling and necrosis at the injection site; excess dosage or too-frequent administration of injections into the same site may cause local subcutaneous atrophy, which, due to the properties of the drug, will only return to normal after several months. As with all glucocorticoids, an exacerbation of symptoms or “flare-up” may occur following injection. Local atrophy, burning, flushing, pain and swelling may occur.

Cardiovascular: cardiac failure; arrhythmias, bradycardia, cardiac arrest, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis.

Dermatologic: hyperpigmentation or hypopigmentation, impaired wound healing, thin and fragile skin, petechiae and ecchymoses, facial erythema, increased sweating, purpura, striae, acneiform eruptions, hives, rash, acne, allergic dermatitis, cutaneous and subcutaneous atrophy, dry scaly skin, edema, sterile abscess, striae, suppressed reactions to skin tests, thinning scalp hair, urticaria.

Endocrine: menstrual irregularities, amenorrhoea and postmenopausal vaginal bleeding, hirsutism, development of a Cushingoid state, secondary adrenocortical and pituitary unresponsiveness, particularly during periods of stress (e.g. trauma, surgery or illness), manifestation of latent diabetes mellitus, decreased carbohydrate and glucose tolerance, glycosuria, hypertrichosis, increased requirements for insulin or oral hypoglycemic agents in diabetics, suppression of growth in pediatric patients.

Gastrointestinal disorders: peptic ulcers with possibility of subsequent perforation and haemorrhage, pancreatitis, abdominal distention, bowel/bladder dysfunction (after intrathecal administration), elevation in serum liver enzyme levels (usually reversible upon discontinuation), hepatomegaly, increased appetite, nausea, perforation of the small and large intestine (particularly in patients with inflammatory bowel disease), ulcerative esophagitis.

Immune system disorders: anaphylactoid reactions, anaphylaxis, angioedema, exacerbation or masking of infections.

Metabolic: negative nitrogen balance owing to protein catabolism.

Musculoskeletal: tendon rupture, loss of muscle mass, osteoporosis, aseptic necrosis of the heads of the humerus and femur, spontaneous fractures, Charcot-like arthropathy, calcinosis

(following intra-articular or intralesional use), muscle weakness, pathologic fracture of long bones, post-injection flare (following intra-articular use), steroid myopathy, vertebral compression fractures.

Neurologic/Psychiatric: vertigo; increased intracranial pressure with papilloedema (pseudotumor cerebri) usually after treatment; headache, insomnia; exacerbation of existing psychiatric symptoms; depression (sometimes severe); euphoria; mood swings; psychotic symptoms, convulsions, emotional instability, neuritis, neuropathy, paresthesia, personality changes, psychic disorders, vertigo. Arachnoiditis, meningitis, paraparesis/paraplegia, and sensory disturbances have occurred after intrathecal administration

Ophthalmic: posterior subcapsular cataracts, increased intraocular pressure, glaucoma, blurred vision, exophthalmos, rare instances of blindness associated with periocular injections.

Renal and urinary: Increased calcium excretion.

DRUG INTERACTIONS

Overview

The drug-drug interactions listed in Table 1 below outline the potential interactions associated with corticosteroid injectable products.

Drug-Drug Interactions

Table 1 - Established or Potential Drug-Drug Interactions

Triamcinolone Hexacetonide	Ref	Clinical comment
Amphotericin B injection and potassium-depleting agents	T	Patients should be monitored for additive hypokalaemia.
Anticholinesterases	T	The effect of anticholinesterase agent may be antagonised.
Anticholinergics (e.g. atropine)	T	Additional increase of intraocular pressure is possible.
Anticoagulants (oral)	T	Corticosteroids may potentiate or decrease anticoagulant effect. For this reason, patients receiving oral anticoagulants and corticosteroids should be closely monitored
Antidiabetics (e.g. sulfonylurea derivatives) and insulin	T	Corticosteroids may increase the levels of glucose in the blood. Diabetic patients should be monitored, especially on instigation and discontinuation of treatment of corticosteroids and if the dosage is changed.
Antihypertensives, including diuretics	T	The reduction in arterial blood pressure may be diminished.
Antituberculosis drugs	T	Isoniazid serum concentrations may be decreased.

Triamcinolone Hexacetonide	Ref	Clinical comment
Cyclosporine	T	When used concomitantly, this substance may produce an increase in both cyclosporine and corticosteroid activity.
Digitalis glycosides	T	Concomitant administration may increase the likelihood of digitalis toxicity.
Hepatic Enzyme Inducers (e.g. barbiturates, phenytoin, carbamazepine, rifampicin, primidone, aminoglutethimide)	T	There may be increased metabolic clearance of triamcinolone hexacetonide. Patients should be carefully observed for possible reduced effect of triamcinolone hexacetonide, and the dosage should be adjusted accordingly.
Hepatic enzyme inhibitors	T	Protease inhibitors (including ritonavir) or ketoconazole may decrease corticosteroid clearance via CYP3A4 inhibition resulting in increased effects such as Cushing's syndrome and adrenal suppression. Patients should be monitored for undesirable effects due to triamcinolone and the dose should be adjusted if needed.
Human growth hormone (somatropin)	T	The growth-promoting effect may be inhibited during long-term therapy with triamcinolone hexacetonide.
Non-depolarising muscle relaxants	T	Corticosteroids may decrease or enhance the neuromuscular blocking action.
Non-steroidal anti-inflammatory agents (NSAIDs)	T	Corticosteroids may increase the incidence and/or severity of gastrointestinal bleeding and ulceration associated with NSAIDs. Corticosteroids may also reduce serum salicylate levels and therefore decrease their efficacy. Conversely, discontinuing corticosteroids during high-dose salicylate therapy may result in salicylate toxicity. Caution must be exercised during concomitant use of acetylsalicylic acid and corticosteroids in patients with hypoprothrombinaemia.
Oestrogens, including oral contraceptives	T	Corticosteroid half-life and concentration may be increased and clearance decreased.
Thyroid drugs	T	Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustments to the dosage of adrenocorticoids.
Vaccines	T	Neurological complications and a diminished antibody response may occur when patients taking corticosteroids are vaccinated. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. If possible, routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued.

Triamcinolone Hexacetonide	Ref	Clinical comment
Medications that prolong the QT interval or induce torsade de pointes	T	<p>Concomitant treatment with triamcinolone hexacetonide and class Ia antiarrhythmic agents such as disopyramide, quinidine and procainamide, or other class II antiarrhythmic agents such as amiodarone, bepridil and sotalol, is not recommended.</p> <p>Extreme caution is required in cases of concomitant administration with phenothiazines, tricyclic antidepressants, terfenadine and astemizole, vincamine, erythromycin i.v., halofantrine, pentamidine and sultopride.</p> <p>Combination with agents that cause electrolyte disturbances such as hypokalaemia (potassium-depleting diuretics, amphotericin B i.v. and certain laxatives), hypomagnesaemia and severe hypocalcaemia is not recommended.</p>

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

Drug-Laboratory Interactions

Corticosteroids may interfere with the nitroblue tetrazolium test for bacterial infection, producing false-negative results.

Athletes should be informed that this medicinal product contains an ingredient (triamcinolone hexacetonide) that may produce a positive result in anti-doping tests.

DOSAGE AND ADMINISTRATION

Dosing Considerations

Triamcinolone Hexacetonide Injectable Suspension contains benzyl alcohol (see CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS – Special Populations, Pediatrics).

At each session, several injections may be given into multiple joints. Do not administer into unstable joints.

This formulation is intended for intra-articular, periarticular and intrasynovial use. It must not be used for intravenous, intra-ocular, epidural or intrathecal use.

Patients should be monitored for undesirable effects related to triamcinolone, and the dose should be adjusted if necessary.

Recommended Dose and Dosage Adjustment

The lowest effective dose should be used, and injections should not be repeated unless clinically indicated.

Intra-Articular Injection (dosage for adults and adolescents) for all indications:

Average Dose: 2 to 20 mg (0.1 mL to 1.0 mL)

The dose depends on the size of the joint to be injected, the degree of inflammation and the amount of articular fluid present. In general, large joints (such as knee, hip, shoulder) require 10 to 20 mg (0.5 – 1.0 mL) and medium-sized joints require 5-10 mg (0.25 – 0.5 mL). For small joints, (such as interphalangeal, metacarpophalangeal), 2 to 6 mg may be employed. When the amount of synovial fluid is increased, aspiration may be performed before administering Triamcinolone Hexacetonide Injectable Suspension. Subsequent dosage and frequency of injections can best be judged by clinical response.

The usual frequency of injection into a single joint is every three to four weeks (although in many cases patients may experience longer relief of symptoms), and injection more frequently than that is generally not advisable. Triamcinolone hexacetonide is long-acting, and therefore administration of injections into individual joints more frequently than at 3-4 week intervals is not recommended. To avoid possible joint destruction from repeated use of intra-articular corticosteroids, injection should be as infrequent as possible, consistent with adequate patient care. Attention should be paid to avoid deposition of drug along the needle path, which might produce atrophy of surrounding tissues.

Dosage for intra-articular use in children aged 3 to 12 years with Juvenile Idiopathic Arthritis:

The dosage regime for triamcinolone hexacetonide intra-articular injection for JIA in children (3-12 years old) is 1 mg/kg for large joints (knees, hips, and shoulders) and 0.5 mg/kg for smaller joints (ankles, wrists and elbows). For the hands and feet, 1-2 mg/joint for metacarpophalangeal/metatarsophalangeal (MCP/MTP) joints, and 0.6-1 mg/joint for proximal interphalangeal (PIP) joints may be used.

Peri-Articular Injection (dosage for adults and adolescents only):

Bursitis/Epicondylitis: Generally the dose is 10-20 mg (0.5-1.0 mL) depending on the size of the bursa and the severity of the disease. In the majority of cases a single treatment is sufficient.

Synovitis/Tendinitis: Generally the dose is 10-20 mg (0.5-1.0 mL). The need for additional injections should be determined on the basis of response to treatment.

Administration

Strict aseptic administration technique is mandatory. The injection site should be sterilised using the same technique as for lumbar puncture. Topical ethyl chloride spray may be used locally before injection. Over-distention of the joint capsule and deposition of the steroid along the needle track should be avoided. Do not administer into unstable joints.

The product is a milky white suspension in which some white or grey crystals may be visible before use. No filter should be used during administration.

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. The presence of visible crystals is normal as the product is a suspension. To open, firmly grasp the top portion in your dominant hand, between thumb and forefinger. Hold the bottom of the ampoule in the other hand. Apply firm but gentle pressure near the blue dot to break the neck of the ampoule.

If necessary, Triamcinolone Hexacetonide Injectable Suspension may be mixed with 1% or 2% lidocaine hydrochloride. Triamcinolone Hexacetonide Injectable Suspension should be drawn into the syringe before drawing in the lidocaine to prevent contamination of triamcinolone hexacetonide. The syringe should then be shaken gently, and the resulting solution used immediately thereafter. Since Triamcinolone Hexacetonide Injectable Suspension has been designed for ease of administration, a small bore needle (25 or 26 gauge) may be used.

The use of solvents containing methylparaben, propylparaben, phenol, etc. should be avoided, since they may cause precipitation of the steroid.

The ready-to-use crystal suspension should be used immediately after opening. Any unused portion should be discarded after use and must not be reused.

OVERDOSAGE

Treatment of acute overdose is by supportive and symptomatic therapy. Excess dosage or too-frequent administration of injections into the same site may cause local subcutaneous atrophy. If this occurs, recovery may take several months due to the long-term effect of the drug.

There is no satisfactory treatment or antidote known.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Triamcinolone Hexacetonide Injectable Suspension is supplied in ampoules of 1 mL per vial, 20 mg/mL.

Medicinal Ingredient: triamcinolone hexacetonide

Non-medicinal Ingredients: benzyl alcohol (preservative) 9.0 mg, polysorbate 80 4.0 mg, sorbitol liquid 650.0 mg and water for injection.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Triamcinolone Hexacetonide Injectable Suspension contains the synthetic long-acting glucocorticoid, triamcinolone hexacetonide, as a sterile aqueous suspension. It has a prolonged anti-inflammatory action.

The product is a microcrystalline water suspension with a depot effect. Triamcinolone Hexacetonide Injectable Suspension is a relatively water insoluble derivative of triamcinolone acetonide (0.0002% at 25°C in water). It is not rapidly removed from the site of injection after intra-articular administration, nor is it rapidly metabolized *in situ*.

Pharmacodynamics

Triamcinolone Hexacetonide Injectable Suspension is a synthetic glucocorticoid with pronounced anti-inflammatory activity. TAH, the *t*-butylacetic acid ester of triamcinolone acetonide, is almost insoluble in water and therefore dissolution/dispersion in the tissue at the injection site is generally slow, taking a few weeks to several months. Esterification at C21 of the steroid ring prevents glucocorticoid activity, but once in solution the *t*-butylacetic acid ester group is hydrolysed to release the active anti-inflammatory moiety, triamcinolone acetonide. TAH forms a depot in/around the affected joint, resulting in extremely low systemic levels, although systemic absorption is almost complete.

The anti-inflammatory potency of triamcinolone on a milligram by milligram comparison is approximately five times that of hydrocortisone. Triamcinolone has practically no mineralocorticoid effect, therefore no sodium retention occurs.

Pharmacokinetics

The hexacetonide ester is almost insoluble in water, so dissolution is slow and the effect in the tissue of the injection site lasts for a long time, from a few weeks to several months. Generally, the onset of effect after Triamcinolone Hexacetonide Injectable Suspension administration occurs after 24 hours and normally lasts for 4 to 6 weeks.

Triamcinolone hexacetonide is hydrolysed by human serum *in vitro* (43% hydrolysed after 24 hours), but following intra-articular injection the substance does not disperse *in situ*.

Special Populations and Conditions

Pediatrics: Published studies and current therapeutic guidelines on the treatment of Juvenile Idiopathic Arthritis (JIA) indicate efficacy and safety of Triamcinolone Hexacetonide Injectable Suspension in children and adolescents with this condition.

STORAGE AND STABILITY

Keep out of the reach or sight of children.
Store between 15°C – 30°C.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

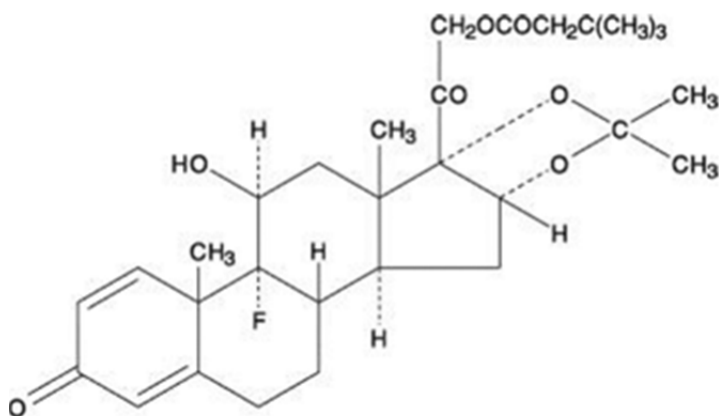
Proper name: triamcinolone hexacetonide

Chemical name: 9-fluoro-11 β ,16 α ,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone 21-(3,3-dimethylbutyrate)

Molecular formula: C₃₀H₄₁FO₇

Molecular mass: 532.6 g/mol

Structural formula:



Physicochemical properties: Triamcinolone hexacetonide is a white or cream coloured powder, insoluble in water.

NON-CLINICAL TOXICOLOGY

General Toxicology

Based on conventional studies of safety pharmacology and repeat dose toxicology studies, no unexpected hazards have been identified. The median lethal dose in mice after 7, 14 and 21 days was in excess of 4000 mg/kg, 2000 mg/kg and 1000 mg/kg respectively following subcutaneous administration. The median lethal dose in rats after 7 and 14 days was 419 mg/kg and 21 mg/kg, following subcutaneous administration.

Sub-acute and chronic toxicity studies in animals did not produce any findings that could be attributed to the drug, other than those which are associated with the pharmacologic activities of steroids, (decreased body weight gain, the reduction in resistance to infection, hematologic abnormalities, effects on adrenals, thymus, etc.).

Carcinogenicity

Long-term studies in animals have not been performed to evaluate carcinogenic potential.

Genotoxicity

There was no evidence of a potential for genetic and chromosome mutations when tested in limited studies performed in bacterial and mammalian cells.

Reproductive and Developmental Toxicology

Corticosteroids have been shown to reduce fertility when administered to rats.

Triamcinolone hexacetonide is a potent teratogen in many animals. Cleft palate has been reported in mice, rats, rabbits, and hamsters at doses equivalent to the human dose. CNS anomalies and cranial malformations have been observed in monkeys following gestational exposure. To date however, no signs of teratogenicity of corticosteroids have been observed in humans.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

Triamcinolone Hexacetonide Injectable Suspension

Read this carefully before you start taking **Triamcinolone Hexacetonide Injectable Suspension** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Triamcinolone Hexacetonide Injectable Suspension**.

What is Triamcinolone Hexacetonide Injectable Suspension used for?

Triamcinolone Hexacetonide Injectable Suspension is used in adults and adolescents to treat the symptoms of subacute and chronic inflammatory joint diseases including:

- Rheumatoid arthritis
- Juvenile Idiopathic Arthritis (JIA)
- Osteoarthritis and post-traumatic arthritis
- Inflammation of the membrane that lines the joint (synovitis).
- Inflammation or irritation of the tendon, a thick cord that attaches bone to muscle (tendinitis).
- Inflammation or irritation of the bursa, the fluid filled sac located between tissues such as bone, muscle, tendons and skin that decreases rubbing and irritation (bursitis).
- Inflammation of the tendons around an epicondyle, the end of a bone, often in the elbow (epicondylitis).

Triamcinolone Hexacetonide Injectable Suspension is also used in children aged 3 – 12 years to treat the symptoms of Juvenile Idiopathic Arthritis (JIA).

How does Triamcinolone Hexacetonide Injectable Suspension work?

The medicinal ingredient in Triamcinolone Hexacetonide Injectable Suspension, reduces the inflammation in joints when injected.

What are the ingredients in Triamcinolone Hexacetonide Injectable Suspension?

Medicinal ingredients: triamcinolone hexacetonide

Non-medicinal ingredients: benzyl alcohol, polysorbate 80, sorbitol solution, water for injection

Triamcinolone Hexacetonide Injectable Suspension comes in the following dosage forms:
Suspension

Do not use Triamcinolone Hexacetonide Injectable Suspension if:

- you have a fungal infection affecting your whole body, including your organs (systemic).
- you are infested or infected with parasites (parasitoses).

- you have active tuberculosis, a bacterial infection affecting mainly the lungs.
- you have a viral infection of the eye called herpes simplex keratitis.
- you are suffering from a serious mental health problem with hallucinations (seeing or hearing things that aren't real) or delusions (believing things that are not true).
- used in infants and children up to 3 years of age. Triamcinolone Hexacetonide Injectable Suspension contains benzyl alcohol, which may cause toxic reactions in children under 3 years of age.
- you are allergic (hypersensitive) to triamcinolone hexacetonide or any other ingredient in the product or container.
- injected in the space around the spine or brain.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Triamcinolone Hexacetonide Injectable Suspension. Talk about any health conditions or problems you may have, including if you:

- have joint pain caused by a gonorrhea or tuberculosis infection
- have heart problems
- have high blood pressure (hypertension)
- have or have a history of blood clots
- have myasthenia gravis; a disease of the immune system that causes muscle weakness
- have osteoporosis; thinning of the bones
- have gut problems including stomach ulcer, inflammation of the intestines, ulcerative colitis or have had recent surgery
- have had recent viral infections causing rashes (i.e. chicken pox, measles, etc.) or mumps or come into contact with someone who has one of these infections
- have high levels of the hormone cortisol in your blood (Cushing's syndrome)
- have diabetes mellitus
- have low levels of thyroid hormone (Hypothyroidism)
- have kidney problems
- have liver problems
- have infections that cannot be treated with antibiotics
- have cancer that has spread to another part of your body (metastatic)
- have mental health problems including sleep disorders, depression, intense feelings of well-being and happiness (euphoria), believing things that aren't real (delusions) or seeing and hearing things that aren't real (hallucinations) and personality disorders
- are going to receive any vaccinations or shots
- are pregnant or planning to become pregnant. Triamcinolone Hexacetonide Injectable Suspension should not be used in pregnancy unless the benefit to the mother outweighs the risk to the unborn baby. If you are pregnant or think you might be pregnant discuss this with your healthcare professional.
- are breastfeeding or planning to breastfeed. Triamcinolone Hexacetonide Injectable Suspension passes into breastmilk.

Other warnings you should know about:

Long-term and repeated use of Triamcinolone Hexacetonide Injectable Suspension in weight-bearing joints may cause the joint to break down. Triamcinolone Hexacetonide Injectable

Suspension should be used at the lowest dose possible to help with your symptoms and for the shortest period of time to help avoid joint break down. You should not overuse the joints you have had treated with Triamcinolone Hexacetonide Injectable Suspension, even if they feel better, if they are still swollen and inflamed.

Triamcinolone Hexacetonide Injectable Suspension contains sorbitol. If you have hereditary problems of fructose intolerance, you should not take this medicine.

Athletes should be aware that Triamcinolone Hexacetonide Injectable Suspension contains an ingredient that can cause them to test positive in anti-doping tests.

Medicines like Triamcinolone Hexacetonide Injectable Suspension can affect the growth and development of children. It is therefore important that the growth and development of children treated with Triamcinolone Hexacetonide Injectable Suspension be monitored by a healthcare professional.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Triamcinolone Hexacetonide Injectable Suspension:

- Medicines used to treat fungal infections such as amphotericin B injection and ketoconazole
- Medicines that cause your body to lose potassium such as laxatives
- Anticholinesterases used to treat conditions such as Alzheimer's disease
- Anticholinergics (e.g. atropine) and other muscle relaxants used to keep you relaxed and asleep during surgery
- Anticoagulants taken orally used to thin the blood and prevent blood clots
- Antidiabetics (e.g. sulfonylurea derivatives) and insulin used to treat diabetes
- Medicines used to lower high blood pressure, including diuretics or "water pills"
- Medicines used to treat tuberculosis
- Cyclosporine used to suppress the immune system after organ transplants
- Digitalis glycosides used to treat heart problems
- Human growth hormone (somatropin)
- Medicines used to treat HIV/AIDS such as ritonavir
- Non-steroidal anti-inflammatory agents (NSAIDs) used to treat pain and inflammation
- Estrogens, including oral contraceptives or "the pill"
- Medicines used to treat thyroid problems
- Vaccines
- Medicines used to treat heart problems including irregular heart beat such as disopyramide, quinidine, procainamide, amiodarone, bepridil and sotalol
- Medicines used to treat mental health problems such as pheothiazine and sultopride
- Medicines used to treat depression known as tricyclic antidepressants
- Medicines used to treat allergic conditions such as terfenadine and astemizole
- Halofantrine used to treat malaria
- Pentamidine an antimicrobial medicine

How to take Triamcinolone Hexacetonide Injectable Suspension:

Triamcinolone Hexacetonide Injectable Suspension will be given to you by a healthcare professional trained in the proper technique for giving injections.

Several injections may be given into multiple joints during a single treatment session.

Usual dose:

Your healthcare professional will decide on the dose and the number of treatments that is right for you based on your specific medical condition.

Overdose:

Using too much Triamcinolone Hexacetonide Injectable Suspension or using it too often can cause damage to the skin and other tissue. Recovery may take several months. There is no known treatment or antidote.

If you think you have been given too much Triamcinolone Hexacetonide Injectable Suspension, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

What are possible side effects from using Triamcinolone Hexacetonide Injectable Suspension?

These are not all the possible side effects you may feel when taking Triamcinolone Hexacetonide Injectable Suspension. If you experience any side effects not listed here, contact your healthcare professional.

Side effects with Triamcinolone Hexacetonide Injectable Suspension may include:

Skin:

- thin fragile skin
- poor wound healing
- swelling
- spots caused by ruptured blood vessels
- reddish spot containing blood that appears in skin
- stretch marks
- dry, scaly skin
- rash
- redness
- itching
- acne
- increased sweating
- lightening or darkening of an area of skin
- thinning hair or unusual hair growth

Metabolism:

- weight gain
- abnormal fat deposits

Digestion:

- nausea, vomiting, abdominal pain, bloating
- diarrhea, indigestion, increased appetite

Muscles:

- loss of muscle mass, muscle weakness, muscle pain,
- malaise (feeling of general discomfort or uneasiness),
- osteoporosis

Nervous System:

- headache
- vertigo
- pain and tenderness
- problems with sensation, strength, and reflexes
- sensation of tingling, tickling, prickling, or burning of your skin
- memory problems (amnesia)
- dizziness

Sexual Function/Reproduction:

- menstrual irregularities
- increased or decreased motility and number of sperm

Other:

- hiccups, fatigue, irritability

Triamcinolone Hexacetonide Injectable Suspension can cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<u>RARE</u>			
Burst or bleeding ulcers: stomach pain, bleeding from the back passage, black or bloodstained stools and/or vomiting blood			√
Flare up of previous Tuberculosis (TB): coughing blood or pain in the chest			√
Serious allergic reaction: rash, itching/swelling (especially of the			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
face/tongue/throat), severe dizziness and trouble breathing			
Signs of infection: persistent fever/cough/sore throat, painful urination, eye pain/discharge		√	
High blood pressure: headaches or generally feeling unwell		√	
Fast/pounding/irregular heartbeat		√	
Cramps and Spasms		√	
Eye problems: vision changes, pain, bulging of the eye, blindness			√
Diabetes: increased thirst and urination, hunger		√	
Tendon pain		√	
Bone/joint pain		√	
Easy bruising and bleeding		√	
Injection site reaction: pain redness and swelling at injection site	√		
Unusual skin growth		√	
Septic arthritis (serious infection in the joint): increase in pain in the affected joint, swelling, lack of movement in the joint, fever, generally feeling unwell			√
Serious heart problems including heart attack and heart failure: crushing chest pain that radiates to your arm or jaw, shortness of breath, sweating, nausea, swelling of the legs, ankles and feet			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Low blood pressure: dizziness, fainting, lightheadedness May occur when you go from lying or sitting to standing up.	√		
Blood clot or swelling of a vein: red, warm, painful vein in the arm or leg, can lead to difficulty breathing or coughing up blood			√
Abscess: hard or firm swelling with pain, tenderness, warmth, redness, pus, fever, chills		√	
Cushingoid state (cause by too much corticosteroids): moon face (enlargement of chin and forehead) thinning of the skin, weakness, weight gain, bruising, lack of menstrual periods in women		√	
Suppression of the pituitary-adrenal axis: flu-like symptoms, fever, chills, headache, diarrhea, cramping, vomiting, weakness, fatigue			√
Bowel or bladder problems		√	
Seizures or fits			√
Mental health problems: depression, emotional instability, euphoria (intense feelings of well-being, elation, happiness, excitement and joy), insomnia, mood swings, personality changes, thoughts of suicide, delusion, hallucination, confusion, schizophrenia, anxiety			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 15°C – 30°C.

Keep out of reach and sight of children.

If you want more information about Triamcinolone Hexacetonide Injectable Suspension:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](http://hc-sc.gc.ca/index-eng.php) (<http://hc-sc.gc.ca/index-eng.php>); the manufacturer's website (www.medexus.ca) or by calling 1-877-633-3987

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