

## SHORT PRODUCT INFORMATION

### 1. NAME OF THE MEDICINAL PRODUCT ARTROPAN 20

mg/ml suspension for injection Sterile

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Every 1 ml;

#### Active ingredient:

Triamcinolone hexacetonide	20mg
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#### Excipient(s):

Benzyl alcohol	9mg
Sorbitol 70%	500mg
Sodium hydroxide	km pH 4.0-8.0

For excipients, see 6.1.

### 3. PHARMACEUTICAL FORM

Injectable Suspension

### 4. CLINICAL FEATURES

#### 4.1. Therapeutic indications

ARTROPAN is indicated for intraarticular, intrasynovial or periarticular use in the symptomatic treatment of rheumatoid arthritis, juvenile idiopathic arthritis (JIA), osteoarthritis and post-traumatic arthritis, and subacute and chronic inflammatory joint diseases, including synovitis, tendinitis, bursitis, and epicondylitis in adults and adolescents.

ARTROPAN can also be used for intra-articular use in children 3-12 years of age with Juvenile Idiopathic Arthritis (see Posology).

#### 4.2. Posology and method of administration

**Intra-articular injection for all indications (dose for adults and adolescents)**

The average dose is 2 – 20 mg.

The dose depends on the size of the joint to be injected and the amount of fluid present. In general, 10 – 20 mg (0.5-1 ml) for large joints (e.g. knee, shoulder, hip), 5-10 mg (0.25-0.5 ml) for medium-sized joints, and 2 – 6 mg (0.1-ml) for small joints. 0.3 ml) is required. When the amount of synovial fluid increases, aspiration should be performed before the administration of ARTROPAN. The next dose and frequency of injection should be determined based on clinical response.

Because ARTROPAN is long-acting, an injection interval of more than 3 or 4 weeks is generally not recommended for a single joint.

Accumulation of the drug at the injection site should be avoided because it can cause atrophy.

### **Periarticular injection (dose for adults and adolescents only)**

Bursitis / Epicondylitis: It is usually 10-20 mg (0.5-1 ml) depending on the severity of the disease and the size of the bursa. In most cases, a single treatment is sufficient.

Synovitis / Tendinitis: Usually 10-20 mg (0.5-1 ml). The need for additional injections should be determined by response to treatment.

#### **Method of Application:**

Asepsis should be observed in the use of this product. The vial should be carefully shaken to ensure suspension before use. The injection site should be sterilized using the same technique as for a lumbar puncture.

In each treatment session, one injection can be given into up to two joints. Application is not made on unstable joints.

**This formulation is intended for intraarticular, periarticular, and intrasynovial use and should not be used for intravenous, intraocular, epidural, or intrathecal use.**

*Precautions to be taken before preparation or administration of the medicinal product*

For instructions on dilution of the medicinal product before administration, see section 6.6.

**Additional information on special****populations: Kidney failure:**

May cause sodium retention resulting in edema and potassium loss in patients using corticosteroids. Therefore, it should be used with caution in patients with renal insufficiency.

**Liver failure:**

In patients with hepatic insufficiency, the effect of corticosteroids is increased. Therefore, it should be used with caution.

**Pediatric population:**

*Dosage for intra-articular use in children 3-12 years of age with Juvenile Idiopathic Arthritis*

The triamcinolone hexacetonide intra-articular injection dose regimen for JIA in children is 1 mg/kg for large joints (knees, hips, and shoulders) and 0.5 mg/kg for smaller joints (ankles, wrists, and elbows). For hands and feet, 1–2 mg/joint for metacarpophalangeal/metatarsophalangeal (MCP/MTP) joints and 0.6-1 mg/joint for proximal interphalangeal (PIP) joints can be used.

**Geriatric population:**

The above-mentioned doses are used.

Especially in the long-term treatment of the elderly, treatment should be carefully planned in terms of serious corticosteroid-related side effects such as osteoporosis, diabetes, hypertension, infection tendency, and thinning of the skin. Close monitoring of the patient is necessary to avoid life-threatening reactions.

**4.3. Contraindications**

Hypersensitivity to the active substance or to the excipients listed in section 6.1. This medicinal product should not be given to newborns or preterm infants because it contains benzyl alcohol. May cause toxic and anaphylactoid reactions in children under 3 years of age, therefore it should not be used in infants and children up to 3 years of age.

Triamcinolone hexacetonide is contraindicated in the following conditions:

- active tuberculosis
- Herpes simplex keratitis,

- acute psychoses,
- systemic mycoses and parasitoses (strong infections).

#### **4.4. Special warnings and precautions for use**

This product contains a potent glucocorticoid and therefore should be used with caution in patients suffering from the following conditions:

- cardiac failure, acute coronary artery disease,
- hypertension,
- thrombophlebitis, thromboembolism
- myasthenia gravis,
- osteoporosis,
- gastric ulcer, diverticulitis, ulcerative colitis, hindgut anastomosis,
- exanthematous diseases,
- psychosis,
- Cushing's syndrome,
- diabetes mellitus,
- hypothyroidism,
- renal failure, acute glomerulonephritis, chronic nephritis,
- cirrhosis,
- infections that cannot be treated with antibiotics,
- metastatic carcinoma.

All corticosteroids can increase calcium excretion.

The product should not be administered intravenously, intraocularly, epidurally or intrathecally.

Intra-articular injection should not be performed in the presence of active infection in or near the joints. The prepared injection should not be used to relieve joint pain caused by infectious conditions such as gonococcal or tuberculous arthritis.

The load on particularly strained joints should be relieved immediately after injection to avoid overloading. Repeated injections can damage the joints. With repeated intra-articular injections for a long time, severe joint destruction with bone necrosis may occur.

Undesirable effects can be minimized by using the lowest effective dose for the minimum duration. Frequent patient review is required to titrate the dose against disease activity (see 4.2).

Adrenal cortical atrophy develops during long-term treatment and may persist for years after stopping treatment.

Discontinuation of corticosteroids after prolonged therapy should always be done gradually to prevent acute adrenal insufficiency and should be tapered gradually over weeks or months, depending on the dose and duration of therapy. Any illness, trauma, or surgical procedure during long-term therapy may require a temporary increase in dose. If corticosteroids have been stopped after long-term therapy, they may need to be temporarily reintroduced.

Patients should carry steroid therapy cards, which, if necessary, provide clear guidance on measures to minimize risk and detail the prescription, drug, dose, and duration of therapy.

Patients should not be immunized or vaccinated with live vaccines while on treatment with medium- or high-dose corticosteroids for more than 2 weeks of therapy, as a possible lack of antibody response may predispose to medical and especially neurological complications. The use of intraarticular and periarticular corticosteroids, or steroids given for less than 2 weeks, or the use of live vaccines in long-term regular doses of 10 mg daily are not considered contraindications.

If the patient develops serious reactions or acute infections during treatment, treatment should be stopped and appropriate therapy given.

Caution should be exercised in case of exposure to chickenpox, measles or other infectious diseases. Because the course of certain viral diseases, such as chickenpox and measles, can be particularly severe in patients treated with glucocorticoids. Particular risk is in immunocompromised (immunosuppressed) children and individuals without a history of chickenpox or measles infection. If these individuals come into contact with chickenpox or measles patients during treatment with triamcinolone hexacetonide, prophylactic treatment should be considered as appropriate.

Menstrual irregularities may occur and vaginal bleeding has been observed in postmenopausal women. This possibility should be mentioned to female patients and, as noted, should not preclude appropriate investigations.

Effect on female fertility, see section 4.6.

Co-administration of triamcinolone hexacetonide with CYP3A4 inhibitors is not recommended unless the potential benefit of treatment outweighs the risk of systemic corticosteroid effects. If the potential benefit of co-administration increases the risk of systemic corticosteroid side effects, patients should be monitored for these effects (see section 4.5).

Visual impairment may be reported with systemic and topical corticosteroid use. If a patient develops symptoms such as blurred vision or other visual disturbances, the patient should be referred to an ophthalmologist for evaluation of possible causes, including rare diseases such as cataracts, glaucoma, or central serous chorioretinopathy (CSCR) that have been reported after systemic and topical corticosteroid use.

### *Pediatric population*

It is recommended to monitor the growth and development of children on long-term corticosteroid therapy.

ARTROPAN contains 9 mg of benzyl alcohol per 1 ml. It should not be applied to premature babies and newborns. May cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years of age.

Benzyl alcohol has been associated with fatal adverse reactions and death, particularly in pediatric patients. Excessive exposure to benzyl alcohol has been associated with toxicity (hypotension and metabolic acidosis), especially in neonates, and an increased incidence of kernicterus, mostly in premature infants. Rare cases of death have occurred due to exposure to very high amounts of benzyl alcohol, mostly in premature infants.

"Gasping Syndrome" has been linked to benzyl alcohol. While normal therapeutic doses of this product will contain significantly lower amounts of benzyl alcohol than those associated with "Gasping Syndrome", the minimum amount of benzyl alcohol that can cause toxicity is unknown.

Premature and low birth weight infants, as well as patients receiving high doses are more likely to have toxicity.

This medicinal product contains less than 1 mmol (23 mg) sodium per dose; so it's actually "sodium free".

ARTROPAN contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

#### **4.5. Interactions with other medicinal products and other forms of interaction**

Amphotericin B injection and potassium-depleting substances: Patients should be monitored for additive hypokalemia.

Anticholinesterases: The action of the anticholinesterase agent may be antagonized.

Anticholinergics (eg atropine): Additional intraocular pressure increase is possible.

Anticoagulants, oral: Corticosteroids can potentiate or reduce the anticoagulant effect. Therefore, patients taking oral anticoagulants and corticosteroids should be closely monitored.

Antidiabetics (eg, sulfonylurea derivatives) and insulin: Corticosteroids can increase blood glucose levels. Diabetic patients should be monitored, particularly in the case of initiation and discontinuation of corticosteroid therapy and dose changes.

Antihypertensives, including diuretics: The reduction in arterial blood pressure may be reduced.

Antituberculous drugs: Isoniazid serum concentrations may be reduced.

Cyclosporine: When used concomitantly, this active substance may cause an increase in both cyclosporine and corticosteroid activity.

Digitalis glycosides: Concomitant administration may increase the likelihood of digitalis toxicity.

Hepatic Enzyme Inducers: (eg, barbiturates, phenytoin, carbamazepine, rifampicin, primidone, aminoglutethimide): There may be increased metabolic clearance of triamcinolone hexacetonide. For the possible reduced effect of triamcinolone hexacetonide, patients should be carefully monitored and the dose adjusted accordingly.

Human growth hormone (somatropin): The growth-promoting effect may be inhibited during long-term treatment with triamcinolone hexacetonide.

Hepatic enzyme inhibitors: protease inhibitors (including ritonavir) or ketoconazole may decrease corticosteroid clearance through inhibition of CYP3A4, resulting in enhanced effects such as Cushing's syndrome and adrenal suppression. Co-administration of triamcinolone hexacetonide with CYP 3A inhibitors (including products containing cobicistat) is not recommended unless the potential benefit of treatment outweighs the risk of systemic corticosteroid effects. If the potential benefit of co-administration increases the risk of systemic corticosteroid adverse events, patients should be monitored for these effects (see section 4.4).

Non-depolarizing muscle relaxants: Corticosteroids may decrease or increase the neuromuscular blocking effect.

Non-steroidal anti-inflammatory agents (NSAIDs): 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 reduce their effectiveness. Conversely, discontinuation of corticosteroids during high-dose salicylate therapy may lead to salicylate toxicity. Caution should be exercised during the concomitant use of acetylsalicylic acid and corticosteroids in patients with hypoprothrombinemia.

Estrogens, including oral contraceptives: May increase corticosteroid half-life and concentration and decrease clearance.

Thyroid drugs: Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in the patient's thyroid status may require adjustments to the dose of adrenocorticoids.



Vaccines: Neurological complications and decreased antibody response may occur when patients receiving corticosteroids are vaccinated. (see section 4.3)

Drugs that prolong the QT interval or induce torsade de pointes: Concomitant use with class Ia antiarrhythmic agents such as triamcinolone hexacetonide and disopyramide, quinidine and procainamide, or with other class II antiarrhythmic drugs such as amiodarone, bepridil and sotalol is not recommended.

Extreme caution should be exercised in case of concomitant administration with phenothiazines, tricyclic antidepressants, terfenadine and astemizole, vincamine, erythromycin iv, halofantrine, pentamidine and sultoprid.

Combination with agents causing electrolyte disturbances such as hypokalemia (potassium-depleting diuretics, amphotericin B iv and some laxatives), hypomagnesemia and severe hypocalcemia is not recommended.

#### *Interactions with lab tests*

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

Athletes should be informed that this medicinal product contains a component (eg, triamcinolone hexacetonide) that may give a positive result in anti-doping tests.

#### **Additional information on special populations:**

#### **Pediatric population:**

Clinical interaction studies in the pediatric population have not been conducted.

#### **4.6. Pregnancy and Lactation**

##### **General advice**

Pregnancy category: C

#### **Women of childbearing potential/Contraception**

There is no information on the effect of corticosteroids on birth control methods. The effects of corticosteroids may be increased when used with oral contraceptives (see section 4.5).

#### **Pregnancy period**

Triamcinolone crosses the placenta. Corticosteroids are teratogenic in animal experiments. The significance of this fact for humans is not fully known, but corticosteroid use has so far not been shown to increase the incidence of malformations. Long-term use of corticosteroids in humans and animals has resulted in reductions in placental and neonatal weights.

Long-term corticosteroid therapy is also associated with an increased risk of adrenocortical suppression in the newborn. This medicinal product should be used during pregnancy only if the benefit to the mother clearly outweighs the risk to the foetus.

There are no adequate data on the use of ARTROPAN in pregnant women. Animal studies have shown reproductive toxicity. They can impair sperm motility. The potential risk for humans is unknown.

ARTROPAN should not be used during pregnancy unless necessary.

#### **Lactation period**

Systemically administered corticosteroids are found in human milk and may suppress growth, interfere with endogenous corticosteroid production, or cause other undesirable effects. Caution should be exercised when using in nursing mothers.

#### **Reproductive ability/Fertility**

Women: Corticosteroid therapy can cause menstrual disorders and amenorrhea.

#### **4.7. Effects on the ability to drive and use machines**

Patients should be warned that side effects such as vertigo and blurred vision may occur, and they should be advised not to drive or use machines if they experience these symptoms during the use of ARTROPAN.

#### **4.8. undesirable effects**

The frequency grouping of undesirable effects is as follows:

very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1000$ ); very rare ( $< 1/10,000$ ); unknown (cannot be estimated from the available data).

Adverse effects depend on dose and duration of treatment. Systemic adverse effects 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. Concomitant use of corticotropin and oral steroids increases this effect.

#### **immune system diseases**Very rare:

anaphylactic-type reactions

Not known: exacerbation or masking of infections

#### **endocrine diseases**

Not known: menstrual irregularities, amenorrhea and postmenopausal vaginal bleeding; hirsutism; development of a cushingoid condition; secondary adrenocortical and pituitary unresponsiveness, especially during periods of stress (eg, trauma, surgery, or illness); decreased carbohydrate tolerance; overt manifestation of latent diabetes mellitus

#### **psychiatric diseases**

Not known: insomnia; exacerbation of existing psychiatric symptoms; depression (sometimes severe); euphoria; sudden changes in mood; psychotic symptoms

#### **nervous system**

**diseases**Rare: vertigo

Not known: increased intracranial pressure with papilledema (pseudotumor cerebri), usually after treatment; headache

#### **Eye diseases**

Not known: posterior subcapsular cataracts; increased intraocular pressure; glaucoma; blurred vision (see also section 4.4)

## **cardiac diseases**

Not known: heart failure; arrhythmias

## **Vascular diseases**

Very rare: thromboembolism

Not known: hypertension

## **Gastrointestinal diseases**

Not known: peptic ulcers with possible subsequent perforation and haemorrhage; pancreatitis

## **Skin and subcutaneous tissue diseases**

Very rare: hyperpigmentation or hypopigmentation

Not known: delayed wound healing; thin and easily damaged skin; petechiae and ecchymoses; facial erythema; increased sweating; purpura; striae; acneiform rashes; urticaria; redness

## **Musculoskeletal and connective tissue**

**diseases** Very rare: calcinosis; tendon rupture

Not known: loss of muscle mass; osteoporosis; femur and humerus  
early aseptic necrosis; spontaneous fractures; Charcot-like arthropathy

## **Kidney and urinary tract diseases**

Not known: negative nitrogen balance due to protein catabolism

## **General disorders and administration site conditions**

Common: Local reactions include sterile abscesses at the injection site, post-injection erythema, pain, swelling, and necrosis.

Infrequent: Overdose or too frequent administration of injections to the same area may cause local subcutaneous atrophy, which will return to normal after a few months due to the properties of the drug.

## Pediatric population

Glucocorticoids can cause growth suppression in children.

#### Reporting of suspected adverse reactions

Reporting suspected drug adverse reactions after authorization is of great importance. Reporting allows continuous monitoring of the benefit/risk balance of the drug. Healthcare professionals are required to report any suspected adverse reaction to the Turkish Pharmacovigilance Center (TÜFAM), [www.titck.gov.tr](http://www.titck.gov.tr); email: [tufam@titck.gov.tr](mailto:tufam@titck.gov.tr); tel: 0 800 314 00 08; fax: 0 312 218 35 99).

#### **4.9. Overdose and its treatment**

High doses of systemic hypercorticism and adrenal suppression may occur in the extended period. In this case, corticosteroid intake is discontinued. In acute overdose, supportive and symptomatic treatment is applied. In severe disease conditions, chronic overdose requires continued steroid therapy, the corticosteroid dose may be temporarily reduced, or the next day treatment started.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1. Pharmacodynamic properties**

Pharmacotherapeutic group: Glucocorticoids,

ATC code: H02AB08

Glucocorticoids are synthetic and naturally occurring adrenocortical steroids that are easily absorbed from the gastrointestinal tract. Naturally occurring glucocorticoids (hydrocortisone and cortisone) have salt-forming properties and are used in replacement therapy in cases of adrenocortical insufficiency. Synthetic analogs are primarily used for their anti-inflammatory effects in many organ system deficiencies due to their anti-inflammatory properties.

Mechanism of action:

It exerts an anti-inflammatory effect by suppressing the formation, release and activity of endogenous inflammatory mediators including prostaglandins, kinins, histamine, liposomal enzymes and the whole system. It also alters the body's immune response.

#### **5.2. Pharmacokinetic properties**

##### **General properties**

Absorption: The hexacetonide ester is practically insoluble in water, so dissolution is slow and the effect on the tissue of the injection site persists for a long time, from several weeks to several months.

it does. In general, onset of action occurs after 24 hours after administration of triamcinolone hexacetonide and normally lasts for 4 to 6 weeks.

Distribution: There is no data.

Biotransformation: Triamcinolone hexacetonide is hydrolyzed with human serum in vitro (43% hydrolysis after 24 hours), but following intra-articular injection, the substance is not dispersed in situ.

Elimination: No data available.

Linearity/Non-linear case: There is no data.

**Characteristics of patients** There is no data.

### **5.3. Preclinical safety data:**

Triamcinolone hexacetonide is a potent teratogen in many animals. For example, cleft palate has been reported in mice, rats, rabbits and hamsters. Central nervous system anomalies and cranial malformations have been observed in monkeys following gestational exposure. However, to date, no teratogenicity of corticosteroids has been observed in humans.

## **6. PHARMACEUTICAL PROPERTIES**

### **6.1. List of excipients**

Polysorbate 80,  
Sorbitol 70% non-crystalline,  
Benzyl alcohol,  
Hydrochloric acid,  
Sodium hydroxide,  
Water for injection.

### **6.2. incompatibilities**

There is no incompatibility between the substances in the formulation.

### **6.3. Shelf life**

24 months

### **6.4. Special precautions for storage**

Store at room temperature below 25°C and protect from light. Do not freeze. Keep out of sight and reach of children and in its package.

### **6.5. The nature and content of the packaging**

In ampoules of colorless Type I glass containing 1 ml of suspension.

### **6.6. Disposal of residues from the medicinal product for human use and other special measures**

There are no special requirements.

It should be disposed of in accordance with the principles of "Regulation on Control of Medical Wastes" and "Regulation on Control of Packaging Wastes".

## **7. LICENSE OWNER**

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## **8. LICENSE NUMBER**

223/49

## **9. FIRST LICENSE DATE/LICENSE RENOVATION DATE**

First license date: 09.02.2010 License renewal date:

## **10. RENEWAL DATE OF SCU**