PROFESSIONAL INFORMATION

SCHEDULING STATUS **S4**

1. NAME OF THE MEDICINE
TAGALON 4 mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml contains 4,0 mg dexamethasone sodium phosphate
Preservatives: methylhydroxybenzoate 0,13 % m/v, propylhydroxybenzoate 0,02 % m/v
Antioxidant: sodium metabisulphite
Sugar free.
For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Injection
A clear, colourless, light yellow solution, free from foreign particles, in a 1 ml colourless, type 1, glass ampoule.

4. CLINICAL PARTICULARS
Therapeutic indications
TAGALON 4 mg/ml injection is indicated in conditions where the anti-inflammatory and immunosuppressive effects are required

Posology and method of administration
Posology
Usual adult dosage ranges from 0,5 to 20 mg daily, depending on the severity of the disorder.
The parenteral administration must be reserved for administration in emergencies or intensive therapy.
Intra-articular, intralesional, intramuscular or soft tissue injection: 0,8 to 4 mg (depending on the size of the joint).

Method of administration
TAGALON 4 mg/ml injection may be administered by slow intravenous injection or intramuscularly.

Contraindications
Hypersensitivity to dexamethasone sodium phosphate, other corticosteroids, or to any components of the TAGALON 4 mg/ml formulation.

TAGALON 4 mg/ml injection should not be administered intrathecally or subconjuctivally (see section 4.2).

TAGALON 4 mg/ml is also contra-indicated in the following conditions:
- possible or confirmed tuberculosis
- ocular herpes simplex
- primary glaucoma
- acute psychosis and psychoneurosis
- systemic infection
- peptic ulcer
- osteoporosis

Special warnings and precautions for use
Adverse events may result from withdrawal or from continued use or large doses.

Sudden cessation of administration is dangerous.

TAGALON 4 mg/ml should be used with extreme caution in the presence of:
- heart failure
- hypertension
- diabetes mellitus
- infectious diseases
- chronic renal failure
- uraemia
- elderly patients

TAGALON 4 mg/ml should be used with great caution in the presence of heart failure, recent myocardial infarction or hypertension, in patients with diabetes mellitus, epilepsy, hypothyroidism, hepatic failure and renal impairment. The elderly too may be at greater risk from adverse effects.

Patients with active or doubtful quiescent tuberculosis should not be given TAGALON 4 mg/ml. (See section 4.3)

The risks of chickenpox and probably of severe herpes zoster are increased in non-immune patients receiving therapeutic doses of TAGALON 4 mg/ml and patients should avoid close personal contact with either infection. Passive immunisation is recommended for non-immune patients on TAGALON 4 mg/ml who do come into contact with chickenpox. Similar precautions apply to measles. Live vaccines should not be given within 3 months of discontinuation of TAGALON 4 mg/ml. Killed vaccines or toxoids may be given although the response may be attenuated.

During prolonged courses of TAGALON 4 mg/ml patients should be examined regularly. Sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of the fluid intake and output, and daily weight records may give early warning of fluid retention.
Back pain may signify osteoporosis.
Children are at special risk from raised intracranial pressure.

Infections may be masked by anti-inflammatory and anti-pyretic effects of TAGALON 4 mg/ml.

The increased severity of varicella and measles may lead to a fatal outcome in non-immune patients receiving systemic TAGALON 4 mg/ml therapy.

Rapid intravenous injection of TAGALON 4 mg/ml may cause cardiovascular collapse and injections should therefore be given slowly or by infusion.

Dexamethasone withdrawal:
Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of TAGALON 4 mg/ml after prolonged therapy must therefore always be gradual to avoid acute adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment.

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg TAGALON 4 mg/ml) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of TAGALON 4 mg/ml is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of TAGALON 4 mg/ml but there is uncertainty about hypothalamic-pituitary-adrenal (HPA) suppression, the dose of TAGALON 4 mg/ml may be reduced to physiological doses. Once a daily dose of 1 mg TAGALON 4 mg/ml is reached, dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of TAGALON 4 mg/ml treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses of up to 6 mg daily of TAGALON 4 mg/ml for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression in the majority of patients. In the following patient groups, gradual withdrawal of TAGALON 4 mg/ml therapy should be considered even after courses lasting 3 weeks or less:
• Patients who have had repeated courses of TAGALON 4 mg/ml, particularly if taken for greater than 3 weeks.
• When a short course has been prescribed within one year of cessation of long-term therapy (months or years).
• Patients who may have reasons for adrenocortical insufficiency other than exogenous TAGALON 4 mg/ml therapy.
• Patients receiving doses of systemic corticosteroid greater than 6 mg daily of TAGALON 4 mg/ml.
• Patients repeatedly taking doses in the evening.

During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

In post marketing experience tumour lysis syndrome (TLS) has been reported in patients with malignancies, including haematological malignancies and solid tumours, following the use of systemic corticosteroids alone, including MEDROL, or in combination with other chemotherapeutic medicines. Patients at high risk of TLS, such as patients with tumours that have a high proliferative rate, high tumour burden and high sensitivity to cytotoxic medicines, should be monitored closely and appropriate precautions should be taken.

Important information about some of the ingredients
DEXAMETHASONE 4 mg/ml:
TAGALON 4 mg/ml contains two preservatives namely methylhydroxybenzoate and propylhydroxybenzoate. These may cause anaphylaxis, that may not occur immediately. The signs may include skin rash or pruritus. A small number of patients may have difficulty breathing. In cases of severe hypersensitivity reactions, TAGALON 4 mg/ml should be immediately discontinued.

Paediatric population
Children may be at increased risk of side-effects; TAGALON 4 mg/ml may cause growth retardation with prolonged use.

Interaction with other medicines and other forms of interaction
Concurrent use of barbiturates, carbamazepine, phenytoin, primidone or rifampicin may enhance the metabolism and reduce the effects of TAGALON 4 mg/ml.
Conversely oral contraceptives or ritonavir may increase plasma concentrations of TAGALON 4 mg/ml.

The use of corticosteroids, such as TAGALON 4 mg/ml, with potassium-depleting diuretics, such as thiazides or furosemide, may cause excessive potassium loss.

There is also an increased risk of hypokalaemia with concurrent amphotericin B or bronchodilator therapy with xanthines (theophylline) or beta$_2$ agonists.

There may be an increased incidence of gastro-intestinal bleeding and ulceration when TAGALON 4 mg/ml is given with non-steroidal anti-inflammatory medicines (NSAIDs). Response to anticoagulants may be altered by TAGALON 4 mg/ml and requirements of antidiabetic medicines and antihypertensives may be increased.
TAGALON 4 mg/ml may decrease serum concentrations of salicylates and may decrease the effect of antimuscarinics in myasthenia gravis.

Fertility, pregnancy and lactation
Women of childbearing potential /Contraception in males and females
No data available.

Pregnancy
Studies have shown that corticosteroids administered to pregnant women did not have adverse effects on the foetus in terms of neuro-development or growth and general health factors.

TAGALON 4 mg/ml given during pregnancy may cause foetal or neonatal adrenal suppression.

Breastfeeding
No data available.

Fertility
No data available.

Effects on ability to drive and use machines
The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Undesirable effects may occur during treatment with TAGALON 4 mg/ml. If affected, patients should not drive or operate machinery.

Undesirable effects
Tabulated list of adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Infections and infestations	Less frequent	Impaired tissue repair and immune function can lead to delayed wound healing, and increased susceptibility to infection. Increased susceptibility to any kind of infection, including septicaemia, tuberculosis, fungal and viral infections.
Blood and lymphatic system disorders	Frequency not known	Increase in the coagulability of blood may lead to thrombo-embolic complications.
Endocrine disorders	Less frequent	Hyperglycaemia with accentuation or precipitation of the diabetic state. The insulin requirements of diabetic patients are increased. Large doses may produce symptoms typical of overactivity of the adrenal cortex, with moon-face, sometimes with hirsutism, buffalo hump, flushing, increased bruising, ecchymoses, striae and acne, sometimes leading to a fully developed Cushing's syndrome.
		Adrenal atrophy (sometimes after 7 days treatment); this produces secondary adrenocortical insufficiency, which may become manifest after overly rapid withdrawal of treatment or insufficiency may occur during prolonged treatment or on cessation of treatment and may be precipitated by some stress such as infection or trauma.
Metabolism and nutrition disorders	Less frequent	Excessive metabolic effects may lead to mobilisation of calcium and phosphorous, with osteoporosis and spontaneous fractures, protein catabolism. Increased excretion of potassium with the possibility of hypokalaemic alkalosis.
Psychiatric disorders	Less frequent	Mental and neurological disturbances.
Eye disorders	Less frequent	Ocular changes, including development of cataract and glaucoma.
Cardiac disorders	Less frequent	Oedema, hypertension. Cardiac failure and cardiovascular collapse after large intravenous doses too rapidly.
Vascular disorders	Less frequent	Intracranial hypertension
Gastrointestinal disorders	Less frequent	Peptic ulceration, acute pancreatitis.
Skin and subcutaneous tissue disorders	Less frequent	Skin thinning.
Musculoskeletal and connective tissue disorders	Less frequent	Aseptic necrosis of bone. Growth retardation in children.
Reproductive system and breast disorders	Less frequent	Menstrual irregularities, amenorrhoea.
General disorders and administration site conditions	Less frequent	Increased appetite, hyperhydrosis.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Overdose
(See section 4.4).
Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Category and class: A 21.5.1 Corticosteroids and analogues.
Dexamethasone sodium phosphate is a corticosteroid derivative with anti-inflammatory and immunosuppressive properties.

Pharmacokinetic properties
Absorption
Dexamethasone is readily absorbed from the site of administration and rapidly distributed to all body tissues.

Distribution
Dexamethasone half-life in plasma is about 190 minutes.
Binding of dexamethasone to plasma proteins is about 77 %.

Elimination
Up to 65 % of a dose is excreted in urine within 24 hours.

Paediatric population
Clearance in premature neonates is reported to be proportional to gestational age, with a reduced elimination rate in the most premature. It readily crosses the placenta with minimum inactivation.

It has little or no effect on sodium and water retention.

6. PHARMACEUTICAL PARTICULARS
List of excipients
Creatinine,
Methylhydroxybenzoate 0,13 % m/v (preservative),
Propylhydroxybenzoate 0,02 % m/v (preservative),
Sodium citrate,
Sodium hydroxide,
Sodium metabisulphite (antioxidant) and
Water for injection

Incompatibilities
Not applicable.

Shelf life
18 months

Special precautions for storage
Store at or below 25 ˚C. Protect from light. Do not remove ampoule from carton until required for use.

Nature and contents of container
10 or 100 x 1 ml clear colourless, type 1, glass ampoules packed in containers.

Special precautions for disposal and other handling
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Trinity Pharma (Pty) Ltd
106 16th Road, Building 2,
Midrand,
1686, South Africa

8. REGISTRATION NUMBER(S)
41/21.5.1/0814

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
07/12/2012

10. DATE OF REVISION OF THE TEXT
22/11/2024