

IRISH MEDICINES BOARD ACT 1995, as amended

Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended

PA0002/023/001

Case No: 2052303

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Bristol-Myers Squibb Pharmaceuticals Ltd

Swords, Co. Dublin, Ireland

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Kenalog Suspension for Injection 40mg/ml

the particulars of which are set out in the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **25/06/2010**.

Signed on behalf of the Irish Medicines Board this

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kenalog Suspension for Injection 40 mg/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Triamcinolone acetonide 40mg/ml.

Excipients: contains 15mg/ml Benzyl Alcohol

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection

White fluid with slight odour of benzyl alcohol.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the local management of inflammation involving joints such as seen with rheumatoid arthritis, osteoarthritis, psoriatic arthropathy, and bursae and tendons.

In the management of corticosteroid responsive conditions such as allergic asthma, rheumatoid arthritis, certain connective tissue disorders, where depot therapy is indicated.

4.2 Posology and method of administration

Route of administration:

- Intra-articular.
- Intramuscular (deep intragluteal only).

Kenalog is only for intra-articular or intra-muscular (deep intragluteal only) use and should not be given by any other route.

The injection should be shaken well before use to achieve uniformity of suspension. Careful technique should be employed to avoid intravascular administration. An aseptic technique should be used. Since the duration of effect is variable, subsequent doses should be given when symptoms recur and not at set intervals.

Intra-articular injection:

Adults and children over 12 years:

For intra-articular administration or injection into tendon sheaths and bursae, the dose of Kenalog injection may vary from 5mg to 10mg (0.125 – 0.25ml) for smaller joints and up to 40mg (1.0ml) for larger joints, depending on the specific disease entity being treated. Single injections in to several sites for multiple joint involvement, up to a total of 80mg, have been given without undue reactions.

It is recommended that, when injections are given into the sheaths of short tendons, Adcortyl injection (triamcinolone acetonide 10mg/ml) should be used. (See under Precautions re Achilles tendon.)

Intra-muscular injection:

Adults and children over 12 years:

The suggested initial dose is 40mg (1.0ml) injected deeply into the upper, outer quadrant of the gluteal muscle. To avoid the danger of subcutaneous fat atrophy, the deltoid should not be used. Alternate sides should be used for subsequent injections.

Subsequent dosage depends on the patient's response and period of relief. Patients with hay fever or pollen asthma who do not respond to conventional therapy may obtain a remission of symptoms lasting throughout the pollen season after a single dose of 40-100mg given when allergic symptoms appear.

Children from 6-12 years:

The suggested initial dose of 40mg (1.0ml) injected deeply into the gluteal muscle should be scaled according to the severity of symptoms and the age and weight of the child.

Children under 6 years:

Kenalog is not recommended for children under six years. (See Precautions).

Elderly:

Treatment of elderly patients, particularly if long term, should be planned bearing in mind the more serious consequences of the common side effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, susceptibility to infection and thinning of the skin.

4.3 Contraindications

Hypersensitivity to any of the ingredients. Systemic infections unless specific anti-infective therapy is employed. Administration by intravenous, intrathecal or intraocular injection.

4.4 Special warnings and precautions for use

Administration by non-approved routes. (See Route of Administration).

Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.

Chicken pox and measles are of particular concern since these normally minor illnesses may be fatal in immunosuppressed patients. Unless they have had chickenpox, patients receiving parenteral corticosteroids for purposes other than replacement should be regarded as being *at risk of severe chickenpox*. Manifestations of fulminant illness include pneumonia, hepatitis and disseminated intravascular coagulation; rash is not necessarily a prominent feature. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; varicella-zoster immunoglobulin should preferably be given within 3 days of exposure and not later than 10 days. Confirmed chickenpox warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.

Patients should be advised to avoid exposure to measles and to seek medical advice without delay if exposure occurs. Prophylaxis with normal immunoglobulin may be needed.

In common with other steroids, Kenalog Injection should be used with caution in patients with recent intestinal anastomoses, thrombophlebitis, psychotic tendencies, exanthematous disease, chronic nephritis, metastatic carcinoma, osteoporosis, in patients with an active peptic ulcer (or a history of peptic ulcer); latent or healed tuberculosis; in acute glomerulonephritis. Hypertension; glaucoma (or a family history of glaucoma), previous steroid myopathy or epilepsy.

Intra-articular injection should not be carried out in the presence of active infection in or near joints. The preparation should not be used to alleviate joint pain arising from infectious states such as gonococcal or tubercular arthritis.

Diabetes may be aggravated, necessitating a higher insulin dosage. Latent diabetes mellitus may be precipitated.

Adequate studies to demonstrate the safety of Kenalog use by intra-turbinal, subconjunctival, sub-tenons, retrobulbar and intraocular (intravitreal) injections have not been performed. Endophthalmitis, eye inflammation, increased intraocular pressure and visual disturbances including vision loss have been reported with intravitreal administration. Several instances of blindness have been reported following injection of corticosteroid suspensions into the nasal turbinates and intralesional injection about the head.

There have been a few reports in the literature of the development of cataracts in patients who have been using corticosteroids for prolonged periods of time. Prescribers should be aware of the possible role of corticosteroids in cataract development.

Patients on long-term systemic therapy with Kenalog may require supportive corticosteroid therapy in time of stress, e.g. intercurrent illness, anaesthesia, surgical procedures, both during the treatment period and for a year afterwards.

Rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroids, especially when a patient has a history of drug allergies.

All corticosteroids increase calcium excretion.

Corticosteroid effects may be enhanced in patients with hypothyroidism or cirrhosis.

Avoid abrupt cessation of corticosteroids as this may result in acute adrenal insufficiency or acute rebound exacerbation of disease, particularly polyarteritis.

Patients should be provided with a source of information with clear guidance on the precautions to be taken to minimise risk, together with details of the prescriber, drug, dosage and duration of treatment.

This product contains 15mg/ml benzyl alcohol and must not be given to premature babies or neonates. Benzyl Alcohol may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years old.

Children:

Prolonged use in children may lead to growth retardation. Although some recovery may occur on discontinuing therapy, growth and development of children on prolonged corticosteroid therapy should be carefully observed.

Intra-articular injection:

Patients should be specifically warned to avoid over-use of joints in which symptomatic benefit has been obtained. Severe joint destruction with necrosis of bone may occur if repeated intra-articular injections are given over a long period of time. Care should be taken if injections are given into tendon sheaths to avoid injection into the tendon itself. Repeated injection into inflamed tendons should be avoided as it has been shown to cause tendon rupture.

Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with depot corticosteroids.

Intra-muscular injection:

During prolonged therapy a liberal protein intake is essential to counteract the tendency to gradual weight loss sometimes associated with negative nitrogen balance and wasting of skeletal muscle.

4.5 Interaction with other medicinal products and other forms of interaction

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

Anticholinesterases: Effects of anticholinesterase agent may be antagonised.

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.

Antihypertensives, including diuretics: Corticosteroids antagonise the effects of antihypertensives and diuretics. The hypokalaemic effect of diuretics, including acetazolamide, Loop diuretics, thiazide diuretics and carbenoxolone, is enhanced.

Anti-tubercular drugs: Isoniazid serum concentrations may be decreased.

Cyclosporin: Monitor for evidence of increased toxicity of cyclosporin when the two are used concurrently.

Digitalis glycosides: Co-administration may enhance the possibility of digitalis toxicity.

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

Hepatic enzyme inducers (e.g barbiturates, phenytoin, carbamazepine, rifampicin, primidone, aminogluthetimide): There may be increased metabolic clearance of Adcortyl. Patients should be carefully observed for possible diminished effect of steroid, and the dosage should be adjusted accordingly.

Human growth hormone: The growth-promoting effect may be inhibited.

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

Nondepolarising 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 GI 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. Aspirin should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinaemia.

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 4.4 Special Warnings and Special Precautions for Use).

4.6 Pregnancy and lactation

Corticosteroids should only be used in pregnancy if considered essential by the physician. Corticosteroids have been shown to be teratogenic in animals. To date, there is no confirmed report of a similar effect in human beings.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Where adverse reactions occur they are usually reversible on cessation of therapy. Corticosteroid administration will result in certain effect, the severity, significance and extent of which vary with the dosage and duration of treatment and the particular corticosteroid used.

Absorption of triamcinolone following injection by the intra-articular route is rare. However, patients should be watched closely for the following adverse reactions which may be associated with any corticosteroid therapy:

Dyspepsia, peptic ulceration with perforation and haemorrhage, abdominal distension, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis.

Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture.

Sodium and water retention, hypertension, hypokalaemic alkalosis, congestive heart failure in susceptible patients, cardiac arrhythmias or ECG changes due to potassium deficiency.

Impaired healing, skin atrophy, bruising, striae, telangiectasia, acne.

Suppression of the hypothalamo-pituitary adrenal axis, growth suppression in childhood and adolescence, menstrual irregularity and amenorrhoea. Cushingoid facies, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, negative nitrogen balance.

Euphoria, psychological dependence, depression, insomnia, headache. Intracranial hypertension has been reported in children on cessation of long term steroid therapy. Aggravation of schizophrenia.

Anaphylactic reactions and hypersensitivity reactions such as rash, pruritis and urticaria, particularly where there is a history of drug allergies.

Increased intra-ocular pressure, glaucoma, exophthalmos, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease.

Opportunistic infection, recurrence of dormant tuberculosis, leucocytosis, hypersensitivity, thromboembolism, increased appetite, nausea, malaise.

On withdrawal fever, myalgia, arthralgia or adrenal insufficiency may occur.

Intra-articular injection:

Reactions following intra-articular administration have been rare. In a few instances transient flushing and dizziness have occurred. Local symptoms such as post-injection flare, transient pain, irritation, sterile abscesses, hyper- or hypo-pigmentation, Charcot-like arthropathy and occasional increase in joint discomfort may occur. Local fat atrophy may occur if the injection is not given into the joint space, but is temporary and disappears within a few weeks to months.

Intramuscular injection:

Severe pain has been reported following intramuscular administration. Sterile abscesses, cutaneous and subcutaneous atrophy, hyperpigmentation, hypopigmentation and Charcot-like arthropathy have also occurred.

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Triamcinolone acetonide is a synthetic glucocorticoid with marked anti-inflammatory and anti-allergic actions.

Intra-articular injection: Following the local injection, relief of pain and swelling, with greater freedom of movement, is usually obtained within a few hours.

Intramuscular injection: Provides an extended duration of therapeutic effect and fewer side-effects of the kind associated with oral corticosteroid therapy, particularly gastrointestinal reactions such as peptic ulceration. Studies indicate that, following a single intramuscular dose of 80mg triamcinolone acetonide, adrenal suppression occurs within 24-48 hours and then gradually returns to normal, usually in approximately three weeks. This finding correlates closely with the extended duration of therapeutic action of triamcinolone acetonide.

5.2 Pharmacokinetic properties

Triamcinolone acetonide may be absorbed into the systemic circulation from synovial spaces. However clinically significant systemic levels after intra-articular injection are unlikely to occur except perhaps following treatment of large joints with high doses. Systemic effects do not ordinarily occur with intra-articular injections when the proper techniques of administration and the recommended dosage regimens are observed.

Triamcinolone acetonide is absorbed slowly, though almost completely, following depot administration by deep intramuscular injection; biologically active levels are achieved systemically for prolonged periods (weeks to months). In common with other corticosteroids, triamcinolone is metabolised largely hepatically but also by the kidney and is excreted in urine. The main metabolic route is 6-beta-hydroxylation; no significant hydrolytic cleavage of the acetonide occurs.

In view of the hepatic metabolism and renal excretion of triamcinolone acetonide, functional impairments of the liver or kidney may affect the pharmacokinetics of the drug.

5.3 Preclinical safety data

See 4.6 Pregnancy and Lactation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Polysorbate 80
Carmellose sodium
Sodium chloride
Water for injections

6.2 Incompatibilities

The injection should not be physically mixed with other medicinal products.

6.3 Shelf Life

Unopened: 3 years.

Chemical and physical in-use stability has been demonstrated for 28 days at up to 25°C. From a microbiological point of view, once opened, the product may be stored for a maximum of 28 days at 25°C. Other in-use times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze. Keep the container in the outer carton to protect from light.

6.5 Nature and contents of container

1ml or 2ml ready-filled glass syringe.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The injection should be shaken well before use to achieve uniformity of suspension. An aseptic technique should be used. For single use only. Discard any unused contents.

7 MARKETING AUTHORISATION HOLDER

Bristol-Myers Squibb Pharmaceuticals Limited
Swords
Co. Dublin

8 MARKETING AUTHORISATION NUMBER

PA 2/23/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1978

Date of last renewal: 01 April 2008

10 DATE OF REVISION OF THE TEXT

June 2010