SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Kenalog Intra-articular / Intramuscular Injection 40mg/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Kenalog Intra-articular / Intramuscular Injection contains triamcinolone acetonide 40 mg per ml of sterile suspension.

Excipient(s) with known effect: 15 mg/ml Benzyl alcohol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Sterile aqueous suspension for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Intra-articular use: for alleviating the joint pain, swelling and stiffness associated with rheumatoid arthritis and osteoarthrosis, with an inflammatory component; also for bursitis, epicondylitis, and tenosynovitis.

Intramuscular use: Where sustained systemic corticosteroid treatment is required: *Allergic states*: bronchial asthma. (see section 4.2); *Endocrine disorders*, e.g. primary or secondary adrenocortical insufficiency. *Collagen disorders*, e.g. during an exacerbation of maintenance therapy of selected cases of SLE or acute rheumatic carditis; *Dermatological diseases*, e.g. pemphigus, severe dermatitis and Stevens Johnson Syndrome; *Rheumatic, Gastrointestinal or Respiratory disorders* - as an adjunctive, short-term therapy; *Haematological disorders*, e.g. acquired (autoimmune) haemolytic anaemia; *Neoplastic diseases*, e.g. palliative management of leukaemia and lymphomas; *Renal disease*, such as acute interstitial nephritis, minimal change nephrotic syndrome or lupus nephritis.

4.2 Posology and method of administration

Kenalog is for Intra-articular/Intramuscular injection ONLY. The safety and efficacy of administration by other routes has yet to be established (see sections 4.3 and 4.4). Strict aseptic precautions should be observed. Since the duration of effect is variable, subsequent doses should be given when symptoms recur and not at set intervals.

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

It is recommended that, when injections are given into the sheaths of short tendons, Adcortyl Injection (triamcinolone acetonide 10 mg/ml) should be used (see section 4.4 re Achilles tendon).

Intramuscular Injection: To avoid the danger of subcutaneous fat atrophy, it is important to ensure that deep intramuscular injection is given into the gluteal site. The deltoid should not be used. Alternate sides should be used for subsequent injections.

Adults and Children over 12 Years:

The suggested initial dose is 40 mg (1.0 ml) injected deeply into the upper, outer quadrant of the gluteal muscle. Subsequent dosage depends on the patient's response and period of relief. Patients with asthma who do not respond to conventional therapy may obtain a remission of asthmatic symptoms after a single dose of 40-100 mg given when allergic symptoms appear (see section 4.4).

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. Close clinical supervision is required to avoid life-threatening reactions.

Children from 6-12 Years of Age:

The suggested initial dose of 40 mg (1.0 ml injected deeply into the gluteal muscle should be scaled according to the severity of symptoms and the age and weight of the child. Kenalog is not recommended for children under six years. Growth and development of children on prolonged corticosteroid therapy should be carefully observed. Caution should be used in the event of exposure to chickenpox, measles or other communicable diseases (see section 4.4).

Triamcinolone withdrawal: In patients who have received more than physiological doses of Kenalog (more than one injection during a three week period), withdrawal should not be abrupt. The dose should be reduced and the dosage interval increased

until a dose of not more than 40 mg and a dosage interval of at least three weeks have been achieved as the dose of systemic corticosteroid is reduced. Clinical assessment of disease activity may be needed.

Abrupt withdrawal of short term systemic corticosteroid treatment is appropriate if it is considered that the disease is unlikely to relapse. A single dose, which is not repeated within a three week period, is unlikely to lead to clinically relevant hpa-axis suppression in the majority of patients. However, in the following patient groups, gradual withdrawal of systemic corticosteroid therapy should always be considered:

Patients who have had repeated courses of systemic corticosteroids.

When a course of Kenalog 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 corticosteroid therapy.

4.3 Contraindications

Hypersensitivity to any of the ingredients.

Systemic infections unless specific anti-infective therapy is employed.

Administration by intravenous, intrathecal, epidural or intraocular injection.

4.4 Special warnings and precautions for use

Warnings:

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.

Cases of serious anaphylactic reactions and anaphylactic shock, including death, have been reported in individuals receiving triamcinolone acetonide injection, regardless of the route of administration.

(Intra-Articular Injection):

Corticosteroids should not be injected into unstable joints.

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.

(Intramuscular 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.

Precautions:

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.

Undesirable effects may be minimised using the lowest effective dose for the minimum period, and by administering the daily requirement, whenever possible, as a single morning dose on alternate days. Frequent patient review is required to titrate the dose appropriately against disease activity (see section 4.2).

Adrenal cortical atrophy develops during prolonged 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 will require a temporary increase in dosage. If corticosteroids have been stopped following prolonged therapy they may need to be reintroduced temporarily.

Patients should carry steroid treatment cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.

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.

Chickenpox 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.

During corticosteroid therapy antibody response will be reduced and therefore affect the patient's response to vaccines. Live vaccines should not be administered.

Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 pharmacokinetic interactions that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Special Precautions:

Particular care is required when considering use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

Recent intestinal anastomoses, diverticulitis, thrombophlebitis, existing or previous history of severe affective disorders (especially previous steroid psychosis), exanthematous disease, chronic nephritis, or renal insufficiency, metastatic carcinoma, osteoporosis (post-menopausal females are particularly at risk); in patients with an active peptic ulcer (or a history of peptic ulcer). Myasthenia gravis. Latent or healed tuberculosis; in the presence of local or systemic viral infection, systemic fungal infections or in active infections not controlled by antibiotics. In acute psychoses; in acute glomerulonephritis. Hypertension; congestive heart failure; glaucoma (or a family history of glaucoma), previous steroid myopathy or epilepsy. Liver failure.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects. During post marketing use, there have been reports of clinically significant drug interactions in patients receiving triamcinolone acetonide and

ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, co-administration of triamcinolone acetonide and ritonavir is not recommended unless the potential benefit of treatment outweighs the risk of systemic corticosteroid effects (see section 4.5).

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

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

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

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

All corticosteroids increase calcium excretion

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

This product contains 15 mg/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.

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

<u>Use in Children:</u>

Kenalog is not recommended for children under six years. Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence which may be irreversible, therefore growth and development of children on prolonged corticosteroid therapy should be carefully observed.

<u>Use in Elderly:</u>

The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

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, 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, aminoglutethimide): There may be increased metabolic clearance of Kenalog. 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.

CYP 3A4 inhibitors: Triamcinolone acetonide is a substrate of CYP3A4. Co-administration with strong CYP3A4 inhibitors (eg, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin) with triamcinolone is not recommended because increased systemic corticosteroid adverse effects may occur (see section 4.8). If the potential benefit of co-administration outweighs the increased risk of systemic corticosteroid side-effects, patients should be monitored for these effects. During post marketing use, there have been reports of clinically

significant drug interactions in patients receiving triamcinolone acetonide and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression (see section 4.4).

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 section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy:
The ability of corticosteroids to cross the placenta varies between individual drugs, however triamcinolone does cross the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate / lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important.

As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential, however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Breast-feeding:

Corticosteroids may pass into breast milk, although no data are available for triamcinolone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The list of undesirable effects shown below is presented by system organ class, MedDRA preferred term, and frequency. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (≥1/10,000); Not known (cannot be estimated from the available data).

System Organ Class	Frequency	MedDRA Terms
Infections and infestations	Common	Infection
	Uncommon	Injection site abscess sterile, Infection masked, Tuberculosis, Candida infection, Eye infection viral, Eye infection fungal, Rhinitis, Conjunctivitis
Immune system disorders	Uncommon	Anaphylactoid reaction Anaphylactic reaction Anaphylactoid shock
Endocrine disorders	Uncommon	Cushingoid, Adrenal suppression, Secondary adrenocortical insufficiency, Hypopituitarism
Metabolism and nutrition disorders	Uncommon	Sodium retention, Fluid retention, Alkalosis hypokalaemic, Hyperglycaemia, Diabetes mellitus

		inadequate control, Calcium deficiency, Increased appetite
Psychiatric disorders	Uncommon	Psychiatric symptom, Depression, Euphoric mood, Mood swings, Psychotic disorder, Personality change, Insomnia, Drug dependence, Mental disorder, Irritability, Suicidal ideation, Anxiety, Cognitive disorder
Nervous system disorders	Common	Headache
	Uncommon	Convulsion, Epilepsy, Syncope, Benign intracranial hypertension, Neuritis, Paraesthesia, Intracranial pressure increased, Dizziness
Eye disorders	Uncommon	Blindness, Cataract, Glaucoma, Exophthalmos, Corneal perforation, Papilloedema.
	Not known	Vision, blurred (see also section 4.4)
Ear and labyrinth disorders	Uncommon	Vertigo
Cardiac disorders	Uncommon	Cardiac failure congestive, Arrhythmia
Vascular disorders	Uncommon	Hypertension, Embolism, Thrombophlebitis, Vasculitis necrotising, Hypotension, Flushing
Gastrointestinal disorders	Uncommon	Peptic ulcer, Peptic ulcer perforation, Peptic ulcer haemorrhage, Pancreatitis, Abdominal distension, Oesophagitis ulcerative, Dyspepsia

Skin and subcutaneous tissue disorders	Uncommon	Urticaria, Rash, Skin hyperpigmentation, Skin hypopigmentation, Skin atrophy, Skin fragility, Petechiae, Ecchymosis, Erythema, Hyperhidrosis, Purpura, Skin striae, Hirsutism, Dermatitis acneiform, Cutaneous lupus erythematosus, Angioedema, Pruritus
Musculoskeletal connective tissue and bone disorders	Common	Arthralgia
	Uncommon	Osteoporosis, Osteonecrosis, Pathological fracture, Fracture delayed union, Musculoskeletal discomfort, Muscular weakness, Myopathy, Muscle atrophy, Growth retardation, Neuropathic arthropathy, Myalgia
Renal and urinary disorders	Uncommon	Glycosuria
Reproductive system and breast disorders	Uncommon	Menstrual irregularities, Amenorrhoea and Postmenopausal vaginal bleeding
General disorders and administration site conditions	Common	Injection site reaction
	Uncommon	Synovitis, Pain, Injection site irritation, Injection site discomfort, Fatigue, Impaired healing, Hyperthermia

Investigations	Uncommon	Blood potassium decreased, Electrocardiogram change, Carbohydrate tolerance decreased, Nitrogen balance negative, Intraocular pressure increased, Laboratory test interference, Weight decreased, Blood calcium abnormal, Protein total abnormal
Injury and poisoning	Uncommon	Spinal compression fracture

4.9 Overdose

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

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 local injection, relief of pain and swelling and greater freedom of movement are 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 gastro-intestinal 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 section 4.6.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol, polysorbate 80, carmellose sodium, sodium chloride, water.

6.2 Incompatibilities

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

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze. Store in an upright position.

6.5 Nature and contents of container

Carton containing glass ampoules 5 x 1ml or individually cartoned multidose vials of 5ml or individually cartoned 1ml and 2ml syringes.

6.6 Special precautions for disposal

No special handling instructions.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Bristol-Myers Squibb Pharmaceuticals Unlimited Company

Plaza 254, Blanchardstown Corporate Park 2,

Dublin 15, Dublin, D15 T867

8 MARKETING AUTHORISATION NUMBER(S)

PL 12038/0005

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