Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Adcortyl Intra-articular/Intra-Dermal Injection 10mg/ml suspension for injection, 1 ml.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Triamcinolone acetonide 10 mg per ml (10 mg per 1 ml ampoule).

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

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for Injection (injection).

White, Sterile aqueous suspension with a slight odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Intra-articular use:
in the local management of inflammation involving joints, bursae or tendon sheaths such as occurs in rheumatoid arthritis, osteoarthritis, bursitis, synovitis, tendinitis, epicondylitis and trauma.

Intradermal use:
for inflammatory dermal lesions such as lichen simplex, lichen planus, psoriasis, granuloma annulare, keloids and for alopecia.

4.2 Posology and method of administration

Adcortyl Injection is only for intra-articular or intra-dermal use and should not be given by any other route. 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.

Adcortyl Injection should only be given in an appropriate setting where there is access to emergency medical care.

Adults:
The dose of Adcortyl Injection for intra-articular administration, and injection into tendon sheaths and bursae, is dependent on the size of the joint to be treated and on the severity of the condition.

Doses of 2.5 - 5 mg (0.25 - 0.5 ml) for smaller joints and 5 - 15 mg (0.5 - 1.5 ml) for larger joints usually alleviate the symptoms. Triamcinolone acetonide 40 mg/ml (Kenalog) is available to facilitate administration of larger doses. (see section 4.4 re Achilles tendon.)

Intradermal dosage is usually 2 - 3 mg (0.2 - 0.3 ml), depending on the size of the lesion. No more than 5 mg (0.5 ml) should be injected at any one site. If several sites are injected the total dosage administered should not exceed 30 mg (3 ml). The injection may be repeated if necessary, at one or two week intervals.

Children:
Adcortyl is not recommended in children under 6 years. Adcortyl intra-articular / intradermal may be used in older children in suitably adjusted dosages. Growth and development of children on prolonged corticosteroid therapy should be carefully observed.

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, hypokalaemia, susceptibility to infection and thinning of the skin. Close supervision is required to avoid life-threatening reactions.

4.3 Contraindications

In patients with an active peptic ulcer (or a history of peptic ulcer). Active or latent or healed tuberculosis; in the presence of local or systemic viral infection, systemic fungal infections or in active bacterial infections not controlled by antibiotics. In acute psychoses. In those with allergy or hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1. Administration by intravenous, intrathecal or intraocular injection.

4.4 Special warnings and precautions for use

Adcortyl is not suitable for intravenous, intramuscular, intraocular, epidural or intrathecal use.

In common with other steroids, Adcortyl Injection should be used with caution in patients with recent intestinal anastomoses, thrombophlebitis, psychotic tendencies, exanthematous disease, chronic nephritis, metastatic carcinoma, osteoporosis (post-menopausal females are particularly at risk); in acute glomerulonephritis, hypertension, congestive heart failure, glaucoma (or a family history of glaucoma), previous steroid myopathy or epilepsy; liver failure.

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.

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.

Patients on long-term systemic therapy with Adcortyl may require supportive corticosteroid therapy in times of stress, general anaesthesia or during surgery, both during the treatment period and for a year afterwards. During corticosteroid therapy antibody response will be reduced and therefore affect the patient’s response to vaccines.

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.Appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug (see section 4.2).

All corticosteroids increase calcium excretion.

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

Corticosteroid administration will result in certain effects, the severity, significance and extent of which vary with the dosage and duration of treatment and the particular corticosteroid used. These include disturbance in electrolyte balance, mineral metabolism, glucose metabolism and gluconeogenesis, nitrogen depletion, diminished lymphoid tissue and immune response, inhibition of pituitary function, Cushingoid syndrome, increase in blood coagulability, diminished response.

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

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 (see section 4.8). 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 4.8). Therefore, caution is advised in co-administration of triamcinolone acetonide and ritonavir (see section 4.5).

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 for exposed non-immune patients receiving systemic corticosteroids or for those 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 dosage 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.

Prolonged use in children may lead to growth retardation. Some recovery may occur on discontinuing therapy.

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 on prolonged therapy should obtain and carry with them a steroid treatment card from their pharmacist which gives clear guidance on the precautions to be taken to minimise risk and which provides details of prescriber, drug, dosage and the duration of treatment.

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 section 4.5), 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.

Adequate studies to demonstrate the safety of Adcortyl 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.

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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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

Anticholinesterases: Effects of anticholinesterase agents 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, aminoglutethimide): 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.

CYP 3A4 inhibitors: Triamcinolone acetonide is a substrate of CYP3A4. Caution is advised in co-administration with strong CYP3A4 inhibitors (eg, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin) with triamcinolone because increased systemic corticosteroid adverse effects may occur (see section 4.8). 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 and 4.8).

Non-depolarising muscle relaxants: Corticosteroids may decrease or enhance the neuromuscular blocking action.

Non-steroidal 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
Corticosteroids are not recommended for pregnant patients, particularly in the first trimester, or for nursing mothers, except when the disease for which they are indicated warrants their use. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

There is evidence of harmful effects in pregnancy in animals. There may be a small risk of cleft palate and intra-uterine growth retardation. Hypoadrenalism may occur in the neonate. Patients with pre-eclampsia or fluid retention require close monitoring.

Breast-feeding
Corticosteroids are found in breast milk.

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).

Where adverse reactions occur they are usually reversible on cessation of therapy. The incidence of predictable side-effects, including hypothalamic-pituitary-adrenal suppression correlate with the relative potency of the drug, dosage, timing of administration and duration of treatment (see section 4.4).

Absorption of triamcinolone following Adcortyl injection, especially when given 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:

System Organ Class	**Frequency**	**MedDRA Terms**
Infections and infestations	*Common*	infection, increased susceptibility and severity of infections such as sepsis, necrotising fasciitis
	Uncommon	injection site abscess sterile, candida infection, eye infection viral, eye infection fungal, infection masked, tuberculosis

Metabolism and nutrition disorders	*Uncommon*	sodium retention, fluid retention, alkalosis hypokalaemic, hyperglycaemia, diabetes mellitus, diabetes mellitus inadequate control, calcium deficiency, increased appetite
Musculoskeletal connective tissue and bone disorders	*Uncommon*	muscular weakness, myopathy, muscle atrophy, osteoporosis, osteonecrosis, fracture delayed union, pathological fractures, neuropathic arthropathy, musculoskeletal discomfort, growth retardation
Immune system disorders	*Uncommon*	~~A~~anaphylactoid reaction, anaphylactic reactions, anaphylactic shock
Gastrointestinal disorders	*Uncommon*	peptic ulcer with possible subsequent perforation and haemorrhage, pancreatitis, abdominal distension, oesophagitis ulcerative, dyspepsia
Skin and subcutaneous tissue disorders	*Uncommon*	rash, pruritus, urticaria (particularly where there is a history of drug allergies), skin hyperpigmentation, skin hypopigmentation, skin atrophy, skin fragility, petechiae, ecchymosies, erythema, hyperhidrosis, purpura, skin striae, hirsutism, dermatitis acneiform, cutaneous lupus erythematous, angioedema
Nervous system disorders	*Common*	headache
	Uncommon	convulsion, syncope, benign intracranial hypertension usually after treatment, neuritis, paraesthesia, epilepsy
Reproductive system and breast disorders	*Uncommon*	menstrual irregularities, amenorrhoea and postmenopausal vaginal bleeding
Endocrine disorder	*Uncommon*	cushingoid, adrenal suppression, secondary adrenocortical and pituitary unresponsiveness
Eye disorders	*Uncommon*	blindness, cataract, glaucoma, exophthalmos, papilloedema, corneal or scleral thinning, corneal perforation
Ear and labyrinth disorders	*Uncommon*	vertigo
Cardiac disorders	*Uncommon*	cardiac failure congestive, arrhythmia
Vascular disorders	*Uncommon*	hypertension, vasculitis necrotising, thrombophlebitis, embolism,leucocytosis, flushing

Psychiatric disorders	*Uncommon*	irritability, euphoric mood, depression, mood swings,suicidal ideation), psychotic disorders,personality changes, anxiety, insomnia, cognitive disorders including amnesia, psychiatric symptom
General disorders and administration site conditions	*Common*	injection site reaction
	Uncommon	synovitis, pain, injection site irritation, injection site discomfort, fatigue, impaired wound healing
Investigations	*Uncommon*	blood potassium decreased, electrocardiogram change, carbohydrate tolerance decreased, weight increase, nitrogen balance negative, blood calcium abnormal, intraocular pressure increased, laboratory test interference
Injury and poisoning	*Uncommon*	spinal compression fracture, tendon rupture

Psychiatric disorders may occur in both adults and children.

Withdrawal Symptoms and Signs:
On withdrawal, psychological effects have been reported with corticosteroids, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight decreased may occur, the frequency is uncommon. Too rapid a reduction in dose following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4).

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: HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glucocorticoids, ATC code: H02AB08

Triamcinolone acetonide is a synthetic glucocorticoid, with marked anti-inflammatory and anti-allergic actions. Following local injection of Adcortyl, relief of pain and swelling and greater freedom of movement are usually obtained within a few hours; such administration avoids the more severe side-effects which may accompany parenteral or oral corticosteroid administration.

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.

The systemic effects of intradermally administered triamcinolone acetonide have not been extensively studied. The risk of systemic absorption, though minimal, should be taken into consideration especially when repeated intralesional administrations may be necessary.

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 for injection

6.2 Incompatibilities

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

6.3 Shelf life

Unopened: 3 years
Once opened: For single use only. Discard any unused contents immediately after use.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze or refrigerate. Protect from light.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Carton containing 5 x 1 ml clear Type I glass ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Store in an upright position. Shake well before use.

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

7 MARKETING AUTHORISATION HOLDER

Bristol-Myers Squibb Pharmaceuticals uc
Plaza 254, Blanchardstown Corporate Park 2, Ballycoolin
Dublin 15, D15 T867
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8 MARKETING AUTHORISATION NUMBER

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