Adrenocortical Steroid

BFI MYS-002
R.O.C. Reg. No.:031695

BUFENCON INJECTION 5ML VIAL

Description: A white to off-white suspension.

Ingredients: Each mL contains:
Betamethasone (as dipropionate) 5mg
Betamethasone (as phosphate disodium) 2mg
Preservatives:
Benzyl Alcohol 5mg
Methyl Paraben 1.8mg
Propyl Paraben 0.2mg

Pharmacology:
Pharmacodynamic:
Betamethasone is a glucocorticoid that, when given systemically, has potent glucocorticoid activity and binds with high affinity to the glucocorticoid receptor. Betamethasone thus has catabolic effects on proteins in peripheral tissues, cause resistance to insulin and impair peripheral utilization of glucose, and immuno suppressive from bone. Betamethasone has both local anti-inflammatory and immunosuppressive activity. Thus, Betamethasone inhibits the adherence of neutrophils and monocytemacrophages to the capillary endothelial cells of the inflamed area. The drug blocks the effect of macrophage migration inhibitory factor and decreases the activation of plasminogen to plasmin.
Finally, by inhibition of phospholipase A2 activity, via formation of lipocortin, Betamethasone reduces the formation of prostaglandins and leukotrienes in local tissue.
Pharmacokinetic:
1. Betamethasone decreases or prevents tissue responses to inflammatory processes, thereby reducing the development of symptoms of inflammation without affecting the underlying cause. It inhibits accumulation of inflammatory cells including macrophages and leukocytes at sites of inflammation.
2. Prompt therapeutic activity in corticosteroid-responsive conditions is achieved by the soluble ester, betamethasone sodium phosphate, which is quickly absorbed after injection. Sustained activity is provided by betamethasone dipropionate, which is only slightly soluble and affords a repository for slow absorption, thereby controlling symptoms over a prolonged period.
3. Betamethasone is primarily metabolized in the liver, other is in the kidney and tissue, to mostly inactive metabolites which are excreted in the urine.

Indications:
BUFENCON INJECTION 5ML VIAL is indicated for the treatment of acute and chronic corticosteroid-responsive disorders. Corticosteroid hormone therapy is an adjunct to, and not a replacement for, conventional therapy.
Musculoskeletal and Soft Tissue Conditions: Rheumatoid arthritis; osteoarthritis; bursitis; ankylosing spondylitis; epicondylitis; radiculitis; coccydynia; sciatica; lumbago; torticollis; ganglion cyst; exostasis; fasciitis.
Allergic Conditions: Chronic bronchial asthma (including adjunctive therapy for status asthmaticus); hay fever; angioneurotic edema; allergic bronchitis; seasonal or perennial allergic rhinitis; drug reactions; serum sickness; insect bites.
Dermatologic Conditions: Atopic dermatitis (nummular eczema); neurodermatitis (circumscribed lichen simplex); contact dermatitis; severe solar dermatitis; urticaria; hypertropic lichen planus; necrobiosis lipoidica diabeticorum; alopecia areata; discoid lupus erythematosus; psoriasis; keloids; pemphigus; dermatitis herpetiformis; cystic acne.
Collagen Diseases: Disseminated lupus erythematosus; scleroderma; dermatomyositis; periarteritis nodosa.
Neoplastic Diseases: For palliative management of leukemias and lymphomas in adults; acute leukemia of childhood.
Other Conditions: Adrenogenital syndrome; ulcerative colitis; regional ileitis; sprue; podiatric conditions (bursitis under heloma durum, hallux rigidus, digiti quinti varus); affections requiring subconjunctival injection; corticosteroid-responsive blood dyscrasias; nephritis, and nephritic syndrome.
Primary and secondary adrenocortical insufficiency may be treated with BUFENCON INJECTION 5ML VIAL but should be supplemented with mineralocorticosteroids, if applicable.
BUFENCON INJECTION 5ML VIAL is recommended for (1) intramuscular injection in conditions responsive to systemic corticosteroids; (2) injection directly into the affected soft tissues where indicated; (3) intra-articular and periarticular injection in arthritides; (4) intralesional injection in various dermatologic conditions; and (5) local injection in certain inflammatory and cystic disorders of the foot.

Route of Administration:
Parenteral (Non I.V.)

Dosage and administration:
DOSING REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE SPECIFIC DISEASE, ITS SEVERITY AND THE RESPONSE OF THE PATIENT.
The initial dose should be maintained or adjusted until a satisfactory response is observed. If a satisfactory clinical response does not occur after a reasonable period of time, treatment with BUFENCON INJECTION 5ML VIAL should be discontinued and other appropriate therapy initiated.
Systemic Administration: For systemic therapy, treatment is initiated with 1 to 2 ml in most conditions and repeated as necessary. Administration is by deep intramuscular (I.M.) injection in the gluteal region. Dosage and frequency of administration will depend on the severity of the patient's condition and the therapeutic response. Two ml might be required initially in a severe illness, such as lupus erythematosus or status asthmaticus which has been resolved by appropriate life-saving procedures.
A wide variety of dermatologic conditions respond effectively to an IM injection of 1 mL BUFENCON INJECTION 5ML VIAL, repeated according to the response of the conditions.
In respiratory tract disorders, onset of relief from symptoms has occurred within a few hours after I.M. injection of BUFENCON INJECTION 5ML VIAL.
Effective control of symptoms with 1 to 2 mL is obtained in bronchial asthma, hay fever, allergic bronchitis and allergic rhinitis.
In the treatment of acute or chronic bursitis, excellent results are obtained with 1 to 2 mL I.M. injection of BUFENCON INJECTION 5ML VIAL, repeated as necessary.
Local Administration: Concomitant use of a local anesthetic is rarely necessary. If coadministration of a local anesthetic is desired, BUFENCON INJECTION 5ML VIAL may be mixed (in a syringe, not the vial) with 1% or 2% procaine hydrochloride or lidocaine, using formulations which do not contain parabens. Similar local anesthetics may also be used. Anesthetics containing methylparaben, propylparaben, phenol, etc. should be avoided. The required dose of BUFENCON INJECTION 5ML VIAL is first withdrawn from the vial into the syringe. The local anesthetic is then drawn in, and the syringe is shaken briefly.
In acute subdeltoid, subacromial, oleocranon, and prepatellar bursitis, an intrabursal injection of 1 to 2 mL of BUFENCON INJECTION 5ML VIAL may relieve pain and restore full range of movement within a few hours. Chronic bursitis may be treated with reduced dosage once acute symptoms are controlled. In acute tenosynovitis, tendinitis, and peritendinitis, one injection of BUFENCON INJECTION 5ML VIAL should alleviate the condition. In chronic forms of these conditions, it may be necessary to repeat the injection as the patient's condition requires.
Following 0.5 to 2 mL intra-articular administration of BUFENCON INJECTION 5ML VIAL, relief from pain, soreness, and stiffness associated with rheumatoid arthritis and osteoarthritis may be experienced within two to four hours. Duration of relief, which varies widely in both diseases, is four or more weeks in the majority of cases.
An intra-articular injection of BUFENCON INJECTION 5ML VIAL is well tolerated in the joint and periarticular tissues.
Recommended doses for intra-articular injection are: large joints (knee, hip, shoulder), 1 to 2 mL; medium joints (elbow, wrist, ankle), 0.5 to 1 mL; small joints (foot, hand, chest), 0.25 to 0.5 mL.
Dermatologic conditions may respond to intralesional administration of BUFENCON INJECTION 5ML VIAL. Response of some lesions not treated directly may be due to a slight systemic effect of the drug. In intralesional treatment, an intradermal dosage of 0.2 mL/cm^2 of BUFENCON INJECTION 5ML VIAL evenly injected with a tuberculin syringe and a 26-gauge needle is recommended. The total amount of BUFENCON INJECTION 5ML VIAL injected at all sites each week should not exceed 1 mL.
BUFENCON INJECTION 5ML VIAL may be used effectively in disorders of the foot that are responsive to corticosteroid therapy. Bursitis under heloma durum may be controlled with two successive injections of 0.25 mL each. In some conditions, such as hallux rigidus, digiti quinti varus and acute gouty arthritis, onset of relief may be rapid. A tuberculin syringe with a 25-gauge needle is suitable for most injections. Recommended doses at intervals of approximately one week: bursitis under heloma durum or molle, 0.25 to 0.5 mL; bursitis under calcaneal spur, 0.5 ml; bursitis over hallux rigidus, 0.5 ml; bursitis over digiti quinti varus, 0.5 ml; synovial cyst, 0.25 to 0.5 ml; Morton's neuralgia (metatarsalgia), 0.25 to 0.5 ml; tenosynovitis, 0.5 ml; periostitis of cuboid, 0.5 ml; acute gouty arthritis, 0.5 to 1 ml.
After a favorable response is obtained, the proper maintenance dosage should be determined by decreasing the initial dose in small decrements at appropriate time intervals until the lowest dose which will maintain an adequate clinical response is determined.
Exposure of the patient to stressful situations unrelated to the existing disease may necessitate an increased dose of BUFENCON INJECTION 5ML VIAL. If the drug is to be discontinued after long-term therapy, the dose should be decreased gradually.
To be administered only by a physician.

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Contraindications:
Contraindicated in patients hypersensitive to Betamethasone, other corticosteroids and to any components of this product.
As with other corticosteroid preparations, Bufencon Injection is contra-indicated in systemic infections.
Corticosteroids should not be injected into unstable joints, infected areas, or intervertebral spaces.

Precautions:
1. Bufencon Injection is not for intravenous use.
2. Long-term intramuscular administration of corticosteroids is known to cause secondary adrenocortical insufficiency. Patients treated for extended periods should be given gradually reduced dosages.
3. When local or systemic infections are present, therapy with Bufencon Injection is not recommended.
4. This product contains two betamethasone esters one of which, betamethasone sodium phosphate disappears rapidly from the injection site. The potential systemic effect produced by the soluble portion should therefore be taken into account by the physician when using the drug.
5. While on corticosteroid therapy patients should not be vaccinated againts smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially in high doses because of possible hazards of neurological complications and lack of antibody response.
6. Because rare instances of anaphylactoid reactions have occured in patients receiving parenteral corticosteroids therapy, appropriate precautionary measures should be taken prior to administration, especially when the patients has allergy to any drug.
7. Intra-articular injection of corticosteroid may produce systemic as well as local effects.
   Appropriate examination of any joint fluid present is necessary to exclude a septic process.
8. The injection contains polysorbate 80. Premature life-threatening syndrome consisting of liver and renal failure, pulmonary deterioration, thrombocytopenia, and ascites has been associated with an injectable vitamin E products containing polysorbate 80.
9. Since adequate human reproduction have not been studied with corticosteroids, the use of this drug in pregnancy, nursing mothers, or women of child bearing potential requires that the risk benefit ratio should be considered.

Warnings
As this preparation contains benzyl alcohol, its use should be avoided in children under two years of age.
Not to be used in neonates.

Interaction with other medicaments:
Steroids may reduce the effects of anticholinesterases in myasthenia gravis, cholecystographic X-ray media and non-steroidal anti-inflammatory agents.
Rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, aminoglutethimide and ephedrine enhance the metabolism of corticosteroids; thus the corticosteroid therapeutic effect may be reduced.
The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.
The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.
The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.
The risk of hypokalaemia is increased with theophylline, ulcer healing drugs such as carbenoxolone and antifungals such as amphotericin B.
Increased toxicity may result if hypokalaemia occurs in patients on cardiac glycosides.
Ritonavir and oral contraceptives may result in increased plasma concentrations or corticosteroids.
The effect of corticosteroids may be reduced for 3-4 days after mifepristone.
The growth promoting effect of somatropin may be inhibited by corticosteroids.
An increase in the incidence of gastrointestinal bleeding may occur if NSAIDS are taken concomitantly with corticosteroids.
Corticosteroids may antagonise the effects of neuromuscular blocking drugs such as vecuronium.
Concurrent use of corticosteroids and fluoroquinolones may result in increased risk of tendon rupture.
Concomitant use of betamethasone with quetiapine may result in the increased metabolism of quetiapine and, depending on the clinical response, a higher dose of quetiapine may need to be considered.
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.
Corticosteroids may enhance the metabolism of tretinoin resulting in decreased levels of tretinoin.

Adverse reactions:
Fluid and electrolyte disturbances: sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension.
Musculoskeletal: muscle weakness; steroid myopathy; loss of muscle mass; osteoporosis; vertibral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fractures of long bones.
Gastrointestinal: peptic ulcer with possible subsequent perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis.
Dermatologic: impaired wound healing; thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating; may suppress reaction to skin tests.
Neurological: convulsions; increased intracranial pressure with papellidema (pseudotumor cerebri) usually after treatment; vertigo; headache.
Endocrine: menstrual irrigularities; development of cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, trauma, surgery, or illness; decreased carbohydrate tolerance; manifestation of latent diabetes mellitus; increased requirements for insulin or oral hypoglycemic agents in diabetics.
Ophthalmologics: posterior subcapsular cataracts; increased intraocular pressure; glaucoma; exophthalmos.
Metabolic: negative nitrogen balance due to protein catabolism.
The following adverse reactions are related to parenteral corticosteroid therapy. Rare instances of blindness associated with intralesional therapy around the face and head; hyperpigmentation or hypopigmentation; subcutaneous and cutaneous atrophy; sterile abscess; post-injection flare (following intra-articular use); Charcot-like arthropathy.

Pregnancy and lactation:
Since adequate human reproduction studies have not been studied with corticosteroids, the use of this drug in pregnancy, nursing mothers, or women of child bearing potential requires that the risk benefit ratio should be considered.

Symptoms and treatment for overdosage, and antidote(s), if any:
A single overdose of a corticosteroid would not be expected to produce acute symptoms. Hypercorticoid effects are not anticipated unless there has been repeated administration of high doses.
Systemic effects of chronic overdosage with steroids include effects on sodium and water retention, increased appetite, mobilisation of calcium and phosphorus with osteoporosis, nitrogen depletion, hyperglycaemia, effects on tissue repair, increased susceptibility to infection, adrenal insufficiency, adrenal cortex hyperactivity, mental and neurological disturbances and muscular weakness.
In case of an acute overdose, maintain adequate fluid intake and monitor electrolytes in serum and urine, with particular attention to sodium and potassium balance. In case of chronic toxicity, slowly withdraw the drug. Treat electrolyte imbalance if necessary.

Incompatibilities:
Do not mix with diluents or local anesthetics containing preservatives (eg. paraben, phenol) because flocculation of suspension may result

Storage conditions:
Store at temperature not exceeding 30℃.
Shake well before use. Protect from light.
Avoid freezing.

Shelf-life:
3 years from date of manufacture.

Packaging:
1 mLx50 Ampules/Box; 5 mLx10 Vials/Box

Manufacturer:
YUNG SHIN PHARMACEUTICAL IND. CO., LTD.
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