PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr CELESTONE® SOLUSPAN®

Betamethasone Sodium Phosphate and Betamethasone Acetate Injectable Suspension

Injectable Suspension, 3 mg/mL Betamethasone Sodium Phosphate and 3 mg/mL Betamethasone Acetate, intra-articular, intrabursal, intradermal, intramuscular

USP

Injectable Glucocorticoid

Organon Canada Inc.

16766, route Trans-Canadienne
Kirkland, QC, Canada, H9H 4M7
www.organon.ca

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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism	12/2021
8 ADVERSE REACTIONS, 8.1 Adverse Reaction Overview	12/2021

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Intramuscular injection

CELESTONE® SOLUSPAN® (betamethasone sodium phosphate and betamethasone acetate injectable suspension) is indicated in allergic, dermatologic, rheumatic, and other conditions responsive to systemic corticosteroids, including bursitis.

Injection directly into the affected tissues

CELESTONE® SOLUSPAN® (betamethasone sodium phosphate and betamethasone acetate injectable suspension) is indicated in bursitis and associated inflammatory disorders of tendons such as tenosynovitis, and inflammatory disorders of muscle such as fibrosis and myositis.

Intra-articular and periarticular injection

CELESTONE® SOLUSPAN® (betamethasone sodium phosphate and betamethasone acetate injectable suspension) is indicated in rheumatoid arthritis and osteoarthritis.

Intralesional injection

CELESTONE® SOLUSPAN® (betamethasone sodium phosphate and betamethasone acetate injectable suspension) is indicated in various dermatologic conditions.

Local injection

CELESTONE® SOLUSPAN® (betamethasone sodium phosphate and betamethasone acetate injectable suspension) is indicated in certain inflammatory and cystic disorders of the foot.

1.1 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use (see 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism, Ophthalmologic, and Special Populations: Pregnant Women, Pediatrics and 8 ADVERSE REACTIONS, 8.1 Adverse Reaction Overview).

1.2 Geriatrics

Geriatrics: No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

CELESTONE® SOLUSPAN® is contraindicated in patients:

- who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- with herpes simplex of the eye
- with systemic fungal infections
- with vaccinia

- with cerebral malaria
- in idiopathic thrombocytopenia purpura when administered intramuscularly

Regional corticosteroid therapy is contraindicated in areas that are locally infected, although infection elsewhere in the body is not a contraindication to the use of corticosteroid regionally.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Dosage must be adjusted according to the severity of the condition, the response obtained, and the patient's tolerance to the corticosteroid. 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 CELESTONE® SOLUSPAN® should be discontinued and other appropriate therapy initiated.

4.2 Recommended Dose and Dosage Adjustment

- **For system effect**

Treatment is initiated with 1 mL intramuscular in most conditions and repeated weekly, or more often, if necessary. In severe illness, such as status asthmaticus or disseminated lupus erythematosus, 2 ml might be required initially. In dermatologic disorders, including neurodermatitis, psoriasis, hypertrophic lichen planus, lichen simplex, eczema, contact dermatitis, and dermatitis medicamentosa, intramuscular dosage is usually 1 mL at intervals of 3 days to a week. In respiratory tract disorders, including bronchial asthma, hay fever, allergic bronchitis, and perennial allergic rhinitis, intramuscular dosage is usually 1 to 2 mL at weekly intervals. Bursitis may be treated with intramuscular injections of 1 mL repeated weekly if necessary.

- **For local effect**

In acute bursitis (subdeltoid, subacromial and prepatellar), one intrabursal injection of 1 ml relieves pain and restores the full range of movement in a few hours. Several intrabursal injections at intervals of 1 to 2 weeks are usually required in recurrent acute bursitis and in acute exacerbations of chronic bursitis. Partial relief of pain and some increase in mobility may be expected in both conditions after 1 or 2 injections. In tendonitis, myositis, fibrositis, tenosynovitis, peritendonitis, and periarticular inflammatory conditions, 3 or 4 local injections of 1 ml each at intervals of 1 to 2 weeks between injections are given in most cases. Injection should be made into the affected tendon sheaths rather than into the tendons themselves. In periarticular inflammatory conditions, the painful area should be infiltrated. In ganglions of joint capsules, 0.5 ml is injected directly into the ganglion cysts. In rheumatoid arthritis and osteoarthritis, relief of pain, soreness and stiffness may be experienced in 2 to 4 hours after intra-articular injection. Using sterile technique, a 20 to 24 gauge needle on an empty syringe for aspiration is inserted into the synovial cavity and a few drops of synovial fluid are withdrawn to confirm that the needle is in the joint. The aspirating syringe is replaced by the syringe containing CELESTONE® SOLUSPAN® and the injection is then made into the joint (see Table 1).

Table 1 – CELESTONE® SOLUSPAN® Intra-articular Injection

Size of Joint	Location	Dose (mL)
Very Large	Hip	1.0 to 2.0

Large	Knee Ankle Shoulder	1.0
Medium	Elbow Wrist	0.5 to 1.0
Small (Metacarpophalangeal Intraphalangeal Sternoclavicular)	Hand Chest	0.25 to 0.5

Pain with intra-articular injection of CELESTONE® SOLUSPAN® has not been a problem. However, should the physician want to administer it with a local anaesthetic, it can be mixed in the syringe with an equal volume of 1% or 2% lidocaine hydrochloride, procaine hydrochloride, or similar local anesthetics using formulations which do not contain parabens. Anesthetics containing methylparaben, propylparaben, phenol, etc. should be avoided. The required dose of CELESTONE® SOLUSPAN® is first withdrawn from the vial into the syringe. The local anesthetic is then drawn in, and the syringe is shaken briefly. Do not inject local anaesthetic into the vial of CELESTONE® SOLUSPAN®.

Dermatologic conditions that have responded to intralesional treatment with CELESTONE® SOLUSPAN® include: localized neurodermatitis, psoriasis, nummular eczema, alopecia areata, hypertrophic lichen planus, circumscribed lichen simplex, keloids, and chronic discoid lupus erythematosus.

- **In intralesional treatment**

0.2 mL of CELESTONE® SOLUSPAN® is injected intradermally (not s.c.) per cm2 of lesion using a tuberculin syringe with a 25 gauge, 13 mm needle. Care should be taken to deposit a uniform depot of medication intradermally. A total of no more than 1 mL at weekly intervals is recommended.

- **Disorders of the foot responsive to corticosteroids injected locally**

For most injections into the foot, a tuberculin syringe with a 25 gauge, 2 cm needle is used. Treatment is given at intervals of 3 days to a week. In bursitis under heloma durum (hard corn), bursitis under heloma molle (soft corn), synovial cysts, and Morton's neuralgia (metatarsalgia) 0.25 to 0.5 mL are recommended. For bursitis under calcaneal spurs, bursitis under hallux rigidus (flexion deformity of the great toe), bursitis over digiti quinti varus (inward deviation of the fifth toe) tenosynovitis, and periosistitis of the cuboid, 0.5 mL is recommended; in acute gouty arthritis 0.5 to 1 mL are recommended.

4.4 Administration

Suspension for injection. Shake well before using.

Intramuscular injections of corticosteroids should be given deep into large muscle masses to avoid local tissue atrophy.

4.5 Missed Dose

If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not double doses.

5 OVERDOSAGE

Treatment of acute overdose is by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy, the dosage of the corticosteroid may be reduced only temporarily.

Complications resulting from the metabolic effects of the corticosteroid or from deleterious effects of the basic or concomitant illnesses or resulting from drug interactions should be handled as appropriate. Maintain adequate fluid intake and monitor electrolytes in serum and urine, with particular attention to sodium and potassium balance. Treat electrolyte imbalance if necessary.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Injection	Suspension / 3 mg betamethasone acetate and 3 mg betamethasone (as betamethasone sodium phosphate)/1 mL	benzalkonium chloride, disodium edetate, sodium phosphate dibasic dihydrate, sodium phosphate monobasic dihydrate, nitrogen and water for injection.

CELESTONE® SOLUSPAN® is supplied in multiple dose vials of 1 mL and 5 mL.

7 WARNINGS AND PRECAUTIONS

General

Strict aseptic technique is mandatory in the use of CELESTONE® SOLUSPAN® injection. CELESTONE® SOLUSPAN® is not intended for intravenous or subcutaneous use.

Following intra-articular injection, a portion of the administered dose of CELESTONE® SOLUSPAN® is absorbed systematically. In patients being treated concomitantly with peroral and parenteral corticosteroids, especially those receiving large doses, the systemic absorption of the drug should be considered in determining intra-articular dosage.

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation may be recommended.

The lowest possible dose of corticosteroid should be used to control the condition under treatment; when dosage reduction is possible, the reduction should be gradual.

With long-term corticosteroid therapy, transfer from parenteral to oral administration should be considered after weighing the potential benefits and risks.

Advise patients to inform subsequent physicians of the prior use of corticosteroids.

Corticosteroids should not be injected into unstable joints, infected areas or intervertebral spaces. Repeated injections into joints of osteoarthritis may increase joint destruction. Avoid injecting

corticosteroids directly into the substance of tendons because delayed appearance of tendon rupture has resulted.

Following intra-articular corticosteroid therapy, care should be taken by the patient to avoid overuse of the joint in which symptomatic benefit has been obtained.

Examination of any joint fluid present is necessary to exclude a septic process. Local injection into a previously infected joint is to be avoided. A marked increase in pain and local swelling, further restriction of joint motion, fever and malaise are suggestive of septic arthritis. If the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.

Carcinogenesis

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

Cardiovascular

Literature reports suggest an apparent association between use of corticosteroids and left ventricular free wall rupture after a recent myocardial infarction; therefore, therapy with corticosteroids should be used with great caution in these patients.

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with congestive heart failure or hypertension.

Endocrine and Metabolism

Average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be considered. All corticosteroids increase calcium excretion.

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual dosage reduction. Such relative insufficiency may persist for months after discontinuation of therapy; therefore, if stress occurs during that period, corticotherapy should be reinstituted. If the patient is receiving corticosteroids already, dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticosteroid should be administered concurrently.

There is an enhanced effect of corticosteroids in patients with hypothyroidism. Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (ie, decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in pediatric patients and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (ie, postmenopausal women) before initiating corticosteroid therapy.

Fat embolism has been reported as a possible complication of hypercorticism.

Pheochromocytoma crisis, which may be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified

pheochromocytoma after an appropriate risk/benefit evaluation.

Gastrointestinal

Corticosteroids should be used with caution in: nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer.

Hematologic

Use acetylsalicylic acid (ASA, Aspirin) cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Hepatic/Biliary/Pancreatic

There is an enhanced effect of corticosteroids in patients with cirrhosis.

Immune

Rare instances of anaphylactoid/anaphylactic reactions with a possibility of shock have occurred in patients receiving parenteral corticosteroid therapy. Appropriate precautionary measures should be taken with patients who have a history of allergic reactions to corticosteroids.

While on corticosteroid therapy, patients should not be vaccinated against smallpox because of potential complications. Other immunization procedures should not be undertaken in patients receiving corticosteroids, especially high doses, because of possible hazards of neurological complications and lack of antibody response. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison disease.

Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice. This is of particular importance in children.

Patients who are on corticosteroids are more susceptible to infections than are healthy individuals. Corticosteroids may mask some signs of infection, and new infections may appear during use. There may be decreased resistance and inability to localize infection when corticosteroids are used. If corticosteroids have to be used in the presence of bacterial infections, institute appropriate vigorous anti-infective therapy.

Infection with any pathogen (viral, bacterial, fungal, protozoan, or helminthic) in any location of the body may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents. These infections may be mild to severe. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases.

Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control drug reactions. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.

Corticosteroid use may lead to activation of latent disease or an exacerbation of intercurrent infections due to pathogens, including those caused by Amoeba, Candida, Cryptococcus, Mycobacterium, Nocardia, Pneumocystis, and Toxoplasma.

It is recommended that latent amebiasis or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea.

Similarly, corticosteroids should be used with great care in patients with known or suspected

Strongyloides (threadworm) infestation. In such patients, corticosteroidinduced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Chickenpox and measles can have a more serious or even fatal course in patients on corticosteroids. In patients who have not had these diseases, particular care should be taken to avoid exposure. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents should be considered.

The use of corticosteroids in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for management in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary since reactivation of the disease may occur. During prolonged corticosteroid therapy, patients should receive chemoprophylaxis. If rifampin is used in a chemoprophylactic program, its enhancing effect on metabolic hepatic clearance of corticosteroids should be considered; adjustment in corticosteroid dosage may be required.

Monitoring and Laboratory Tests

Corticosteroids may suppress reactions to skin tests.

Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

Dosage adjustments may be required with remission or exacerbation of the disease process, the patient's individual response to therapy and exposure of the patient to emotional or physical stress such as serious infection, surgery or injury. Monitoring may be necessary for up to one year following cessation of long-term or high-dose corticosteroid therapy.

Neurologic

Serious neurologic events, some resulting in death, have been reported with epidural injection of corticosteroids. Specific events reported include, but are not limited to, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, and stroke. These serious neurologic events have been reported with and without use of fluoroscopy. The safety and effectiveness of epidural administration of corticosteroids have not been established, and corticosteroids are not approved for this use.

Results from a single, multicenter, randomized, controlled study with another corticosteroid, methylprednisolone hemisuccinate, showed an increase of early mortality (at 2 weeks) and late mortality (at 6 months) in patients with cranial trauma who had received methylprednisolone, compared to placebo. The causes of mortality in the methylprednisolone group have not been established. Of note, this study excluded patients who were felt to have a clear indication for corticosteroids.

Corticosteroids should be used with caution in patients with myasthenia gravis.

Ophthalmologic

Prolonged corticosteroid use may produce posterior subcapsular cataracts (especially in children), increased intraocular pressure and glaucoma with possible damage to the optic nerves, and may enhance secondary ocular infections due to fungi or viruses. Ophthalmologic examination should be done periodically, especially in patients on long-term therapy (more than six weeks). Patients on long-term

therapy should have intraocular pressure monitored.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) 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 of visual disturbances 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.

The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes.

Psychiatric

Psychic derangement may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Renal

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with renal insufficiency.

Reproductive Health: Female and Male Potential

- **Fertility**

  Corticosteroids have been shown to impair fertility in animal studies. Steroids may increase or decrease motility and number of spermatozoa in some patients.

Sensitivity/Resistance

Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

7.1 Special Populations

7.1.1 Pregnant Women

Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, or in women of childbearing potential requires that the possible benefits of the drug be weighed against the hazards to the mother and embryo, fetus or infant.

Corticosteroids cross the placental barrier.

When mothers were given betamethasone injections prenatally, the infants had transient suppression of fetal growth hormone and presumably of those pituitary hormones which regulate corticosteroid production by both the definitive and fetal zones of the fetal adrenal glands. However, the suppression of fetal hydrocortisone did not interfere with the pituitary-adrenocortical responses to stress after birth.

Infants born of mothers who were dosed with corticosteroids throughout most or some portion of their pregnancy should be examined carefully for signs of adrenal insufficiency and the possible very rare occurrence of congenital cataracts.

Women who have been on corticosteroids during pregnancy should be monitored during and after labor and delivery for any indication of adrenal insufficiency because of the stresses associated with childbirth.

Corticosteroids are not indicated in the management of hyaline membrane disease after birth and should not be administered to pregnant women with pre-eclampsia, eclampsia, or evidence of placental damage.

Studies have shown an increased risk of neonatal hypoglycaemia following antenatal administration of a short course of betamethasone to women at risk for late preterm delivery.

7.1.2 Breast-feeding

Corticosteroids appear in breast milk of nursing mothers. Because of the potential for adverse effects from CELESTONE® SOLUSPAN® Injection in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

7.1.3 Pediatrics

Growth and development in infants and children on prolonged corticosteroid therapy should be carefully observed (see 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism, and Ophthalmologic).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

There have been a few cases of crystal deposition but no reports of dimpling of the skin after intradermal injection. Nevertheless, because dimpling of the skin is attributable to atrophy of subcutaneous fat and is seen with other injectable corticosteroids, subcutaneous injection should be avoided. Pain has not been reported.

Dermatologic: impaired wound healing; skin atrophy; thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating; suppressed reactions to skin tests; reactions such as allergic dermatitis, urticaria, angioneurotic edema, hyperpigmentation, hypopigmentation, subcutaneous atrophy, cutaneous atrophy; Kaposi's sarcoma.

Endocrine: menstrual irregularities; development of cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements of insulin or oral hypoglycemic agents in diabetics. Neonatal hypoglycemia has been reported after antenatal administration.

Fluid and electrolyte disturbances: sodium retention, potassium loss, hypokalemic alkalosis; fluid retention; congestive heart failure in susceptible patients; hypertension.

Gastrointestinal: hiccups, peptic ulcer with possible perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis.

General disorders and administration site conditions: sterile abscess, post injection flare (following intraarticular use).

Immune system disorders: hypersensitivity, anaphylactoid and hypotensive or shock like reactions.

Metabolic: negative nitrogen balance due to protein catabolism.

Musculoskeletal: muscle weakness, corticosteroid myopathy, loss of muscle mass; aggravation of myasthenic symptoms in myasthenia gravis; osteoporosis; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones; tendon rupture; joint instability (from repeated intra-articular injections), charcot-like arthropathy.

Neurologic: convulsions; increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment; vertigo; headache.

Ophthalmic: posterior subcapsular cataracts; increased intraocular pressure, glaucoma; exophthalmos, instances of blindness associated with intralesional therapy around the face and head, vision blurred.

Psychiatric: euphoria, mood swings; severe depression to frank psychotic manifestations; personality changes; hyperirritability; insomnia.

Vascular disorders: thromboembolism.

9 DRUG INTERACTIONS

9.3 Drug-Behavioural Interactions

The intake of alcohol with corticosteroids may result in an increased occurrence or increased severity of gastrointestinal ulceration.

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 3 - Established or Potential Drug-Drug Interactions

[Proper/Common name]	Effect	Clinical comment
Hepatic Enzyme Inducers, e.g., • barbiturates • phenytoin • carbamazepine • rifampin	Ennhance the metabolism and clearance of corticosteroids	Concurrent use of phenobarbital, phenytoin, rifampin or ephedrine may enhance the metabolism and clearance of corticosteroids, reducing their therapeutic effects.
Estrogens, including Oral Contraceptives	Excessive corticosteroid effects	Patients receiving both a corticosteroid and an estrogen should be observed for excessive corticosteroid effects.

Amphotericin B injection and Potassium-Depleting Agents	Enhance hypokalemia	Concurrent use of corticosteroids with potassium-depleting diuretics may enhance hypokalemia. Concurrent use of corticosteroids with cardiac glycosides may enhance the possibility of arrhythmias or digitalis toxicity associated with hypokalemia. Corticosteroids may enhance the potassium depletion caused by amphotericin B. In all patients taking any of these drug therapy combinations, serum electrolyte determinations, particularly potassium levels, should be monitored closely.
Oral Anticoagulants	Increase or decrease the anticoagulant effects	Concurrent use of corticosteroids with coumarin-type anticoagulants may increase or decrease the anticoagulant effects, possibly requiring adjustment in dosage.
Nonsteroidal anti-Inflammatory Agents (NSAIDS)	Increased occurrence or increased severity of gastrointestinal ulceration	Combined effects of non-steroidal anti-inflammatory drugs with glucocorticosteroids may result in an increased occurrence or increased severity of gastrointestinal ulceration. Corticosteroids may decrease blood salicylate concentrations. Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.
Antidiabetics	Increase blood glucose concentration	Because corticosteroids may increase blood glucose concentration, dosage adjustments of antidiabetic agents may be required.
Somatotropin	Inhibit the response to somatotropin	Concomitant glucocorticosteroid therapy may inhibit the response to somatotropin.
Aminoglutethimide	Loss of corticosteroid-induced adrenal suppression	Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.
Antibiotics	Decrease in corticosteroid clearance	Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.
Anticholinesterases	Produce severe weakness in patients with myasthenia gravis	Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

Antitubercular Drugs	Decrease serum concentrations of isoniazid	Serum concentrations of isoniazid may be decreased.
Cholestyramine	Increase the clearance of corticosteroids	Cholestyramine may increase the clearance of corticosteroids.
Cyclosporine	Increased activity of both cyclosporine and corticosteroids	Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use
Strong CYP3A4 Inhibitors	Increased exposures of corticosteroids	Corticosteroids (including betamethasone) are metabolized by CYP 3A4. Ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60%, leading to an increased risk of corticosteroid side effects. Coadministration with strong CYP3A4 inhibitors, (e.g. itraconazole, clarithromycin, ritonavir, cobicistat-containing products) may lead to increased exposures of corticosteroids and therefore the potential for increased risk of systemic corticosteroid side effects. Consider the benefit of coadministration versus the potential risk of systemic corticosteroid effects, in which case patients should be monitored for systemic corticosteroid side-effects.
Vaccines	Diminished response to toxoids and live or inactivated vaccines.	Patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines due to inhibition of antibody response. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. Routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued if possible (see 7 WARNINGS AND PRECAUTIONS, Immune).

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Corticosteroids may suppress reactions to skin tests.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

CELESTONE® SOLUSPAN® is a combination of soluble and slightly soluble betamethasone esters that provides potent anti-inflammatory, antirheumatic and antiallergic effects in the treatment of corticosteroid-responsive disorders. Prompt therapeutic activity is achieved by betamethasone sodium phosphate, which is absorbed quickly after injection. Sustained activity is provided by betamethasone acetate, which is only slightly soluble and becomes a repository for slow absorption, thereby controlling symptoms over a prolonged period.

10.2 Pharmacodynamics

The information on which the indications were originally approved were not presented in the Product Monograph.

10.3 Pharmacokinetics

The information on which the indications were originally approved were not presented in the Product Monograph.

11 STORAGE, STABILITY AND DISPOSAL

Store at 25°C, excursions permitted between 2 and 30°C. Protect from light.

12 SPECIAL HANDLING INSTRUCTIONS

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

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

The information on which the indications were originally approved were not presented in the Product Monograph.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

The non-clinical toxicology data on which the original indication was authorized is not available.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[PR]CELESTONE® SOLUSPAN®

betamethasone sodium phosphate and betamethasone acetate injectable suspension

Read this carefully before you start taking **CELESTONE® SOLUSPAN®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **CELESTONE® SOLUSPAN®**.

What is CELESTONE® SOLUSPAN® used for?

- For injection directly into the muscle: in allergic, skin, joint, muscle, bone and other conditions that respond to steroids. This also includes bursitis (swelling of the bursa, which are fluid filled sacs near joints).
- For injection directly into the affected tissues: in bursitis and other disorders causing swelling of tendons such as tenosynovitis and swelling of muscle such as fibrosis and myositis.
- For injection into or around joints: in rheumatoid arthritis and osteoarthritis.
- For injection into lesions: in various skin conditions.
- For local injection: in certain swelling and cystic disorders of the foot.

How does CELESTONE® SOLUSPAN® work?

CELESTONE® SOLUSPAN® contains steroid medication called betamethasone. It is used for the treatment of disorders that respond to steroid medications. This medication works to reduce swelling and allergic symptoms in skin, muscles, and joint.

What are the ingredients in CELESTONE® SOLUSPAN®?

Medicinal ingredients: betamethasone acetate and betamethasone (as betamethasone sodium phosphate).

Non-medicinal ingredients: benzalkonium chloride, disodium edetate, sodium phosphate dibasic dihydrate, sodium phosphate monobasic dihydrate, nitrogen and water for injection.

CELESTONE® SOLUSPAN® comes in the following dosage forms:

Injectable suspension: 3 mg betamethasone acetate and 3 mg betamethasone (as betamethasone sodium phosphate)/mL

Do not use CELESTONE® SOLUSPAN® if:

- you are allergic to betamethasone sodium phosphate and betamethasone acetate or any other corticosteroid medicine or any of the ingredients found in CELESTONE® SOLUSPAN® (see What are the ingredients in CELESTONE® SOLUSPAN®?).
- you have herpes simplex of the eye (a type of viral infection of the eye).
- you have a fungal infection or any untreated infection.
- you have vaccinia virus.
- you have malaria that has affected the brain.
- you have a decreased number of platelets when the medication is administered in the muscle.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CELESTONE® SOLUSPAN®. Talk about any health conditions or problems you may have, including if you:

- have or have had an infection (such as a viral, bacterial or fungal infection).
- have a weak immune response. Tell your healthcare professional if you suspect an infection has occurred as corticosteroids can make infections more likely and may mask their signs.
- have recently had or are about to have any vaccination.
- have thyroid problems.
- have liver problems, such as cirrhosis
- have certain eye diseases such as glaucoma, cataracts, herpes infection or any problems with the retina.
- have stomach or gut problems.
- have kidney problems.
- have heart problems (such as heart failure, heart disease or heart attack) or blood pressure problems
- have a history of psychiatric problems or certain mental or mood conditions (such as depression).
- have or are suspected to have pheochromocytoma (tumor developing in an adrenal gland)
- have or are at an increased risk of brittle bone (osteoporosis)
- have a history of allergic reactions to corticosteroids
- have neurologic problems such as myasthenia gravis (neuromuscular disease leading to weakness of muscles).
- if you are breastfeeding or planning to breastfeed
- are pregnant or planning to become pregnant

Other warnings you should know about:

Nervous System:

Serious side effects with your nervous system, some resulting in death, have been reported with injection of corticosteroids into the back around the spinal cord (epidural injection).

These include but are not limited to:

- blockage of blood to the spinal cord
- paralysis of the lower body
- paralysis from the neck down
- blindness due to injury to a part of the brain
- stroke

The safety and effectiveness of corticosteroids in epidural injections is not known and should not be used.

Pregnancy and breastfeeding:

- If you are pregnant, or still able to get pregnant and/or breast-feed, there are specific risks you must discuss with your healthcare professional. Taking CELESTONE® SOLUSPAN® may:
    - slow the growth and cause low birth weight of the baby.
    - cause cataracts in babies. This risk is associated with mothers who take corticosteroids for a long period of time during pregnancy.
- If you are breastfeeding or planning to breastfeed, tell your healthcare professional.

Male fertility:

- Taking CELESTONE® SOLUSPAN® may affect male fertility.

Immunosuppression:

- CELESTONE® SOLUSPAN® may:
    - hide symptoms of infection
    - reactivate dormant infections
    - cause infections due to lowered body resistance
- Tell your healthcare professional you are taking CELESTONE® SOLUSPAN® since it can affect the results of skin tests

Patients, especially children, should avoid exposure to chickenpox or measles while taking CELESTONE® SOLUSPAN®.

Contact your doctor if you experience blurred vision or other visual disturbances.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with CELESTONE® SOLUSPAN®:

- Medications that induce liver enzymes (e.g., barbiturates, phenytoin, carbamazepine, rifampin)
- Estrogens, including oral contraceptives
- Amphotericin B injection (used to treat fungal infections) and potassium-depleting agents
- Oral blood thinners
- Nonsteroidal anti-inflammatory agents (NSAIDS) (used to treat inflammation)
- Medicines for diabetes
- Somatotropin (medicine used to treat conditions of low growth hormone levels)
- Aminoglutethimide (medicine used to treat conditions where the body makes too much of a certain hormone)
- Antibiotics (medicines used to treat bacterial infections)
- Anticholinesterases (medicine used to prevent the breakdown of the neurotransmitter acetylcholine in the body)
- medicines for tuberculosis
- Cholestyramine (medicine used to lower cholesterol levels)
- Cyclosporine (medicine used to lower the risk of organ transplant rejection)
- Strong CYP3A4 Inhibitors
- Vaccines
- Alcohol

How to take CELESTONE® SOLUSPAN®:

- CELESTONE® SOLUSPAN® will be given to you by a healthcare professional in a healthcare setting.

Usual dose:

CELESTONE® SOLUSPAN® is a suspension for injection. The injection is usually administered by your doctor or a healthcare professional. Your doctor will determine the dose depending on your individual needs. Make sure you follow the dose prescribed by your doctor.

CELESTONE® SOLUSPAN® is for injection directly into the muscle, the affected tissues, into or around joints, into lesion and for local injection.

CELESTONE® SOLUSPAN® cannot be used for administration into the spinal canal.

Your doctor will evaluate your health regularly to make sure you get the correct dose.

Overdose:

Overdose may occur if you receive too much medication at one time or over a longer period of time. In case of accidental overdosage of CELESTONE® SOLUSPAN®, contact your doctor or local poison control centre to receive appropriate treatment.

If you think you, or a person you are caring for, have taken too much CELESTONE® SOLUSPAN®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not double doses.

What are possible side effects from using CELESTONE® SOLUSPAN®?

These are not all the possible side effects you may have when taking CELESTONE® SOLUSPAN®. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Skin problems:
    - facial redness
    - increased sweating
    - Petechiae (reddish spot containing blood that appears in the skin) and ecchymoses (bruises caused by ruptured blood vessels)
    - skin reactions such as:
        - allergic skin reactions
        - hives
        - swelling of skin or mucus tissues
        - darkening or lightening of skin
        - loss of fat under the skin
        - thinning of the skin
    - suppressed reactions to skin tests
- Hormone and metabolism problems:
    - for patients with diabetes, needing more insulin to treat their condition
    - symptoms of too much cortisol hormone, including but not limited to:
        - moon face (rounded puffy face)
        - weight gain
        - abnormal fat deposits
    - not enough cortisol made by the body, particularly in times of stress (such as in trauma, surgery or illness)
    - suppression of growth in children

- Fluid and electrolyte problems:
    - sodium retention
    - potassium loss and experiencing symptoms caused by low potassium
- Stomach and gut problems:
    - bloating
    - hiccups
    - swelling of the pancreas
    - formation of ulcers on and swelling of the esophagus
- General disorders and administration problems:
    - increased pain at the injection site following the injection in the joint
    - abscess (a pus filled wound) with no infection
- Immune system problems:
    - decrease in blood pressure or shock like reactions
- Muscle and bone problems:
    - worsening of muscle weakness symptoms in myasthenia gravis
    - loss of bone near the shoulder and hip that is not caused by infection
    - joint instability (from repeated injections into a joint), loss of feeling in the foot and ankle
    - loss of muscle mass
    - partial or complete tear of tendon
    - vertebral compression fractures
- Nervous system problems:
    - headache
    - increased pressure in the skull with swelling of the nerve in the eye (pseudotumor cerebri) usually after treatment
    - dizziness
    - vertigo
- Eye problems:
    - cataracts
    - glaucoma (a condition that damages the optic nerve of the eye)
- Psychiatric problems:
    - euphoria (intense feelings of well-being, elation, happiness, excitement and joy)
    - mood swings
    - severe depression to psychotic manifestations (hallucinations, delusions, confused or disturbed thoughts)
    - personality changes
    - hyperirritability (extremely sensitive)
    - difficulty sleeping

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Kaposi's Sarcoma (a type of cancer caused by human herpes virus 8): symptoms may include purple, red or brown blotches or tumours,		√	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
usually on the skin of the legs, face or in the genital area			
Pheochromocytoma (tumor of the adrenal gland): symptoms may include high blood pressure, headache, heavy sweating, rapid heartbeat, tremors, paleness in the face, shortness of breath, panic attack-type symptoms			√
Neurologic events: blockage of blood to the spinal cord, paralysis of the lower body, paralysis from the neck down, blindness due to injury to a part of the brain, and stroke			√
Heart failure: shortness of breath, fatigue, weakness, dizziness, irregular heart beat			√
Blood clots: swelling, pain or tenderness, usually in the arm or leg		√	
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heart beat, nausea, vomiting, tenderness when touching the abdomen		√	
Fluid retention, swelling		√	
High blood pressure: headaches or feeling unwell			√
Muscle weakness			√
Stomach ulcers (burst or bleeding ulcers): stomach pain, blood in stools and/or vomiting blood			√
Wounds that are slow to heal	√		
Convulsions			√
Psychological disorders: feeling depressed including thinking about suicide, feeling anxious, insomnia		√	
Irregular menstrual periods	√		

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Diabetes: frequent urination, hunger and thirst		√	
Visual problems: failing eyesight, blurry vision, eye pain, increased pressure in your eyes		√	
Reactivation of tuberculosis: coughing blood or pain in the chest)			√
Infections: raised temperature and feeling unwell.			√
Osteoporosis (thin, fragile bones): bone/joint pain, broken bones, back pain that gets worse when standing or walking			√
Allergic reactions: rash, hives, swelling of the face, lips, tongue or throat. Difficulty swallowing or breathing			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at 25°C, excursions permitted between 2 and 30°C. Protect from light.

Keep out of reach and sight of children.

If you want more information about CELESTONE® SOLUSPAN®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.organon.ca, or by calling 1-844-820-5468.

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