## PRESCRIBING INFORMATION

## SOLU-MEDROL™ Sterile Powder

## *(methylprednisolone)*COMPOSITION

**SOLU-MEDROL™ Sterile Powder 40 mg**
**Each 1 ml Act-O-Vial contains:**
I. Powder compartment:
Methylprednisolone (as methylprednisolone sodium succinate) 40 mg
Lactose
Sodium biphosphate monohydrate
Dibasic sodium phosphate
II. Diluent compartment:
Benzyl alcohol 9 mg
Water for injection
**SOLU-MEDROL™ Sterile Powder 125 mg**
**Each 2 ml Act-O-Vial contains:**
I. Powder compartment:
Methylprednisolone (as methylprednisolone sodium succinate) 125 mg
Sodium biphosphate monohydrate
Dibasic sodium phosphate
II. Diluent compartment:
Benzyl alcohol 18 mg
Water for injection
**SOLU-MEDROL™ Sterile Powder 500 mg**
I. Each powder vial contains:
Methylprednisolone (as methylprednisolone sodium succinate) 500 mg
Sodium biphosphate monohydrate
Dibasic sodium phosphate
II. Each diluent vial (7.8 ml) contains:
Benzyl alcohol 70.2 mg
Water for injection
**SOLU-MEDROL™ Sterile Powder 1000 mg**
I. Each powder vial contains:
Methylprednisolone (as methylprednisolone sodium succinate) 1000 mg
Sodium biphosphate monohydrate
Dibasic sodium phosphate
II. Each diluent vial (15.6 ml) contains:
Benzyl alcohol 140.4 mg
Water for injection

## FORMS, WAYS OF ADMINISTRATION AND PACKAGES

Each package contains a sterile powder for injection and a sterile solution.
Intravenous and intramuscular administration.
Packages:
SOLU-MEDROL™ Sterile Powder 40 mg: 1 Act-O-Vial.
SOLU-MEDROL™ Sterile Powder 125 mg: 1 Act-O-Vial.
SOLU-MEDROL™ Sterile Powder 500 mg: l Vial + l Vial.
SOLU-MEDROL™ Sterile Powder 1000 mg: l Vial + l Vial.

**PROPERTIES**

This product is an IM and IV indictable form of methylprednisolone, a synthetic glucocorticosteroid.

This highly concentrated aqueous solution is particularly suitable for the treatment of pathologic conditions in which an effective and rapid hormonal effect is required.

Methylprednisolone has a strong anti-inflammatory, immunosuppressive and anti-allergic activity.

**Pharmacodynamics**

Glucocorticoids diffuse across cell membranes and complex with specific cytoplasmic receptors.

These complexes then enter the cell nucleus, bind to DNA (chromatin), and stimulate transcription of mRNA and subsequent protein synthesis of various enzymes thought to be ultimately responsible for the numerous effects of glucocorticoids after systemic use.

Glucocorticoids not only have an important influence on inflammatory and immune processes, but also affect carbohydrate, protein and fat metabolism. They also act on the cardiovascular system, the skeletal muscles and the central nervous system.

**Effect on the inflammatory and immune process**

The anti-inflammatory, immunosuppressive and anti-allergic properties of glucocorticoids are responsible for most of the therapeutic applications. These properties lead to the following results:

• reduction of the immunoactive cells near the inflammation focus,
• reduced vasodilation,
• stabilization of the lysosomal membranes,
• inhibition of phagocytosis,
• reduced production of prostaglandins and related substances.

A dose of 4 mg methylprednisolone has the same glucocorticosteroid (anti-inflammatory) effect as 20 mg hydrocortisone. Methylprednisolone has only a minimal mineralocorticoid effect (200 mg methylprednisolone are equivalent to 1 mg desoxycorticosterone).

**Effect on carbohydrate and protein metabolism**

Glucocorticoids have a protein catabolic action. The liberated amino acids are converted into glucose and glycogen in the liver by means of the gluconeogenesis process.

Glucose absorption in peripheral tissues decreases, which can lead to hyperglycemia and glucosuremia, especially in patients who are prone to diabetes.

**Effect on fat metabolism**

Glucocorticoids have a lipolytic action. This lipolytic activity mainly affects the limbs. They also have a lipogenic effect which is most evident on chest, neck and head. All this leads to a redistribution of the fat deposits.

Maximum pharmacologic activity of corticosteroids lags behind peak blood levels, suggesting that most effects of the drugs result from modification of enzyme activity rather than from direct actions by the drugs.

**Pharmacokinetics**

In vivo, cholinesterases rapidly hydrolyse methylprednisolone sodium succinate to free methylprednisolone.

In man, methylprednisolone forms a weak dissociable bond with albumin and transcortin. Approximately 40 to 90% of the drug is bound.

Intravenous infusions with 30 mg/kg administered over 20 minutes or 1 g administered over 30 to 60 minutes lead after approximately 15 minutes to peak methylprednisolone plasma levels of nearly 20 μg/ml. About 25 minutes after an intravenous bolus injection of 40 mg peak methylprednisolone plasma values of 42-47 μg/100 ml are measured.

Intramuscular injections of 40 mg give peak methylprednisolone plasma levels of 34 μg/100 ml after some 120 minutes.
Intramuscular injections give lower peak values than intravenous injections. With IM injections plasma values persist for a longer period, with the result that both administration patterns lead to equivalent quantities of methylprednisolone. The clinical importance of these small differences is probably minimal when we consider the mechanism of action of glucocorticoids.
A clinical response is usually observed 4 to 6 hours after administration. In the treatment of asthma, the first beneficial results can already be perceived after 1 or 2 hours. The plasma half-life of methylprednisolone sodium succinate is 2.3 to 4 hours and appears to bear no relation to the administration pattern.
Methylprednisolone is a glucocorticoid with a medium-term activity. It has a biological half-life of 12 to 36 hours. The intracellular activity of glucocorticoids results in a clear difference between plasma half-life and pharmacological half-life. Pharmacological activity persists after measurable plasma levels have disappeared. The duration of anti-inflammatory activity of glucocorticoids approximately equals the duration of hypothalamic-pituitary-adrenal (HPA) axis suppression.
Metabolism of methylprednisolone occurs via hepatic routes qualitatively similar to that of cortisol. The major metabolites are 20 beta-hydroxymethylprednisolone and 20 beta-hydroxy- 6 alpha-methylprednisolone. The metabolites are mainly excreted in the urine as glucuronides, sulfates and unconjugated compounds. Following IV administration of 14C labeled methylprednisolone, 75% of the total radioactivity was recovered in the urine in 96 hours, 9% was recovered in human feces after 5 days and 20% in the bile.

**INDICATIONS**
Glucocorticoids should only be considered as a purely symptomatic treatment, unless in case of some endocrine disorders, where they are used as substitution treatment.

**Anti-inflammatory Treatment**
**Rheumatic disorders**
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:
• Post-traumatic osteoarthritis
• Synovitis of osteoarthritis
• Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
• Acute and subacute bursitis
• Epicondylitis
• Acute nonspecific tenosynovitis
• Acute gouty arthritis
• Psoriatic arthritis
• Ankylosing spondylitis

**Collagen diseases** (immune and complex diseases)
During an exacerbation or as maintenance therapy in selected cases of:
• Systemic lupus erythematosus (and lupus nephritis)
• Acute rheumatic carditis
• Systemic dermatomyositis (polymyositis)
• Polyarteritis nodosa
• Goodpasture’s syndrome

**Dermatologic diseases**
• Pemphigus
• Severe erythema multiforme (Stevens-Johnson syndrome)
• Exfoliative dermatitis
• Bullous dermatitis herpetiformis
• Severe seborrheic dermatitis
• Severe psoriasis
• Mycosis fungoides
• Urticaria

**Allergic states**
Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in:
• Bronchial asthma
• Contact dermatitis
• Atopic dermatitis
• Serum sickness
• Seasonal or perennial allergic rhinitis
• Drug hypersensitivity reactions
• Urticarial transfusion reactions
• Acute noninfectious laryngeal edema (epinephrine is the drug of first choice)

**Ophthalmic diseases**
Severe acute and chronic allergic and inflammatory processes involving the eye, such as:
• Herpes zoster ophthalmicus
• Iritis, iridocyclitis
• Chorioretinitis
• Diffuse posterior uveitis and choroiditis
• Optic neuritis
• Sympathetic ophthalmia

**Gastrointestinal diseases**
To tide the patient over a critical period of the disease in:
• Ulcerative colitis (systemic therapy)
• Regional enteritis (systemic therapy)

**Respiratory diseases**
• Pulmonary sarcoidosis
• Berylliosis
• Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
• Loeffler's syndrome not manageable by other means
• Aspiration pneumonitis

**Edematous states**
• To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

**Immunosuppressive Treatment**
• Organ transplantation

**Treatment of Hematological and Oncological Disorders**
**Hematologic disorders**
• Acquired (autoimmune) hemolytic anemia
• Idiopathic thrombocytopenia purpura in adults (IV only: IM administration is contraindicated)
• Secondary thrombocytopenia in adults
• Erythroblastopenia (RBC anemia)
• Congenital (erythroid) hypoplastic anemia

**Oncological diseases**
For palliative management of:
• Leukemias and lymphomas in adults
• Acute leukemia of childhood

**Treatment of Shock States**
• Shock secondary to adrenocortical insufficiency or shock unresponsive to conventional therapy when adrenal cortical insufficiency may be present. (Hydrocortisone is generally the drug of choice. When mineralocorticold activity is undesirable, methylprednisolone may be preferred).
• Hemorrhagic, traumatic and surgical shock unresponsive to standard therapy.
• Although there are no well controlled (double-blind placebo) clinical trials, data from experimental animal models indicate that SOLU-MEDROL™ may be useful in shock states in which standard therapy (e.g. fluid replacement, etc.) has not been effective. See also SPECIAL PRECAUTIONS regarding septic shock.

**Others**
**Nervous system**
• Cerebral edema from tumor - primary or metastatic and/or associated with surgical or radiation therapy
• Acute exacerbations of multiple sclerosis
• Acute spinal cord injury. The treatment should begin within eight hours of injury.
• Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy
• Trichinosis with neurologic or myocardial involvement
• Prevention of nausea and vomiting associated with cancer chemotherapy
**Endocrine disorders**
• Primary or secondary adrenocortical insufficiency
• Acute adrenocortical insufficiency
For these indications, the drugs of choice are hydrocortisone or cortisone. Synthetic analogues can be used in certain circumstances if they are combined with mineralocorticoids.
• Preoperatively and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful
• Congenital adrenal hyperplasia
• Nonsuppurative thyroiditis
• Hypercalcemia associated with cancer

## DOSAGE AND ADMINISTRATION

### As Adjunctive Therapy in Life Threatening Conditions

The recommended dose is 3 mg per kg, given IV over a period of at least 30 minutes. This dose may be repeated in the hospital every 4 to 6 hours for 48 hours depending on the clinical necessity (see SPECIAL PRECAUTIONS).

### Pulse-therapy

In case of very serious exacerbation and/or unresponsiveness to standard therapy, such as nonsteroidal inflammatory means, gold salts and penicillamine.

Suggested schedules:

**Rheumatoid arthritis**

1 g/day IV for 1, 2, 3 or 4 days or 1 g/month IV for 6 months.

As high doses of corticosteroids can cause an arrhythmogenic action, this therapy should be restricted to hospitals, which dispose of an electrocardiograph and defibrillator.

The regimen should be administered over at least 30 minutes and may be repeated if no improvement has been reported within one week after therapy or if the patient's condition dictates.

**Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy**

Suggested schedules:

**Mild to moderately emetogenic chemotherapy**

Administer SOLU-MEDROL™ 250 mg IV over at least 5 minutes one hour before chemotherapy, at the initiation of chemotherapy and at the time of discharge. A chlorinated phenothiazine may also be used with the first dose of SOLU-MEDROL™ for increased effect.

**Severely emetogenic chemotherapy**

Administer SOLU-MEDROL™ 250 mg IV over at least 5 minutes with appropriate doses of metoclopramide or a butyrophenone one hour before chemotherapy, then SOLU-MEDROL™ 250 mg IV at the initiation of therapy and at time of discharge.

**Acute Spinal Cord Injury**

The treatment should begin within eight hours of injury.

**For patients initiated on treatment within 3 hours of injury**

Start with an IV bolus dose of 30 mg methylprednisolone per kilogram of body weight over a 15-minute period under continuous medical supervision. This administration rate of the talus injection may only be used for this indication, under ECG monitoring and with an available defibrillator. The administration of high doses of methylprednisolone in bolus intravenously (doses of more than 500 mg over a period of less than 10 minutes) may cause arrhythmias, circulatory collapse and cardiac arrest.

After the bolus injection comes a 45-minute pause, followed by a continuous infusion of 5.4 mg/kg per hour for 23 hours.

**For patients initiated on treatment within 3 to 8 hours of injury**

Administer 30 mg/kg as an IV bolus over a 15-minute period, followed by a 45-minute pause, and then a continuous IV infusion of 5.4 mg/kg/h for 47 hours.

For the infusion pump, one should preferably choose another intravenous site than for the bolus injection.

### Other Indications

Initial dosage will vary from 10 to 500 mg depending on the clinical problem being treated.

Larger doses may be required for short-term management of severe, acute conditions such as bronchial asthma, serum sickness, urticarial transfusion reactions and acute exacerbations of multiple sclerosis. The initial dose, up to and including 250 mg, should be given intravenously over a period of at least 5 minutes and doses exceeding 250 mg should be given over at least 30 minutes. Subsequent doses may be given intravenously or intramuscularly at intervals dictated by the patient's response and clinical condition.
Corticosteroid therapy is an adjunct to, and not replacement for, conventional therapy.
Dosage may be reduced for infants and children but should be governed more by the severity of the condition and response of the patient than by age or size. It should not be less than 0.5 mg per kg every 24 hours.
Dosage must be decreased or discontinued gradually when the drug has been administered for more than a few days. If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.
Routine laboratory studies, such as urinalysis, two-hour postprandial blood sugar, determination of blood pressure and body weight, and a chest X-ray should be made at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with an ulcer history or significant dyspepsia.
Medical surveillance is also needed in case of interruption of chronic treatment.
The methylprednisolone sodium succinate solution may be administered by intravenous or intramuscular injection or by intravenous infusion, the preferred method for initial emergency use being intravenous injection. To administer by intravenous (or intramuscular) injection, prepare solution as directed.

**Directions for Use of the Act-O-Vial**
1. Press down on plastic activator to force diluent into the lower compartment.
2. Gently agitate to effect solution.
3. Remove plastic tab covering center of stopper.
4. Sterilize top of stopper with a suitable germicide.
5. Insert needle squarely through center of stopper until tip is just visible. Invert vial and withdraw dose.

**Directions for Use of the Vial**
Under aseptic conditions add the diluent to the vial with sterile powder. Do only use the special diluent.
**Preparation of Perfusion Solutions**
First reconstitute the solution as directed. Therapy may be initiated by administering the methylprednisolone sodium succinate solution intravenously over a period of at least 5 minutes (e.g. doses up to and including 250 mg) to at least 30 minutes (e.g. doses exceeding 250 mg).
Subsequent doses may be withdrawn and administered similarly. If desired, the medication may be administered in dilute solutions by admixing the reconstituted product with dextrose 5% in water, normal saline, dextrose 5% in 0.45% sodium chloride. The resulting solutions are physically and chemically stable for 46 hours.

**CONTRAINDICATIONS**
• Systemic fungal infections
• Known hypersensitivity to components
**Relative Contraindications**
**Special risk groups**
Patients belonging to the following special risk groups should be under strict medical surveillance and should be treated during an as short as possible period (see also

sections SPECIAL PRECAUTIONS and ADVERSE REACTIONS): children, diabetics, hypertensive patients, patients with psychiatric antecedents, certain infectious diseases such as tuberculosis or certain viral diseases such as herpes and zona associated with ocular symptoms.

**ADVERSE REACTIONS**

Systemic adverse reactions may be observed. Although rarely occurring in very short-term therapy, they should always be carefully traced. This is part of the follow-up of any corticotherapy, and does not specifically pertain to any particular product. These possible adverse reactions of glucocorticoids like methylprednisolone are:

**Fluid and Electrolyte Disturbances**

In comparison with cortisone or hydrocortisone, mineralocorticoid effects are less likely to occur with synthetic derivatives such as methylprednisolone. Dietary salt restriction and potassium supplementation may be necessary. All glucocorticosteroids increase calcium excretion.

• Sodium retention
• Fluid retention
• Congestive heart failure in susceptible patients
• Potassium loss
• Hypokalemic alkalosis
• Hypertension

**Musculoskeletal**

• Muscle weakness
• Steroid myopathy
• Osteoporosis
• Vertebral compression fractures
• Aseptic necrosis
• Pathologic fracture

**Gastrointestinal**

• Peptic ulcer with possible subsequent perforation and hemorrhage
• Gastric hemorrhage
• Pancreatitis
• Esophagitis
• Intestinal perforation

**Dermatologic**

• Impaired wound healing
• Thin fragile skin
• Petechiae and ecchymoses
• Repeated local subcutaneous injections may cause local cutaneous atrophy

**Neurological**

• Increased intracranial pressure
• Pseudotumor cerebri
• Seizures
• Psychic derangements may appear when glucocorticoids are used ranging from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations
• Vertigo

**Endocrine**

• Menstrual irregularities
• Development of cushingoid state
• Suppression of growth in children

• Suppression of the pituitary-adrenocortical axis
• Decreased carbohydrate tolerance
• Manifestations of latent diabetes mellitus
• Increased requirements for insulin or oral hypoglycemic agents in diabetics

**Ophthalmic**

Prolonged use of glucocorticoids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Glucocorticoids should be used cautiously in patients with ocular herpes simplex for fear of corneal perforation.

• Increased intraocular pressure
• Exophthalmos

**Metabolic**

• Negative nitrogen balance due to protein catabolism

**Immune System**

• Masking of infections
• Latent infections becoming active
• Opportunistic infections
• Hypersensitivity reactions including anaphylaxis
• May suppress reactions to skin tests

**The Following Additional Reactions Are Related to Parenteral Corticosteroid Therapy**

• Anaphylactic or allergic reactions with or without circulatory collapse
• Cardiac arrest
• Bronchospasm
• Hypotension or hypertension
• Cardiac arrhythmias - there are reports of cardiac arrhythmias and/or circulatory collapse and/or cardiac arrest following the rapid administration of large IV doses of methylprednisolone sodium succinate (greater than 0.5 g administered over a period of less than 10 minutes).

Bradycardia has been reported during or after the administration of large doses of methylprednisolone sodium succinate and may be unrelated to the speed or duration of infusion. After administration of high doses of glucocorticoids, also tachycardia has been reported.

## SPECIAL PRECAUTIONS

**Special Risk Groups**

Patients belonging to the following special risk groups should be under strict medical surveillance and should be treated during as short period as possible.

**Children**

Growth may be suppressed in children receiving long-term, daily-divided doses glucocorticoid therapy. The use of such a regimen should be restricted to those most serious indications.

**Diabetics**

Manifestations of latent diabetes mellitus or increased requirements for insulin or oral hypoglycemic agents.

**Hypertensive patients**

Aggravation of arterial hypertension.

**Patients with psychiatric antecedents**

Existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.
In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting glucocorticosteroids before, during and after the stressful situation is indicated.
Glucocorticosteroids may mask some signs of infection and new infections may appear during their use.
There may be decreased resistance and inability to localize infection when corticosteroids are used.
Data from a clinical study conducted to establish the efficacy of methylprednisolone sodium succinate in septic shock, suggest that a higher mortality occurred in subsets of patients who entered the study with elevated serum creatinine levels or who developed a secondary infection after therapy began.
The use of methylprednisolone sodium succinate in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the glucocorticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen.
If glucocorticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.
Because rare instances of anaphylactic (e.g. bronchospasm) 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.
Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.
There is an enhanced effect of glucocorticosteroids on patients with hypothyroidism and in those with cirrhosis.
Glucocorticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.
Glucocorticosteroids should be used with caution in nonspecific ulcerative colitis.
Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.
Methylprednisolone sodium succinate should not be used routinely to treat head injury as demonstrated by the results of a multicenter study. The study results revealed an increased mortality in the 2 weeks after injury in patients administered methylprednisolone sodium succinate compared to placebo (1.18 relative risk). A causal association with methylprednisolone sodium succinate treatment has not been established.
Some of these presentations contain benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal “gasping syndrome” (respiratory disorder characterized by a persistent gasping for breath) in premature infants.
Corticotherapy has to be considered when interpreting a whole series of biological tests and parameters (e.g. skin tests, thyroid hormone levels).

The duration of the treatment should in general be kept as short as possible. Medical surveillance is recommended during chronic treatment (see also DOSAGE AND ADMINISTRATION). The discontinuation of a chronic treatment should also occur under medical surveillance (gradual discontinuation, evaluation of the adrenocortical function). The most important symptoms of adrenocortical insufficiency are asthenia, orthostatic hypotension and depression.
Injection into the deltoid muscle should be avoided because of the high incidence of subcutaneous atrophy.

**INCOMPATIBILITIES**
The IV compatibility and stability of methylprednisolone sodium succinate solutions and with other drugs in intravenous admixtures are dependent on admixture pH, concentration, time, temperature and the ability of methylprednisolone to solubilize itself. Thus, to avoid compatibility and stability problems, whenever possible it is recommended that solutions of methylprednisolone sodium succinate be administered separately from other drugs and as either IV push, through an IV medication chamber or as an IV “piggy-back” solution.

**PREGNANCY AND LACTATION**
Some animal studies have shown that corticosteroids, when administered to the mother at high doses, may cause fetal malformations.
Since adequate human reproduction studies have not been done with glucocorticosteroids, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential, requires that the possible benefits of the drug be weighed against the potential hazards to the mother, embryo or fetus.
Glucocorticoids should be used during pregnancy only if clearly needed. If a chronic treatment with corticosteroids has to be stopped during pregnancy (as with other chronic treatments), this should occur gradually (see also DOSAGE AND ADMINISTRATION). In some cases (e.g. substitution treatment of adrenocortical insufficiency), however, it can be necessary to continue treatment or even to increase dosage.
Corticosteroids readily cross the placenta. New born infants born of mothers who have received substantial doses of glucocorticosteroids during pregnancy should be carefully observed and evaluated for signs of adrenal insufficiency.
In the case of labor and delivery no effects are known.
Corticosteroids are excreted in breast milk.

**INTERACTIONS**
**Desired Interactions**
• Prevention of nausea and vomiting associated with cancer chemotherapy.
• Mild to moderately emetogenic chemotherapy. For an increased effect, a chlorinated phenothiazine may be used with the first dose of methylprednisolone (one hour before chemotherapy).
• Severely emetogenic chemotherapy. For an increased effect, metoclopramide or a butyrophenon may be used with the first dose of methylprednisolone (one hour before chemotherapy).
• By the treatment of fulminating or disseminated pulmonary tuberculosis and tuberculous meningitis with subarachnoid block or impending block, methylprednisolone is used concurrently with appropriate antituberculous chemotherapy.
• By the treatment of neoplastic diseases like leukemia and lymphoma, methylprednisolone is usually used in conjunction with an alkylating agent, an antimetabolite and a vinca alkaloid.

**Undesired Interactions**
• Combination of glucocorticosteroids with ulcerogenic drugs (e.g. salicylates and NSAIDs) increases the risk of gastrointestinal complications.
• Combination of glucocorticosteroids with thiazide diuretics increases the risk of glucose intolerance.
• Glucocorticosteroids can increase the requirements for insulin or oral hypoglycemic agents in diabetics.
• While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high doses, because of possible hazards of neurological complications and/or lack of antibody response.
• Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.
• Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin.
Concurrent administration of these agents results in a mutual inhibition of metabolism. Therefore it is possible that convulsions and other adverse events associated with the individual use of either drug may be more apt to occur.

**ABILITY TO DRIVE AND TO OPERATE MACHINERY**
Although visual disorders belong to the rare adverse reactions, caution is recommended by patients driving cars and/or using machines.

**OVERDOSAGE**
There is no clinical syndrome of acute overdosage with methylprednisolone sodium succinate.
Chronic overdosage induces typical Cushing symptoms. Methylprednisolone is dialysable.

**STORAGE**
The expiry date (month/year) is mentioned on the package after “EXP.:” (EXP.= expiry date.)
The unreconstituted product should be stored at controlled room temperature below 25°C.
Solutions reconstituted with bacteriostatic water for injection can be stored for 46 hours at controlled room temperature. Bacteriostatic water for injection contains benzyl alcohol.

**DISPENSING IN THE COUNTRY OF ORIGIN**
On medical prescription only.

**MANUFACTURER**
Pfizer Manufacturing Belgium NV/SA

**LICENSE HOLDER**
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*The format of this leaflet was determined by the Ministry of Health and its content was checked and approved.*