SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Depo-Medrol 40 mg/1 mL suspension for injection
Depo-Medrol 80 mg/2 mL suspension for injection
Depo-Medrol 200 mg/5 mL suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The active substance is methylprednisolone.

Depo-Medrol 40 mg/1 mL contains 40 mg methylprednisolone acetate in 1 mL of suspension for injection (40 mg/mL).
Depo-Medrol 80 mg/2 mL contains 80 mg methylprednisolone acetate in 2 mL of suspension for injection (40 mg/mL).
Depo-Medrol 200 mg/5 mL contains 200 mg methylprednisolone acetate in 5 mL of suspension for injection (40 mg/mL).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile suspension for injection, for single use.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Glucocorticoids should be considered as a purely symptomatic treatment, except in some endocrine disorders, in which they are administered as replacement therapy.

A. Intramuscular administration

Methylprednisolone acetate (Depo-Medrol) is not suitable for the treatment of acute life-threatening conditions. If a rapid hormonal effect of maximum intensity is required, a highly soluble glucocorticoid agent such as methylprednisolone sodium succinate (Solu-Medrol) should be administered intravenously.
When oral administration is not feasible and this medicinal product is suitable for the treatment of the condition, the intramuscular use of Depo-Medrol is indicated in the following cases:

Anti-inflammatory treatment
- Rheumatic disorders
  As an adjuvant to maintenance treatment (analgesics, kinesiotherapy, physiotherapy, etc.) and for short-term administration (to tide the patient over an acute episode or exacerbation) in:
  - Psoriatic arthritis
  - Ankylosing spondylitis

  For the following indications, in situ administration of the medicinal product is preferable wherever possible:
  - Post-traumatic osteoarthritis

- Synovitis at site of osteoarthritis
- Rheumatoid arthritis, including the juvenile form (in some cases, low-dose maintenance treatment may be necessary)
- Acute or subacute bursitis
- Epicondylitis
- Acute nonspecific tenosynovitis
- Acute gouty arthritis

- Collagen diseases
  During an exacerbation or as maintenance treatment in selected cases of:
  - Systemic lupus erythematosus
  - Systemic dermatomyositis (polymyositis)
  - Acute rheumatic heart disease
- Skin disorders
  - Pemphigus
  - Severe erythema multiforme (Stevens-Johnson syndrome)
  - Exfoliative dermatitis
  - Mycosis fungoides
  - Bullous dermatitis herpetiformis (sulfones are the treatment of first choice, with systemic administration of glucocorticoids as adjunctive treatment)
- Allergic disorders
  Control of severe or incapacitating allergic conditions unresponsive to appropriate conventional treatment, in cases of:
  - Chronic asthmatic respiratory disorders
  - Contact dermatitis
  - Atopic dermatitis
  - Serum sickness
  - Medicinal product allergy
  - Post-transfusion urticaria
  - Quincke's oedema (adrenaline is the medicinal product of first choice)
- Eye disorders
  Severe acute and chronic allergic and inflammatory processes involving the eye, such as:
  - Herpes zoster ophthalmicus
  - Iritis, iridocyclitis
  - Chorioretinitis
  - Diffuse posterior uveitis
  - Optic neuritis
- Gastrointestinal disorders
  To tide the patient over a critical period in cases of:
  - Ulcerative colitis (systemic treatment)
  - Crohn's disease (systemic treatment)
- Oedema conditions
  - To induce diuresis or remission of proteinuria in cases of nephrotic syndrome without uraemia, of the idiopathic type or due to lupus erythematosus
- Respiratory disorders
  - Symptomatic pulmonary sarcoidosis
  - Berylliosis
  - Fulminant or disseminated pulmonary tuberculosis, in combination with concomitant administration of appropriate anti-tuberculosis medicinal products
  - Loeffler syndrome, unresponsive to conventional treatment
  - Aspiration pneumonia

Treatment of haematology and oncology disorders
- Haematological disorders
  - Acquired (autoimmune) haemolytic anaemia
  - Secondary thrombocytopenia in adults
  - Erythroblastopenia (aplastic anaemia)
  - Congenital (erythroid) hypoplastic anaemia
- Oncology disorders
  For the palliative treatment of:
  - Leukaemia and lymphoma in adults
  - Acute leukaemia in children

Endocrine disorders
- Primary or secondary adrenocortical insufficiency
- Acute adrenocortical insufficiency
- (For these indications, hydrocortisone or cortisone are the medicinal products of choice. In some cases, synthetic analogues may be used provided they are combined with a mineralocorticoid. In children, a mineralocorticoid supplement is particularly important.)
- Congenital adrenal hyperplasia
- Hypercalcaemia associated with cancer
- Non-purulent thyroiditis

Miscellaneous
- Suspected or existing tuberculous meningitis with subarachnoid block, in combination with suitable tuberculostatics
- Trichinosis with neurological or myocardial involvement

B. Intrasynovial, periarticular, intrabursal or soft tissue administration (see also section 4.4)

Depo-Medrol is indicated as an adjuvant in short-term use (to tide the patient over an acute episode or exacerbation) in cases of:
- Synovitis at site of osteoarthritis
- Rheumatoid arthritis
- Acute or subacute bursitis
- Acute gouty arthritis
- Epicondylitis
- Acute nonspecific tenosynovitis
- Post-traumatic osteoarthritis

C. In intralesional administration

Intralesional administration of Depo-Medrol is indicated in the following disorders:
- Keloids
- Localised hypertrophic, infiltrated, inflammatory lesions of: lichen planus, plaque psoriasis, granuloma annulare and lichen simplex chronicus (circumscribed neurodermatitis)
- Discoid lupus erythematosus
- Alopecia areata

Infiltration of Depo-Medrol may also be useful in cystic tumours, aponeurosis or tendinitis (ganglia).

D. Intrarectal instillation
- Ulcerative colitis

4.2 Posology and method of administration

Posology

A. Administration for systemic effect

Intramuscular dosage varies based on the severity of the condition being treated. If a prolonged effect is desired, the weekly dose is calculated by multiplying the daily oral dose by 7 and should be administered as a single intramuscular injection.

Dosage must be adjusted individually according to the severity of the disease and response of the patient. As a general rule, the treatment should be as short as possible. Medical supervision is required.

Hormone therapy is an adjunct to and not a replacement for conventional treatment. Dosage must be decreased or treatment must be discontinued gradually when the medicinal product has been administered for more than a few days. Close medical supervision is recommended when chronic treatment is discontinued.
The severity and expected duration of the disorder and patient response to the medicinal product are primary factors in determining dosage. In cases of spontaneous remission of a chronic disorder, treatment should be discontinued. In chronic treatment, regular laboratory examinations should include urine analysis, blood sugar two hours after eating, blood pressure, body weight and chest X-ray. In patients having suffered from a gastric ulcer or severe dyspepsia, an X-ray of the upper gastrointestinal tract is recommended.

In patients with adrenogenital syndrome, a single intramuscular injection of 40 mg every two weeks may be indicated. For maintenance of patients with rheumatoid arthritis, weekly intramuscular dosage varies from 40 to 120 mg. The usual dosage for patients with skin lesions relieved by systemic corticosteroid therapy is 40 to 120 mg of methylprednisolone acetate administered intramuscularly for one to four weeks. In acute severe dermatitis due to poison ivy, relief may result within 8 to 12 hours following intramuscular administration of a single dose of 80 to 120 mg. In chronic contact dermatitis, it may be necessary to repeat the injection after 5 to 10 days. In seborrheic dermatitis, a weekly dose of 80 mg may be adequate to mitigate symptoms. Following intramuscular administration of 80 to 120 mg to asthmatic patients, relief may result within 6 to 48 hours and may persist for several days to two weeks.

If the disorder is combined with signs of stress, dosage should be increased. If a rapid hormonal effect of maximum intensity is required, the intravenous administration of highly soluble methylprednisolone sodium succinate is indicated.

B. In situ administration for local effect

Treatment with Depo-Medrol does not obviate the need for the conventional measures usually employed. Although this method of treatment relieves symptoms, in no way is it a cure; the hormone has no effect on the cause of the inflammation.

Procedure

1. Rheumatoid and osteoarthritis
   The dose for intra-articular administration depends upon the size of the joint and varies with the severity of the condition in the individual patient. In chronic cases, injections may be repeated

at intervals ranging from one to five or more weeks, depending upon the degree of relief obtained from the initial injection. The following table is provided for information purposes:

Size of joint	Examples	Dosage
Large	Knee Ankle Shoulder	20 to 80 mg
Average	Elbow Wrist	10 to 40 mg
Small	Metacarpophalangeal Interphalangeal Sternoclavicular Acromioclavicular	4 to 10 mg

It is recommended that the anatomy of the joint be extensively reviewed before attempting intra-articular injection. In order to obtain an optimal anti-inflammatory effect, it is important that the injection be made into the synovial space. Using the same sterile technique as for a lumbar puncture, a sterile 20- to 24-gauge needle (on a dry syringe) is quickly inserted into the synovial cavity. Procaine infiltration is elective. The aspiration of only a few drops of joint fluid proves the joint space has been entered by the needle. The injection site for each joint is determined by the location where the synovial cavity is most superficial and most free of large vessels and nerves. With the needle in place, the aspirating syringe is removed and replaced by a second syringe containing the desired amount of Depo-Medrol. A small quantity of synovial fluid is aspirated to make sure the needle is still in the synovial space. After injection, the joint is moved gently a few times to aid mixing of the synovial fluid and the suspension. The injection site is then covered with a small sterile dressing.

Suitable sites for intra-articular injection are the knee, ankle, wrist, elbow, shoulder, phalangeal and hip joints. It is often difficult to enter the hip joint; precautions should be taken to avoid any large blood vessels in the area. Joints not suitable for injection are those that are anatomically inaccessible, such as the spinal and sacroiliac joints, which are devoid of synovial cavity. Treatment failures are most frequently the result of penetration outside the synovial cavity. An injection into the surrounding tissue usually results in little or no benefit. If failures occur when injections into the synovial space are certain (as determined by aspiration of fluid), repeated injections are usually futile. Local treatment does not alter the underlying disease process and should whenever possible be complemented with physiotherapy and orthopaedic correction.

2. Bursitis
   The area around the injection site should be cleaned carefully and an infiltration at the site made with 1% procaine hydrochloride solution. A 20- to 24-gauge needle attached to a dry syringe is inserted into the bursa and the fluid aspirated. The needle is left in place and the aspirating syringe replaced with a small syringe containing the desired dose. After injection, the needle is withdrawn and a small dressing applied.

3. Miscellaneous: ganglia, tendinitis, epicondylitis
   In the treatment of conditions such as tendinitis or tenosynovitis, care should be taken to inject the suspension into the tendon sheath rather than into the substance of the tendon. The tendon may be readily palpated when stretched. When treating epicondylitis, the most painful area should be outlined carefully and the suspension infiltrated into that area. For ganglia of the tendon sheaths, the suspension should be injected directly into the cyst. In many cases, a single

injection results in a marked decrease in the size of the cyst or even its disappearance. According to the severity of the disorder, dosage may range from 4 to 30 mg. In recurrent or chronic disorders, repeated injections may prove necessary.

The usual sterile precautions should be observed for each injection (application of a suitable antiseptic to the skin).

4. Injections for local effect in skin conditions
   Following extensive cleansing with an appropriate antiseptic such as 70% alcohol, 20 to 60 mg is injected into the lesion. In cases of large lesions, it may be necessary to distribute doses of 20 to 40 mg over repeated local injections. Care should be taken to avoid injection of quantities likely to cause discolouration, as this may result in a small necrosis. One to four injections are usually given. The intervals between injections vary with the type of lesion and the duration of improvement produced by the initial injection.

C. Intrarectal administration

Depo-Medrol in doses of 40 to 120 mg administered as retention enemas or by continuous drip three to seven times weekly for periods of two or more weeks, have been shown to be a useful adjunct in the treatment of some patients with ulcerative colitis. The condition of many patients can be controlled with 40 mg of Depo-Medrol administered in 30 to 300 mL of water. Naturally, other accepted therapeutic measures should be instituted.

Paediatric population

Although a lower dose should be administered to children and infants, this dose should nevertheless be determined on the basis of the severity of the disorder rather than on age and body weight.

Method of administration
- Intramuscular
- Intra-articular, periarticular, intrabursal or soft tissues
- Intralesional
- Intrarectal instillation
- Intrasynovial

Depo-Medrol should not be administered by any route other than listed in section 4.1 (see also section "Adverse reactions reported with contraindicated routes of administration" in section 4.8, "Undesirable effects").

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Intrathecal administration
- Intravenous administration
- Epidural administration
- Intranasal or ophthalmic administration, or administration at various injection sites (scalp, oropharynx, sphenopalatine ganglion)
- Systemic mycoses

4.4 Special warnings and precautions for use

This product should not be used for more than one dose. After administration of the desired dose, the remaining suspension should be discarded (see section 6.6).

In order to minimise the incidence of dermal and subdermal atrophy, care must be exercised not to exceed the recommended doses. If possible, multiple small injections should be made in the region of the lesion. The techniques of intra-articular and intramuscular injection should also include precautions against dermal injection or infiltration. Injection into the deltoid muscle should be avoided due to a significant incidence of subcutaneous atrophy.

Severe adverse reactions have been reported in association with the following contraindicated routes of administration: intrathecal/epidural, intranasal, ophthalmic and administration at various injection sites (see section 4.8). Appropriate measures must be taken to avoid intravascular injection.

Intra-articular use
In cases of intra-articular use and/or other local administration, a strict sterile technique is needed to avoid iatrogenic infections.
Following intra-articular corticosteroid administration, care should be taken to avoid overuse of joints in which symptomatic benefit has been obtained. If this instruction is not respected, the therapeutic effect of the steroids may not only be entirely negated, the joint damage may actually be aggravated. Injections into unstable joints are not recommended. In some cases, repeated intra-articular injection may cause joint instability. Any deterioration may be identifiable by X-ray. When a local anaesthetic is administered before injection of Depo-Medrol, the instructions for use of the anaesthetic must be read carefully, and all necessary precautions must be taken.

The following additional precautions apply to glucocorticoids administered parenterally
Intrasynovial injection of corticosteroids may result in both systemic and local effects.
To exclude the possibility of infection, an appropriate examination of the synovial fluid is required.
A marked increase in pain accompanied by local swelling, reduction in joint motion, fever and malaise are potential symptoms of suppurative acute arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, treatment with local injections of glucocorticoids must be discontinued, and appropriate antimicrobial therapy started.
Local injection of steroids should be avoided in cases of pre-existing joint infections.
Glucocorticoids must not be injected into unstable joints. Sterile technique is absolutely necessary to avoid infections and contamination.

Immunosuppressive effects/Increased susceptibility to infection
Corticosteroids may increase susceptibility to infection, may mask some signs of infection and new infections may appear during their use. Corticosteroid use may result in decreased resistance and inability to locate the infection. Infections with any pathogen including viral, bacterial, fungal, protozoan or helminthic organisms, in any location in the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity or neutrophil action. These infections may be moderate, severe and occasionally fatal. The higher the dose of corticosteroids, the higher the incidence of infectious complications.
Do not use intra-articularly, intrabursally or intratendinously for local effect in cases of acute infection. Intramuscular administration should only be considered after an appropriate antimicrobial treatment is started.

Patients taking medicinal products that suppress the immune system are more susceptible to infections than healthy individuals. For example, chickenpox and measles may have a more serious or even fatal course in non-immune children or adults taking corticosteroids.

The administration of live or attenuated live vaccines is not recommendedin patients receiving immunosuppressive doses of corticosteroids. Inactivated and biogenetic vaccines may however be administered in these patients. The therapeutic response to these vaccines may nonetheless be reduced, and the vaccines may even be ineffective. In patients receiving non-immunosuppressive doses of corticosteroids, the necessary vaccinations can be administered as usual.

The use of Depo-Medrol in active tuberculosis should be limited to cases of fulminating or disseminated tuberculosis in which the corticosteroid is associated with an adequate tuberculosis treatment. Close monitoring of patients with latent tuberculosis or presenting a positive tuberculin test is required, as corticosteroids may result in the reactivation of the disease. During prolonged corticosteroid therapy, these patients should receive chemoprophylactic treatment.

Kaposi's sarcoma has been reported in patients treated with corticosteroids. Discontinuation of corticosteroids may result in clinical remission.

The role of corticosteroids in septic shock has been controversial, with early studies reporting both beneficial and detrimental effects. More recently, supplemental corticosteroids have been suggested to be beneficial in patients with established septic shock who exhibit adrenal insufficiency. However, their routine use in septic shock is not recommended.A systematic review of short-term treatment with high-dose corticosteroids did not support their use. However, meta-analyses and a review suggest that longer courses (5-11 days) of low-dose corticosteroids might reduce mortality, especially in patients with septic shock requiring vasopressor treatment.

Effects on the immune system
Allergic reactions may occur. Rare cases of anaphylactic reactions in patients treated with parenteral glucocorticoids have been reported. For this reason, appropriate precautions should be taken prior to administration, especially when the patient has a history of allergy to these medicinal products.

Endocrine effects
In patients treated with corticosteroids who are subject to an unusually stressful event, an increase in the dose of rapid-action corticosteroids is indicated before, during and after the stressful event.
Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration, and duration of corticosteroid therapy. This effect may be minimised by administering the treatment every other day.
In addition, acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly.Secondary medicinal product-induced adrenocortical insufficiency may therefore be minimised by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy. Hormone therapy should therefore be restarted in any situation of stress occurring during that period.
A steroid “withdrawal syndrome”, seemingly unrelated to adrenocortical insufficiency, may also occur following abrupt discontinuation of glucocorticoids. This syndrome includes symptoms such as: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, peeling of the skin, myalgia, weight loss, and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels.

As glucocorticoids may result in or aggravate Cushing's syndrome, they should be avoided in patients with Cushing’s disease.

The effects of corticosteroids increase in patients with hypothyroidism.

Metabolism and nutrition
Corticosteroids, including methylprednisolone, may increase blood glucose, worsen pre-existing diabetes and predispose patients taking long-term corticosteroid therapy to diabetes mellitus.

Psychiatric effects
During corticosteroid therapy, psychic disorders may occur, from euphoria, insomnia, mood swings, personality disorders and severe depression to evident psychotic disorders.Similarly, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Potentially severe psychiatric adverse reactions may occur with systemic steroids. These symptoms typically emerge within a few days or weeks of starting treatment. Most of these reactions disappear after dose reduction or withdrawal, although specific treatment may be necessary. Psychological effects have been reported upon withdrawal of corticosteroids; their frequency is unknown.
Patients/caregivers should be encouraged to seek medical attention if psychological symptoms develop in the patient, especially if depressed mood or suicidal ideation is suspected.
Patients/caregivers should be alert to possible psychiatric disturbances that may occur either during or immediately after dose reduction/withdrawal of systemic steroids.

Nervous system effects
Corticosteroids should be used with caution in patients with epileptic disorders.

Corticosteroids should be used with caution in patients with myasthenia gravis (see also the paragraph on myopathy in section 4.4, Musculoskeletal effects).

Cases of epidural lipomatosis have been reported in patients treated with corticosteroids, usually when used at high doses in the long term.

Ocular effects
Prolonged use of corticosteroids may cause posterior subcapsular and nuclear cataracts (particularly in children), exophthalmos, or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves, and may promote the development of secondary ocular infections due to fungi or viruses.
Given the risk of corneal perforation, glucocorticoids should be administered with caution in patients with ocular herpes simplex or herpes zoster with ophthalmic symptoms.
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.
Corticosteroid treatment has been associated with central serous chorioretinopathy, which is likely to result in retinal detachment.

Cardiac effects
The adverse effects of glucocorticoids on the cardiovascular system, such as dyslipidaemia and hypertension, may predispose treated patients with existing cardiovascular risk factors to additional cardiovascular effects in cases of prolonged treatment at high doses. Accordingly, corticosteroids should be employed judiciously in such patients and attention should be paid to risk modification and additional cardiac monitoring if needed.

In cases of congestive heart failure, systemic corticosteroids should be used with caution, and only if strictly necessary.

Vascular effects
Thrombosis, including venous thromboembolic events, have been reported with the use of corticosteroids. Corticosteroids should therefore be used with caution in patients with thromboembolic disorders, or who may be predisposed to such disorders.

Gastrointestinal effects
High doses of corticosteroids may cause acute pancreatitis.

There is no universal agreement on whether corticosteroids per se are responsible for peptic ulcers encountered during treatment. However, glucocorticoid therapy may mask the symptoms of peptic ulcer so that perforation or haemorrhage may occur without significant pain.Treatment with aglucocorticoid may mask peritonitis or other signs or symptoms associated with gastrointestinal disorders, such as perforation, obstruction or pancreatitis.The risk of developing gastrointestinal ulcers increases in the event of combination with nonsteroidal anti-inflammatories.

Corticosteroids should be used with caution in cases of nonspecific ulcerative colitis if there is an imminent risk of perforation, abscess or other pyogenic infection. Caution should also be exercised in cases of diverticulitis, recent intestinal anastomosis and active or latent peptic ulcer where steroids are usedfor either direct or adjuvant treatment.

Hepatobiliary effects
Medicinal product-induced hepatic lesions, including acute hepatitis, or an increase in hepatic enzymes may be a result of the intravenous administration of methylprednisolone in cyclic intermittent treatment (usually at an initial dose of ≥ 1 g/day). Rare cases of hepatotoxicity have been reported. Its appearance may be delayed by several weeks or more. In the majority of case studies, these adverse reactions resolved after discontinuation of the treatment. Adequate monitoring is therefore required.

Musculoskeletal effects
Acute myopathy has been reported with the use of high doses of corticosteroids, most often occurring in patients with neuromuscular transmission disorders (e.g. myasthenia gravis), or in patients receiving concomitant treatment with anticholinergics, such as neuromuscular blockers (e.g. pancuronium).This acute myopathy is generalised, may involve the ocular and respiratory muscles, and may result in quadriparesis.Elevations of creatine kinase may occur. Clinical improvement or recovery after discontinuation of corticosteroids may require weeks to years.
Osteoporosis is a common but infrequently recognised adverse effect associated with long-term use of large doses of glucocorticoids.

Renal and urinary disorders
Caution is required in patients with systemic sclerosis because an increased incidence of scleroderma renal crisis has been observed with corticosteroids, including methylprednisolone.

Corticosteroids should be used with caution in patients with renal insufficiency.

Investigations
Average and large doses of hydrocortisone or cortisone may cause an increase in blood pressure, sodium and water retention and increased excretion of potassium. These effects are less likely to occur with synthetic derivatives, except when used in large doses. Dietary sodium restriction and

potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Injury, poisoning and procedural complications
Systemic corticosteroids are not indicated and should therefore not be used to treat traumatic brain injury.A multi-site study showed an increase in mortality at 2 weeks and at 6 months after injury in patients receiving methylprednisolone sodium succinate compared to those receiving placebo. A causal relationship with methylprednisolone sodium succinate has not been established.

Other
Caution is recommended with prolonged corticosteroid treatment in the elderly, due to an increased risk of osteoporosis, as well as increased risk of fluid retention that may result in hypertension.

Complications of treatment with glucocorticoids are dependent on the dose and duration of treatment. The risks must therefore be assessed against the benefits expected in each individual case, in order to determine the dose, duration of treatment and schedule of administration (daily or intermittent).

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic sideeffects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid sideeffects, in which case patients should be monitored for systemic corticosteroid sideeffects (see section 4.5).

Acetylsalicylic acid and nonsteroidal anti-inflammatories should be used with caution in patients taking corticosteroids.
In the interpretation of a number of biological tests and parameters (including skin tests and thyroid hormone concentration tests), any use of corticosteroids must be taken into account.

Pheochromocytoma crisis, which can be fatal, has been reported after the administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or diagnosed pheochromocytoma after an appropriate risk/benefit assessment.

Excipients information
This medicine contains less than 1 mmol sodium (23 mg) per 40 mg/1 ml, 80 mg/2 ml and 200 mg/5 ml, that is to say essentially 'sodium-free’.

Pediatric population
The growth and development of infants and children receiving prolonged corticosteroid therapy should be carefully observed. In children receiving prolonged treatment with glucocorticoids in a fractioned daily dose, growth may be slowed. The use of such a regimen should be restricted to the most serious indications.

Infants and children receiving prolonged corticosteroid therapy are exposed to a particular risk of raised intracranial pressure.

High doses of corticosteroids may result in pancreatitis in children.

4.5 Interaction with other medicinal products and other forms of interaction

Methylprednisolone, a substrate of cytochrome P450 (CYP) enzymes, is mainly metabolised by the CYP3A4 enzyme. CYP3A4 is the dominant enzyme of the most abundant CYP subfamily in the liver of adult humans. It catalyses 6β-hydroxylation of steroids, the essential Phase I metabolic step for both endogenous and synthetic corticosteroids. Many other compounds are also substrates of

CYP3A4, some of which (as well as other medicinal products) alter glucocorticoid metabolism by induction (upregulation) or inhibition of the CYP3A4 enzyme.

CYP3A4 INHIBITORS such as ketoconazole, itraconazole, clarithromycin and grapefruit juice generally decrease hepatic clearance and increase the plasma concentration of methylprednisolone. In the presence of a CYP3A4 inhibitor, the dose of methylprednisolone may need to be reducedto avoid steroid toxicity.

CYP3A4 INDUCERS such as rifampicin, carbamazepine, phenobarbital and phenytoin generally increase hepatic clearance and reduce the plasma concentration of methylprednisolone. In the presence of a CYP3A4 inducer, the dose of methylprednisolone may need to be increased to obtain the desired effect.

In the presence of another CYP3A4 substrate, the hepatic clearance of methylprednisolone may be affected. The dosage should therefore be adjusted. It is possible that adverse events associated with the use of either of these medicinal products alone may be more likely to occur with co-administration.

Methylprednisolone also interacts with certain medicinal products unrelated to metabolism by CYP3A4.

Interactions/significant effects of the medicinal product or substance with methylprednisolone

Class or type of medicinal product **- MEDICINAL PRODUCT or SUBSTANCE**	**Interaction or effect**
Antibacterials - ISONIAZID	CYP3A4 INHIBITOR. A further potential effect of methylprednisolone is to increase acetylation rate and isoniazid clearance.
Antibiotics, antituberculosis treatment - RIFAMPICIN	CYP3A4 INDUCER
Anticoagulants (oral)	The effect of methylprednisolone on oral anticoagulants varies. Reports mention both a decrease and an increase in the effects of anticoagulants in concomitant administration with corticosteroids. Therefore, coagulation rates should be checked in order to maintain the desired anticoagulant effects.
Anticonvulsants - CARBAMAZEPINE	CYP3A4 INDUCER (and SUBSTRATE)
Anticonvulsants - PHENOBARBITAL - PHENYTOIN	CYP3A4 INDUCERS
Anticholinergics - NEUROMUSCULAR BLOCKERS	Corticosteroids may influence the action of anticholinergics. 1) Acute myopathy has been observed during concomitant administration of high doses of corticosteroidsand anticholinergics, such as neuromuscular blockers (see section 4.4, “Musculoskeletal effects” for further information). 2) Antagonism of the neuromuscular blocking effects of pancuronium and vecuronium has been reported in patients taking corticosteroids.

Class or type of medicinal product **- MEDICINAL PRODUCT or SUBSTANCE**	**Interaction or effect**
	This interaction may occur with all competitive neuromuscular blockers.
Cholinesterase inhibitors	Steroids may reduce the effects of cholinesterase inhibitors (such as neostigmine or pyridostigmine) in myasthenia gravis and may trigger an attack of myasthenia.
Antidiabetics	As corticosteroids may increase glycaemia, it may be necessary to adjust doses of antidiabetic agents.
Antiemetics - APREPITANT - FOSAPREPITANT	CYP3A4 INHIBITORS (and SUBSTRATES)
Antifungals - ITRACONAZOLE - KETOCONAZOLE	CYP3A4 INHIBITOR (and SUBSTRATE)
Antivirals HIV PROTEASE INHIBITORS	CYP3A4 INHIBITOR (and SUBSTRATE) 1) HIV protease inhibitors, such as indinavir and ritonavir, may increase plasma concentrations of corticosteroids. 2) Corticosteroids may have an inductive effect on the metabolism of HIV protease inhibitors, causing a reduction in plasma concentrations.
Pharmacokinetic enhancers - COBICISTAT	CYP3A4 INHIBITORS Pharmacokinetic enhancers inhibit the activity of CYP3A4 resulting in a decrease of the hepatic clearance and an increase of the plasma concentrations of corticosteroids. A corticosteroid dose adaptation may be necessary (see section 4.4).
Aromatase inhibitor - AMINOGLUTETHIMIDE	The adrenal suppression induced by aminoglutethimide may exacerbate the endocrine changes caused by prolonged treatment with glucocorticoids.
Calcium antagonists - DILTIAZEM	CYP3A4 INHIBITOR (and SUBSTRATE)
Contraceptives (oral) - ETHINYL ESTRADIOL / NORETHINDRONE	CYP3A4 INHIBITOR (and SUBSTRATE)
- GRAPEFRUIT JUICE	CYP3A4 INHIBITOR
Immunosuppressants - CICLOSPORIN	CYP3A4 INHIBITOR (and SUBSTRATE) 1) Concomitant administration of ciclosporin and methylprednisolone causes reciprocal inhibition of their metabolism, which may increase plasma concentrations of one or both substances. The undesirable effects associated with the use of each medicinal product alone may therefore be increased in cases of concomitant administration. 2) Convulsions have been observed during simultaneous administration of methylprednisolone and ciclosporin.

Class or type of medicinal product **- MEDICINAL PRODUCT or SUBSTANCE**	**Interaction or effect**
Immunosuppressants - CYCLOPHOSPHAMIDE - TACROLIMUS	CYP3A4 SUBSTRATE
Macrolide antibiotics - CLARITHROMYCIN - ERYTHROMYCIN	CYP3A4 INHIBITOR (and SUBSTRATE)
Macrolide antibiotics - TROLEANDOMYCIN	CYP3A4 INHIBITOR
NSAIDs (nonsteroidal anti-inflammatory drugs) - High doses of acetylsalicylic acid	1) In cases of concomitant administration of corticosteroids and NSAIDs, the incidence of gastrointestinal haemorrhage and ulcerations may increase. 2) Methylprednisolone may increase the clearance of acetylsalicylic acid administered at high doses, which may cause a reduction in serum salicylate levels. Discontinuation of methylprednisolone treatment may cause an increase in serum salicylate levels, which may cause increased risk of salicylate toxicity. 3) In cases of hypoprothrombinaemia, caution should be exercised in the use of acetylsalicylic acid during corticosteroid treatment.
Agents that increase potassium loss	In cases of concomitant administration of corticosteroids and agents that increase potassium loss (e.g. thiazides and related, loop diuretics), patients should be closely monitored to avoid hypokalaemia. The combination of glucocorticoids and thiazide diuretics increases the risk of glucose intolerance. There is also an increased risk of hypokalaemia in cases of concomitant use of corticosteroids and amphotericin B, xanthenes or beta$_2$-mimetics.
Antibacterials - Quinolones	The risk of tendinitis is increased with concomitant administration of quinolones.
Antihypertensives	Simultaneous administration of antihypertensives may cause partial loss of control of hypertension, as the mineralocorticoid effect of corticosteroids can bring about an increase in blood pressure.
Cardiotonic glycosides - DIGOXIN	The toxicity of cardiotonic glycosides, such as digoxin and related substances, may increase in cases of simultaneous use with corticosteroids, as the mineralocorticoid effect may induce potassium loss.
METHOTREXATE	Methotrexate may influence the effect of methylprednisolone via a synergistic effect on the pathological condition. A dose reduction of the corticosteroid may be considered.
Sympathomimetics	Methylprednisolone may increase the response to sympathomimetics such as salbutamol. This may increase both the efficiency and the potential toxicity of sympathomimetics.
PHENYLBUTAZONE	Simultaneous administration of phenylbutazone may induce

Class or type of medicinal product - MEDICINAL PRODUCT or SUBSTANCE	Interaction or effect
	metabolism of corticosteroids, and therefore reduce their activity.
Vaccines	The administration of live attenuated vaccines is not recommended in patients receiving immunosuppressive doses of corticosteroids. Inactivated vaccines and biogenetically produced vaccines may however be administered to these patients, but the therapeutic response to these vaccines may be reduced or even ineffective. In patients receiving non-immunosuppressive doses of corticosteroids, the necessary immunisation procedures may be undertaken (see section 4.4).

In the treatment of neoplastic diseases such as leukaemia and lymphoma, methylprednisolone is typically used in combination with alkylating agents, antimetabolites and vinca alkaloids.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of methylprednisolone acetate in pregnant women.Corticosteroids do not appear to cause congenital anomalies when given to pregnant women. In the absence of adequate studies of the effects of methylprednisolone on human reproduction, this medicinal product should only be used during pregnancy following careful evaluation of the ratio of benefits to risks for the mother and the foetus.

Corticosteroids readily cross the placenta. A retrospective study found an increased incidence of low birth weight in infants born to mothers receiving corticosteroids.In humans, the risk of low birth weight appears to be linked to the dose, and may be minimised by the administration of the lowest dose of corticosteroids.

Neonates whose mothers have been treated with large amounts of corticosteroids during pregnancy should be closely monitored for symptoms of adrenal insufficiency, although neonatal adrenal insufficiency appears to be rare in infants exposed to corticosteroids in utero.

Cases of cataracts have been observed in infants born to mothers taking corticosteroids in the long term during pregnancy.
Studies in animals have shown reproductive toxicity (see section 5.3).

If long-term treatment with corticosteroids needs to be discontinued during pregnancy (as with other chronic treatments), this should occur gradually (see section 4.2). In certain cases (replacement therapy in adrencortical insufficiency, for example), it may be necessary to continue the treatment, or even to increase the dose.

Lactation
Corticosteroids are excreted in humanmilk.

Corticosteroids excreted in humanmilk may inhibit growth and disturb production of endogenous glucocorticoids in breast-fed infants. This medicinal product should only be used while breastfeeding following careful evaluation of the ratio of benefits to risks for the mother and the infant.

Fertility
Studies in animals have shown that corticosteroids alter fertility (see section 5.3).

4.7 Effects on the ability to drive and use machines

The effect of corticosteroids on the ability to drive and use machines has not been systematically studied. Undesirable effects such as dizziness, vertigo, visual disturbances and fatigue are possible after treatment with corticosteroids. If affected, patients should not drive or use machines. Although visual disorders are a rare undesirable effect, patients driving vehicles and/or using machines should be informed of these adverse reactions.

4.8 Undesirable effects

Safety profile summary
The following undesirable effects are typical of systemic corticosteroids.Hypersensitivity reactions to medicinal products may occur at the start of treatment. Serious infections, including opportunistic infections, may also occur during treatment with corticosteroids. The other adverse medicinal product reactions are as follows: convulsions, pathological and spinal compression fractures, peptic ulcers with perforation or haemorrhage, tendon rupture, psychiic or psychotic disorders, Cushingoid disorders, glucose intolerance disorders, steroid withdrawal syndrome, hypertension, myopathy, glaucoma, cataract, rash, fluid retention, abdominal pain, nausea, headaches and dizziness.

Table of undesirable effects
General undesirable effects may be observed. These rarely occur during treatment of very short duration, but should nevertheless be carefully monitored. This is an inherent aspect of all corticosteroid treatment and is therefore in no way specific to a particular product.

Glucocorticoids such as methylprednisolone may have the following systemic side effects:

The following undesirable effects are listed according to MedDRA system organ class and in order of frequency:

System organ class	Frequency not known (cannot be estimated from the available data)
Infections and infestations	Opportunistic infection, infection, infection at the injection site, peritonitis*.
Blood and lymphatic system disorders	Leucocytosis.
Immune system disorders	Medicinal product hypersensitivity, anaphylactic reaction, anaphylactoid reaction.
Endocrine disorders	Cushingoid syndrome, hypopituitarism, steroid withdrawal syndrome.
Metabolism and nutrition disorders	Metabolic acidosis,epidural lipomatosis, sodium retention, fluid retention, hypokalaemic alkalosis, dyslipidaemia, glucose intolerance disorders, increase in insulin needs (or those of oral glucose-lowering agents in diabetics), lipomatosis,increase in appetite (which may cause weight gain).

System organ class	Frequency not known (cannot be estimated from the available data)
Psychiatric disorders	Affective disorders (including depressed mood, euphoric mood, affective lability, psychological dependence, suicidal ideation), psychotic disorders (including mania, delirium, hallucinations and schizophrenia), mental disorders, changes in personality, confusion, anxiety, mood swings, behavioural disorders, insomnia, irritability.
Nervous system disorders	Increase in intracranial tension (with papillary oedema [benign intracranial hypertension]), seizures, amnesia, cognitive disorder, sensation of dizziness, headache.
Eye disorders	Chorioretinopathy, rare cases of blindness associated with intralesional treatment in the face and head region, cataract, glaucoma, exophthalmia, vision, blurred (see also section 4.4).
Earand labyrinth disorders	Dizziness.
Cardiac disorders	Congestive heart failure (in susceptible patients).
Vascular disorders	Thrombotic events, hypertension, hypotension.
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism, persistent hiccups.
Gastrointestinal disorders	Peptic ulcer (with possibility of perforation or haemorrhage of the peptic ulcer), intestinal perforation, gastric haemorrhage, pancreatitis, ulcerous oesophagitis, oesophagitis, abdominal pain, abdominal distension, diarrhoea, dyspepsia, nausea, vomiting.
Hepatobiliary disorders	Hepatitis, increase in liver enzymes (e.g. AST, ALT)
Skin and subcutaneous tissue disorders	Angio-oedema, hirsutism, petechiae, ecchymosis, cutaneous atrophy, erythema, hyperhidrosis, cutaneous striae, rash, pruritus, urticaria, acne, cutaneous hyperpigmentation, cutaneous hypopigmentation.
Musculoskeletal and connective tissue disorders	Muscle weakness, myalgia, myopathy, muscle atrophy, osteoporosis, osteonecrosis, pathological fractures, neuropathic arthropathy, arthralgia, growth disorder.
Reproductive system and breast disorders	Menstrual irregularity.
General disorders and administration site conditions	Sterile abscess, delayed healing, peripheral oedema, fatigue, malaise, reaction at the injection site.
Investigations	Increase in intraocular pressure, reduced tolerance to carbohydrates, reduced kalaemia, increased calcium in the urine, increased blood alkaline phosphatase, increased blood urea,suppression of reactions to skin tests.
Injury, poisoning and procedural complications	Tendon rupture (especially the Achilles tendon), vertebral compression fractures.

*Peritonitis may be the main sign or symptom of the onset of a gastrointestinal disorder, such as perforation, obstruction or pancreatitis (see section 4.4).

In situ administration
As the medicinal product is absorbed from the administration site into the general circulation, the general undesirable effects mentioned above should be taken into account.
In cases of local administration, dermal and subdermal atrophy may also occur. Although corticosteroid crystals can inhibit inflammatory reactions in the skin, their presence may cause a disintegrationof cellular elements and physiological changes to the fundamental substance of the connective tissue. The resulting dermal and subdermal alterationscan cause cutaneous depressions at the injection site.
The extent of this reaction depends on the quantity of corticosteroid injected (see section 4.4). Regeneration is usually complete after a few months, or once the corticosteroid crystals have been entirely absorbed.

Adverse reactions reported with certain contraindicated routes of administration:
Intrathecal/epidural routes: arachnoiditis, functional gastrointestinal disorder/bladder dysfunction, headache, meningitis, paraparesis/paraplegia, seizures, sensory disturbances. The frequency of these undesirable effects is not known.
Intranasal route
Temporary or permanent visual disorders, possibly leading to blindness; allergic reactions; rhinitis.
Ophthalmic route
Temporary or permanent visual disorders, possibly leading to blindness; increased intraocular pressure, ocular and periocular inflammation and allergic reactions, infections, residue or atrophy at the injection site.
Various injection sites
(scalp, oropharynx, sphenopalatine ganglion): blindness.

Paediatric population
The frequency, type and severity of most of the undesirable effects is expected to be the same as in adults, except for mood swings, behavioural disorders and insomnia, which are more common in children.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions according to their local country requirements.

4.9 Overdose

Symptoms:
No clinical syndrome of acute overdose with methylprednisolone acetate has been reported.

Management:
Cases of acute intoxication and/or death following overdose of corticosteroids are rare. In the event of an overdose, no specific antidote is available; treatment is supportive and symptomatic.

Methylprednisolone is dialysable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: glucocorticoids, ATC code: H02AB04

Mechanism of action
Depo-Medrol is a sterile injectable suspension of methylprednisolone acetate, a synthetic glucocorticoid with powerful and long-lasting anti-inflammatory, immunosuppressive and anti-allergic effects, and has a more potent anti-inflammatory effect than prednisolone. In addition, Depo-Medrol is less likely to cause water and sodium retention than prednisolone. Depo-Medrol may also be administered intramuscularly for prolonged systemic action, or in situ for local treatment. The prolonged activity of Depo-Medrol is explained by the slower release of the active substance.

Methylprednisolone acetate has the general properties of the glucocorticoid methylprednisolone but is less soluble and is metabolised more slowly, which explains its long duration of action. Glucocorticoids diffuse across cell membranes and form complexes with specific receptors in the cytoplasm. These complexes then enter the cell nucleus, bind to DNA (chromatin), and promote the transcription of mRNA and the consecutive synthesis of various enzymes that are ultimately responsible for the varied effects observed in the systemic use of glucocorticoids. In addition to their significant effect on the inflammatory and immune process, glucocorticoids also affect the metabolism of carbohydrates, proteins and fats. They also have an effect 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 the basis of a very substantial number of their therapeutic applications. The main aspects of these properties are as follows:
  - Decrease in immunoactive cells in the source of the inflammation;
  - Decreased vasodilation;
  - Stabilisation of lysosomal membranes;
  - Inhibition of phagocytosis;
  - Reduced production of prostaglandins and related substances.

  A dose of 4.4 mg methylprednisolone acetate (4 mg methylprednisolone) has a glucocorticoid (anti-inflammatory) effect equivalent to a dose of 20 mg hydrocortisone.
  Methylprednisolone has a minimal mineralocorticoid effect (200 mg methylprednisolone is equivalent to 1 mg deoxycorticosterone).

- Effect on the metabolism of carbohydrates and proteins:
  Glucocorticoids stimulate protein catabolism. In the liver, the amino acids released are converted into glucose and glycogen by the process of gluconeogenesis. The absorption of glucose into the peripheral tissue reduces, which leads to hyperglycaemia and glycosuria, especially in patients predisposed to diabetes.

- Effect on lipid metabolism:
  Glucocorticoids have a lipolytic action. This lipolysis is most pronounced in the limbs. They also have an effect on the lipogenesis in the torso, neck and head. All of these effects result in the redistribution of fat deposits.

Pharmacodynamic effects
The maximum pharmacological activity of glucocorticoids is attained later than peak plasma concentrations, suggesting that the principal effects of these substances are not based on direct medicinal action, but on changes in enzyme activity.

5.2 Pharmacokinetic properties

Methylprednisolone acetate is hydrolysed to its active form by plasma cholinesterase. In humans, methylprednisolone binds weakly to albumin and globulin. Approximately 40 to 90% of the medicinal product is bound to proteins. The intracellular activity of glucocorticoids results in a significant difference between the plasma half-life and pharmacological half-life. Pharmacological activity persists after plasma concentrations have ceased to be measurable.

The duration of the anti-inflammatory activity of glucocorticoids is very close to the duration of inhibition of the hypothalamic-pituitary-adrenal (HPA) axis.
After approximately 7.3 ± 1 hours (Tmax), an IM injection of 40 mg/mL results in a peak plasma concentration of methylprednisolone of approximately 1.48 ± 0.86 µg/100 mL (Cmax). The half-life in this case is 69.3 hours. After IM administration of a single dose of 40 to 80 mg of methylprednisolone acetate, the HPA axis may be inhibited for 4 to 8 days.
After 4 to 8 hours, an intra-articular injection of 40 mg into both knees (total dose 80 mg) results in a peak plasma concentration of methylprednisolone of approximately 21.5 µg/100 mL. After intra-articular injection, the duration of both HPA axis inhibition and plasma concentrations of methylprednisolone demonstrate that methylprednisolone acetate diffuses into to the bloodstream from the joints for a period of approximately 7 days.

Methylprednisolone is metabolised at hepatic level, qualitatively similarly to cortisol. The main metabolites are 20-beta-hydroxymethylprednisolone and 20-beta-hydroxy-6-alpha-methylprednisolone. The metabolites are principally excreted in the urine as glucuronides, sulphates and unconjugated compounds. These conjugation reactions occur primarily in the liver, and to a certain extent in the kidneys.

5.3 Preclinical safety data

Conventional studies of safety pharmacology, repeated dose toxicity reveal no special hazard.The toxicities observed in repeated dose studies are as expected during continuous exposure to exogenous adrenocortical steroids.

Carcinogenic potential:
Methylprednisolone has not been formally evaluated in carcinogenicity studies on rodents. Other glucocorticoids have been tested for carcinogenicity on mice and rats with variable results. However, published data indicates that several similar glucocorticoids, in particular, budesonide, prednisolone and triamcinolone acetonide, may increase the incidence of adenomas and hepatocellular carcinomas after oral administration in the drinking water of male rats. These carcinogeniceffects occurred at doses lower than the usual clinical doses expressed in mg/m^2.

Mutagenic potential:

No potential of genetic and chromosomal mutations has been demonstrated in the limited studies conducted on bacterial and mammal cells.

Reproductive toxicity:
It has been demonstrated that corticosteroids administered to rats reduce fertility.In rats, corticosterone induced a reduction in seminal plugs, the number of implantations and viable foetuses.

Corticosteroids have been shown to be teratogenic in many species after administration of doses equivalent to the human dose. In reproductive studies in animals, glucocorticoids such as methylprednisolone were found to induce malformations (cleft palate, skeletal malformations) and delayed intrauterine growth.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol 3350; myristyl-gamma-picoline chloride; sodium chloride; water for injection.

6.2 Incompatibilities

Due to possible physical incompatibilities, Depo-Medrol should not be diluted or mixed with other solutions.

6.3 Shelf life

Do not use Depo-Medrol after the expiry date which is stated on thecarton/ vial label after“EXP”:. The expiry date refers to the last day of that month.

6.4 Special precautions for storage

Store at controlled room temperature (below 30 ° C).

6.5 Nature and contents of container

Depo-Medrol 40 mg/1 mL suspension for injection (40 mg/mL) is available in packs containing one (or three) 1 mL vial(s) or one (or three) 1 mL syringe(s).
Depo-Medrol 80 mg/2 mL suspension for injection (40 mg/mL) is available in packs containing one 2 mL vial or one 2 mL syringe.
Depo-Medrol 200 mg/5 mL suspension for injection (40 mg/mL) is available in packs containing one 5 mL vial.

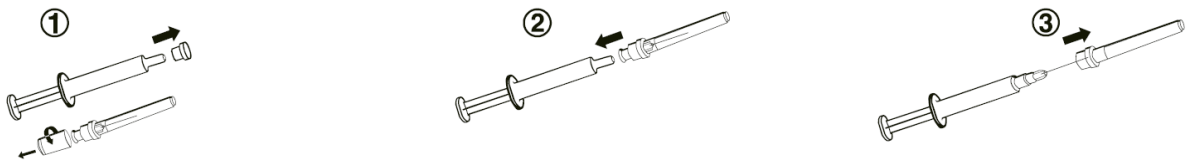
Not all Strengths/Pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Before use, the medicinal products administered parenterally should be inspected visually in order to detect the possible presence of particles or discolouration. Strict aseptic technique is essential to prevent iatrogenic infections. This product is not suitable for intravenous, intrathecal,epidural,intranasal, ophthalmic administration or administration at various injection sites (scalp, oropharynx, sphenopalatine ganglion). Do not use this vialfor more than one dose. After administration of the desired dose, the remaining suspension must be discarded.

How to use the syringe:
Shake the vial well before use to obtain a uniform suspension.
1. Remove the protective cap
2. Place the needle on the syringe

3. Remove the protective needle guard. The syringe is ready for use.



After use, the syringe must be discarded and must not be reused.

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

7. MARKING AUTHORIZATION HOLDER AND MANUFACTURER

Marketing Authorization Holder:
PFIZER S.A., Boulevard de la Plaine 17, 1050 Brussels, Belgium.

Manufacturer:
Pfizer Manufacturing Belgium NV, Rijksweg 12, 2870 Puurs, Belgium.

8. MARKING AUTHORIZATION NUMBER

05395/07341/REN/2020

9. DATE OF RENEWAL OF AUTHORISATION

16-10-2020

10. DATE OF REVISION OF THE TEXT

January 2021.