**LOION 6MG/ML ORAL SOLUTION**  
**PL 21587/0001**

**UKPAR**

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LOION 6MG/ML ORAL SOLUTION
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LAY SUMMARY

On 19\textsuperscript{th} April 2010, the MHRA granted Pharmapol Arzneimittel Vertrieb GMBH a Marketing Authorisation (licence) for Loion 6mg/ml Oral Solution.

Loion 6mg/ml Oral Solution contains prednisolone (as sodium phosphate). Prednisolone belongs to a group of medicines called corticosteroids of steroids. Loion 6mg/ml Oral Solution is used to treat:

- severe asthma
- rheumatoid arthritis
- acute allergic reactions
- certain blood disorders
- severe skin conditions

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits Loion 6mg/ml Oral Solution outweigh the risks; hence a Marketing Authorisation has been granted.
LOION 6MG/ML ORAL SOLUTION
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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Loion 6mg/ml Oral Solution (PL 21587/0001) to Pharmapol Arzneimittel Vertrieb GMBH on 19th April 2010. This prescription only medicine is used to treat:

- bronchial asthma, severe hypersensitivity reactions, anaphylaxis; rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease (excluding systemic sclerosis), polyarteritis nodosa;
- inflammatory skin disorders, including pemphigus vulgaris, bullous pemphigoid and pyoderma gangrenosum;
- minimal change nephrotic syndrome, acute interstitial nephritis;
- ulcerative colitis, Crohn's disease; sarcoidosis;
- rheumatic carditis;
- haemolytic anaemia (autoimmune), acute lymphoblastic and chronic lymphocytic leukaemia, malignant lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura;
- immunosuppression in transplantation.

This application for Loion 6mg/ml Oral Solution is submitted according to Article 10.1 of Directive 2001/83/EC, claiming to be a generic medicinal product to Soluble Prednisolone Tablets 5mg, first authorised in the UK to Glaxo Operations Limited in October 1990, which then underwent a change of ownership to Wagmade PLC on 16th December 1999.

The product contains the active substance prednisolone (supplied as sodium phosphate).

Prednisolone sodium phosphate is a prodrug which is transformed directly into prednisolone by means of the physiologically occurring phosphates of the gastrointestinal tract.

It is considered that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring.

The Marketing Authorisation Holder has provided adequate justification for not submitting a Risk Management Plan (RMP).

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Loion 6mg/ml Oral Solution outweigh the risks; hence Marketing Authorisations have been granted.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE
Prednisolone (sodium phosphate)
INN: Prednisolone (sodium phosphate)
Chemical name: 11β,17-dihydroxy-3,20-dioxpregna-1,4-dien-21-yl disodium phosphate

Structure:

Physical form: White or almost white crystalline powder, slightly hygroscopic.
Solubility: Slightly soluble in water and soluble in alcohol.

Molecular formula: C\textsubscript{21}H\textsubscript{27}Na\textsubscript{2}O\textsubscript{8}P
Molecular weight: 484.39

Prednisolone is the subject of a European Pharmacopoeia monograph.

An Active Substance Master File (ASMF) has been provided covering the manufacture and control of the active substance prednisolone.

Synthesis of the drug substance from the designated starting materials has been adequately described, and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

All potential known impurities have been identified and characterised. Appropriate proof of structure data has been supplied for the active pharmaceutical ingredient.

An appropriate specification is provided for the active substance prednisolone. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification.

Satisfactory Certificates of Analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer.

The specifications and typical analytical test results are provided and are satisfactory.

Satisfactory specifications and Certificates of Analysis have been provided for all aspects of the container-closure system. A declaration has been provided that the primary packaging complies with current regulations concerning contact with foodstuff.
An appropriate retest period has been proposed based on stability data submitted for the active substance prednisolone.

**DRUG PRODUCT**

**Other ingredients**
Other ingredients consist of pharmaceutical excipients liquid (non-crystallising) sorbitol (E 420), glycerol (85 per cent), acetosulfame potassium, disodium edentate, sodium dihydrogen phosphate dehydrate, sodium hydroxide, purified water, cherry flavour.

All excipients with the exception of cherry flavour, comply with their relevant European Pharmacopoeia monographs. Cherry flavour complies with in-house specifications.

None of the excipients used contain material of animal or human origin.

**Product development**
The applicant has provided a suitable product development section. Justifications for the use and amounts of each excipient have been provided and are valid.

**Manufacture**
A description and flow-chart of the manufacturing method has been provided.

In-process controls are satisfactory based on process validation data and controls on batches of the finished product. Process validation has been carried out on three pilot-scale batches of finished product and the results appear satisfactory. The applicant has committed to perform process validation on the first three future production-scale batches.

**Finished product specification**
The finished product specification is satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis for all working standards used have been provided and are satisfactory.

**Container-Closure System**
The product is packaged in a 10 or 20 ml brown glass (type III) bottle with a child-proof, white polypropylene screw cap and a natural coloured polyethylene adapter insert for a metering syringe.
The bottle is enclosed in a carton containing a metering syringe made of polypropylene and silicone (oral syringe, CE0086) with 0.5 to 5.0 ml scale.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 30 months for the product has been set with the storage precautions ‘Do not store above 25°C’ and ‘Store in original package’. It also states that ‘One bottle loion 6mg/ml Oral Solution is intended for single use only’.

**ADMINISTRATIVE**

**Expert Report**
A pharmaceutical expert report has been written by a suitably qualified person and is satisfactory.
Summary of Product Characteristics (SPC)
This is pharmaceutically satisfactory.

Labelling
These are pharmaceutically satisfactory.

Patient Information Leaflet (PIL)
This is pharmaceutically satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
This is pharmaceutically satisfactory.

Conclusion
It is recommended that a Marketing Authorisation is granted for this application.
PRECLINICAL ASSESSMENT

This application for Loion 6mg/ml Oral Solution is submitted according to Article 10.1 of Directive 2001/83/EC, claiming to be a generic medicinal product to Soluble Prednisolone Tablets 5mg, first authorised in the UK to Glaxo Operations Limited in October 1990, which then underwent a change of ownership to Wagmade PLC on 16th December 1999.

No new preclinical data have been supplied with this application and none are required for applications of this type.
CLINICAL ASSESSMENT

No bioequivalence studies have been performed and none are required for this application, as per the Note for Guidance on the Investigation of Bioavailability and Bioequivalence CPMP/EWP/QWP/1401/98,

The finished product is a solution which is being referenced to a soluble tablet which when delivered is in solution, the guidelines state that bioequivalence studies are not required providing the formulation does not affect gastro-intestinal transit, absorption or in-vivo stability of the active.

Therefore a bioequivalence study is not necessary and has not been performed. All aspects for essentially similarity are fulfilled and an abridged application under Art. 10.1 (a)(iii) of Directive 2001/83/EC is therefore justified.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Loion 6mg/ml Oral Solution are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
The pharmacology, pharmokinetics and toxicology of prednisolone are well-known. No new or unexpected safety concerns arise from this application.

EFFICACY
Prednisolone is a well-known drug substance and has been used for many years. No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The data submitted supports the claim that the applicant’s product is of a well-known substance. Extensive clinical experience with prednisolone is considered to have demonstrated the therapeutic value of the compound. The benefit/risk for the indications proposed is, therefore, considered to be positive.
LOION 6MG/ML ORAL SOLUTION  
PL 21587/0001

STEPS TAKEN FOR ASSESSMENT

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<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 25\textsuperscript{th} January 2007.</td>
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<td>Following assessment of the application, the MHRA requested further information relating to the quality dossier on 14\textsuperscript{th} May 2007 and 12\textsuperscript{th} June 2009.</td>
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<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 22\textsuperscript{nd} June 2007 and 12\textsuperscript{th} March 2010 for the quality section.</td>
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<td>The application was determined on 19\textsuperscript{th} April 2010.</td>
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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Loion 6 mg/ml oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
The active ingredient of Loion 6 mg/ml oral solution is prednisolone as the sodium phosphate ester. Each 1 ml oral solution contains 6 mg prednisolone (as sodium phosphate). For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Oral solution
Loion 6 mg/ml oral solution is a colourless, transparent, homogeneous and syrupy solution in a brown glass bottle with a child-proof white screw cap.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are:
- bronchial asthma, severe hypersensitivity reactions, anaphylaxis; rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease (excluding systemic sclerosis), polyarteritis nodosa;
- inflammatory skin disorders, including pemphigus vulgaris, bullous pemphigoid and pyoderma gangrenosum;
- minimal change nephrotic syndrome, acute interstitial nephritis;
- ulcerative colitis, Crohn's disease; sarcoidosis;
- rheumatic carditis;
- haemolytic anaemia (autoimmune), acute lymphoblastic and chronic lymphocytic leukaemia, malignant lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura;
- immunosuppression in transplantation.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
For oral use
Loion 6 mg/ml oral solution is best taken undiluted. Shake well before use.

The lowest dosage that will produce an acceptable result should be used (See precautions section); when it is possible to reduce the dosage, this must be accomplished by stages. During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Adults: The dose used will depend upon the disease, its severity, and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed.

Short-term treatment: 20 to 30mg daily for the first few days, subsequently reducing the daily dosage by 2.5 or 5mg every two to five days, depending upon the response.

Rheumatoid arthritis: 7.5 to 10mg daily. For maintenance therapy the lowest effective dosage is used.

Most other conditions: 10 to 100mg daily for one to three weeks, then reducing to the minimum effective dosage.

Children: Fractions of the adult dosage may be used (e.g. 75% at 12 years, 50% at 7 years and 25% at 1 year) but clinical factors must be given due weight.

Loion 6 mg/ml oral solution may be given early in the treatment of acute asthma attacks in children. For children over 5 years use a dose of 30-40mg prednisolone.
For children aged 2-5 years use a dose of 20mg prednisolone. Those already receiving maintenance steroid tablets should receive 2 mg/kg prednisolone up to a maximum dose of 60mg. The dose of prednisolone may be repeated for children who vomit; but intravenous steroids should be considered in children who are unable to retain orally ingested medication. Treatment for up to three days is usually sufficient, but the length of course should be tailored to the number of days necessary to bring about recovery. There is no need to taper the dose at the end of treatment.

For children under 2 years, Loion 6 mg/ml oral solution can be used early in the management of moderate to severe episodes of acute asthma in the hospital setting, at a dose of 10 mg for up to three days.

4.3 CONTRAINDICATIONS
Systemic infections, unless specific anti-infective therapy is employed. Live virus immunisation. Hypersensitivity to any component of the oral solution.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
In patients who have received more than physiological doses of systemic corticosteroids (approximately 7.5 mg prednisolone or equivalent) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 7.5mg prednisolone is reached, dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses of up to 40 mg daily of prednisolone, or equivalent for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

- Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks
- When a short course has been prescribed within one year of cessation of long-term therapy (months or years),
- Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy,
- Patients receiving doses of systemic corticosteroid greater than 40mg daily of prednisolone (or equivalent),
- Patients repeatedly taking doses in the evening.

Patients should carry 'Steroid treatment' cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must therefore always be gradual to avoid acute adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment. During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Suppression of the HPA axis and other undesirable effects may be minimised by using the lowest effective dose for the minimum period, and by administering the daily requirement as a single morning dose or whenever possible as a single morning dose on alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity. (See dosage section).

Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.
Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. If the patient is a child parents must be given the above advice. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.

Patients should be advised to take particular care to avoid exposure to measles and to seek immediate advice if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.

Live vaccines should not be given to individuals with impaired immune responsiveness caused by high doses of corticosteroids. The antibody response to other vaccines may be diminished.

Because of the possibility of fluid retention, care must be taken when corticosteroids are administered to patients with renal insufficiency or hypertension or congestive heart failure.

Corticosteroids may worsen diabetes mellitus, osteoporosis, hypertension, glaucoma and epilepsy and therefore patients with these conditions or a family history of them should be monitored frequently.

Care is required and frequent patient monitoring necessary where there is a history of severe affective disorders (especially a previous history of steroid psychosis), previous steroid myopathy, peptic ulceration, hypothyroidism, recent myocardial infarction or patients with a history of tuberculosis.

In patients with liver failure, blood levels of corticosteroid may be increased, as with other drugs which are metabolised in the liver. Frequent patient monitoring is therefore necessary.

Physicians should be aware that corticoids have been reported to precipitate porphyria. As well, one case of a reversible Steven-Johnson-Syndrome (SJS) was reported in connection with prednisolone treatment.

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

**Use in Children:** Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible.

**Use in the Elderly:** The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

### 4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, ephedrine and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.

Mifepristone may reduce the effect of corticosteroids for 3-4 days.

Erythromycin and ketoconazole may inhibit the metabolism of some corticosteroids.

Ciclosporin increases plasma concentration of prednisolone. The same effect is possible with ritonavir.

Oestrogens and other oral contraceptives may potentiate the effects of glucocorticoids and dosage adjustments may be required if oral contraceptives are added to or withdrawn from a stable dosage regimen.
The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids.

The growth promoting effect of somatropin may be inhibited by the concomitant use of corticosteroids.

Steroids may reduce the effects of anticholinesterases in myasthenia gravis and cholecystographic x-ray media.

The efficacy of coumarin anticoagulants and warfarin may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Concomitant use of aspirin and Non Steroidal Anti-Inflammatory Drugs (NSAIDs) with corticosteroids increases the risk of gastro-intestinal bleeding and ulceration.

The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

The hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, and carbenoxolone, are enhanced by corticosteroids. The risk of hypokalaemia is increased with theophylline and amphotericin. Corticosteroids should not be given concomitantly with amphotericin, unless required to control reactions.

The risk of hypokalaemia also increases if high doses of corticosteroids are given with high doses of bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline. The toxicity of cardiac glycosides is increased if hypokalaemia occurs with corticosteroids.

Concomitant use with methotrexate may increase the risk of haematological toxicity.

High doses of corticosteroids impair the immune response and so live vaccines should be avoided (see also warnings).

In rare cases the concomitant treatment with corticosteroids and fluoroquinolones may increase the risk of tendon rupture.

4.6 PREGNANCY AND LACTATION
The ability of corticosteroids to cross placenta varies between individual drugs, however, 88% of prednisolone is inactivated as it crosses the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation.

Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Patients with pre-eclampsia or fluid retention require close monitoring.

Depression of hormone levels has been described in pregnancy but the significance of this finding is not clear.

Lactation:
Corticosteroids are excreted in small amounts in breast milk. However doses of up to 40 mg daily of prednisolone are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses
than this may have a degree of adrenal suppression but the benefits of breast-feeding are likely to outweigh any theoretical risk.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None known.

4.8 UNDESIRABLE EFFECTS
The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment. (See other special warnings and precautions)

Endocrine/metabolic:

Corticoids in general may precipitate porphyria.

Anti-inflammatory and Immunosuppressive effects:
Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (See other special warnings and precautions).

Musculoskeletal:
Osteoporosis, vertebral and long bone fractures, avascular osteonecrosis particularly of the femoral head may occur after prolonged corticosteroid therapy or after repeat short courses involving high doses, tendon rupture. Proximal myopathy.

Fluid and electrolyte disturbance:
Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis.

Neuropsychiatric:
Euphoria, psychological dependence, depression, insomnia and aggravation of schizophrenia. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal. Aggravation of epilepsy.

Ophthalmic:
Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases.

Gastrointestinal:
Dyspepsia, peptic ulceration with perforation and haemorrhage, acute pancreatitis, candidiasis, nausea.

Dermatological:
Impaired healing, skin atrophy, bruising, telangiectasia, striae, acne.
One case of a reversible prednisolone induced Steven-Johnson-Syndrome (SJS) was reported.

Cardiovascular:
Myocardial rupture following recent myocardial infarction.

General:
Malaise, hiccups, leucocytosis, thromboembolism.
Hypersensitivity including anaphylaxis has been reported.

Withdrawal symptoms and signs:
Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. (See other special warnings and precautions)
A 'withdrawal syndrome' may also occur including, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

Corticoids in general may precipitate porphyria.
One case of a reversible prednisolone induced Steven-Johnson-Syndrome (SJS) was reported.

4.9 OVERDOSE
Treatment is unlikely to be needed in cases of acute overdosage.

5 PHARMACOLOGICAL PROPERTIES
5.1 PHARMACODYNAMIC PROPERTIES
ATC code: H02AB06
Loion 6 mg/ml oral solution contains the equivalent of 6 mg/ml of prednisolone in the form of the 21-
disodium phosphate ester. Prednisolone sodium phosphate is a synthetic glucocorticoid with the same
general properties as prednisolone itself and other compounds classified as corticosteroids.
Prednisolone is four times as active as hydrocortisone on a weight for weight basis.

Prednisolone sodium phosphate is very soluble in water, and is therefore less likely to cause local
gastric irritation than prednisolone alcohol, which is only slightly soluble. This is important when high
dosages are required, as in immuno-suppressive therapy.

5.2 PHARMACOKINETIC PROPERTIES
Absorption
Prednisolone is readily absorbed from the gastrointestinal tract with peak plasma concentrations
achieved by 1-2 hours after an oral dose. Plasma prednisolone is mainly protein bound (70-90%), with
binding to albumin and corticosteroid-binding globulin. The plasma half-life of prednisolone, after a
single dose, is between 2.5-3.5 hours.

Distribution
The volume of distribution and clearance of total and unbound prednisolone are concentration
dependent, and this has been attributed to saturable protein binding over the therapeutic plasma
concentration range.

Metabolism
Prednisolone is extensively metabolised, mainly in the liver, but the metabolic pathways are not clearly
defined.

Excretion
Over 90% of the prednisolone dose is excreted in the urine, with 7-30% as free prednisolone, and the
remainder being recovered as a variety of metabolites.

5.3 PRECLINICAL SAFETY DATA
No additional data of relevance.

6 PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
Sorbitol, liquid (non-crystallising), E 420
Glycerol (85 per cent)
Acesulfame potassium
Disodium edetate
Sodium dihydrogen phosphate dihydrate
Sodium hydroxide
Water, purified
Cherry flavour

6.2 INCOMPATIBILITIES
None known.

6.3 SHELF LIFE
30 months,
6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 25 °C.
Store in the original package.
One bottle Loion 6 mg/ml oral solution is intended for single use only.

6.5 NATURE AND CONTENTS OF CONTAINER
10 or 20 ml brown glass bottle with a child-proof, white polypropylene screw cap and a natural
coloured polyethylene adapter insert for a metering syringe. The bottle is enclosed in a carton
containing a metering syringe made of polypropylene and silicone (oral syringe, CE0086) with 0.5 to
5.0 ml scale.

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6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
None

7 MARKETING AUTHORISATION HOLDER
Pharmapol Arzneimittelvertrieb-GmbH
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Loion 6 mg/ml oral solution

Active substance: prednisolone (as sodium phosphate)

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
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2. Before you take Loion 6 mg/ml oral solution
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1. What Loion 6 mg/ml oral solution is and what it is used for
Loion 6 mg/ml oral solution is an oral solution containing prednisolone (as sodium phosphate). It is one of a group of medicines called corticosteroids or „steroids“ (They should not be confused with „anabolic“ steroids misused by some bodybuilders and athletes). Loion 6 mg/ml oral solution is used to treat
- severe asthma
- rheumatoid arthritis
- acute allergic reactions
- certain blood disorders
- severe skin conditions.

Many different diseases may be improved by the careful use of medicines like Loion 6 mg/ml oral solution, which mainly works by reducing inflammation in the body. Ask your doctor if you are not sure why you are taking this oral solution.

2. Before you take Loion 6 mg/ml oral solution
DO NOT take Loion 6 mg/ml oral solution
- if you are allergic to the active substance prednisolone (as sodium phosphate) or any of the other ingredients.
- if you just have been immunised or a vaccination is planned.
- if you have a viral infection such as measles, chickenpox or shingles or any other infection.

Take special care with Loion 6 mg/ml oral solution and ask your doctor
- if you ever had tuberculosis (TB), diabetes, epilepsy, depression, raised eye pressure (glaucoma), high blood pressure (hypertension), thinning of the bones (osteoporosis), specific muscle weakness (myasthenia gravis) or stomach ulcers.
- if you have liver or heart disease.
- if you are on a low sodium diet.
- if you are going to have a gall bladder X-ray.
- if you have had a recent heart attack.
- Avoid contact with anyone suffering from measles, chickenpox, or shingles. Tell your doctor immediately, if you have been in personal contact with these patients during treatment or in the past three months, especially if you have not previously had these illnesses yourself.

Carrying a steroid card
If your doctor asks you to carry a STEROID CARD, be sure to keep it with you always.
Show it to any doctor, dentist, nurse or midwife or anyone else who is giving you treatment or vaccinations. Even after your treatment has finished tell any doctor, dentist, nurse or midwife or anyone else who is giving you treatment that you have had steroid treatment.
A steroid card may be obtained from your doctor, pharmacist or local Health Authority. In Scotland, steroid cards are available from your local Scottish Health Board.
Use in children
If **Loion 6 mg/ml oral solution** is prescribed for a child, make sure the oral solution is taken as this patient information or your doctor says. High doses taken for a long time can stunt growth in children.

Use in the Elderly:
Plasma prednisolone concentrations are higher in elderly subjects. Therefore, in old age common adverse effects of steroids may lead to more serious consequences, especially thinning of the bones (osteoporosis), high blood pressure (hypertension), low potassium content of the blood (hypokalaemia), diabetes, susceptibility to infection and thinning of the skin. Regular check-ups at the doctor of elderly patients should be undertaken to minimize complications.

Taking other medicines
The effectiveness of certain treatments may be affected by combination of medicines.
Tell your doctor if you are taking:
- some antiepileptic drugs (carbamazepine, phenobarbitone, phenytoin or primidone),
- some antibiotics (fluoroquinolones, rifampicin, rifabutin or erythromycin),
- active ingredient in cough and cold remedies (ephedrine),
- anticoagulants (e.g. warfarin, acenocoumarol),
- aminoglutethimide (which reduces natural steroids in the body),
- treatments for diabetes (e.g. insulin, glibenclamide, metformin),
- acetazolamide (used for certain eye conditions),
- diuretics (water tablets) such as bendrofluazide and furosemide (used to treat high blood pressure, heart failure, water retention and swelling),
- other medicines used to treat high blood pressure,
- cardiac glycosides such as digoxin (used to treat heart failure and irregular heart beat),
- non-steroidal anti-inflammatory drugs such as ibuprofen, ketoprofen and diclofenac, long-term treatment with aspirin or other salicylates,
- oestrogens (found in contraceptive pills, hormone replacement therapy (HRT), and certain cancer treatments),
- anti fungal treatments (amphotericin or ketoconazole),
- somatropin (used to promote growth),
- theophylline (used to treat asthma and bronchitis),
- high doses of antiasthmatic drugs and drugs against other breathing problems: bambuterol, fenoterol, formoterol, salbutamol, salmeterol and terbutaline;
- ritodrine (used for premature labour),
- carbenoxolone (used to treat oesophageal ulceration),
- ritonavir (used to treat viral infections),
- ciclosporin (used to help the body accept bone marrow or organ transplants),
- anticholinesterases (drugs used to treat the condition myasthenia gravis),
- methotrexate (used for rheumatoid arthritis, psoriasis and certain types of cancer),
- mifepristone (used to terminate pregnancy).

Please note that these statements may also apply to products used some time ago or at some time in the future.
Please tell your doctor or pharmacist if you are taking, or have recently taken, any other medicine; including medicines obtained without a prescription.
Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

If steroids are taken for long periods of time or repeatedly during pregnancy, there may be an increased risk of the baby growing more slowly while in the mother’s womb. However, there are certain clinical situations where it would be more risky to the mother and child to stop taking Loion 6 mg/ml oral solution than carrying on taking them. Your doctor will advise you if you are pregnant or planning to become pregnant.

Breast-feeding: Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

No effects are known

Important information on some of the ingredients of Loion 6 mg/ml oral solution

This medicine contains sorbitol and glycerol. Glycerol may cause headache, stomach upset and diarrhoea. Sorbitol may have a mild laxative effect. The caloric value is 2.6 kcal/g sorbitol. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Loion 6 mg/ml oral solution

Read this instructions carefully. - If you are not sure how much medicine you should take and when to take it, ask your doctor or pharmacist.

- The oral solution is best taken undiluted.
- Shake well before use.
- If you are on long-term therapy make sure your supply of oral solution does not run out.
- Take your Loion 6 mg/ml oral solution as a single dose each morning, unless your doctor has advised you otherwise.
- Dosage depends on the condition being treated and, for an adult, can vary widely between 10 mg and 100 mg daily in divided doses, always reducing to the smallest dose that works.

Prescribed for a CHILD to treat acute asthma attacks:

- For children aged less than 2 years old, 10 mg daily may be given, for up to three days
- For children aged from 2 to 5 years old, 20 mg daily may be given. Treatment for up to three days is usually sufficient, but the length of the course should be tailored to the number of days necessary to recover.
- For children aged more than 5 years old, 30 to 40 mg may be given.

If you have the impression that the effect of Loion 6 mg/ml oral solution is too strong or too weak, talk to your doctor or pharmacist.

If you take more Loion 6 mg/ml oral solution than you should:

If you may have taken more Loion 6 mg/ml oral solution than you should, talk to a doctor or pharmacist or go to the casualty of your nearest hospital immediately.

It is very important to stick to the dose on the label of your medicine. Taking more than this could be dangerous, especially if a great amount of the oral solution is taken at one time.

If you forgot to take Loion 6 mg/ml oral solution:

If you forgot to take a dose, it is important to take another as soon as possible. Then go on as before.

If you stop taking Loion 6 mg/ml oral solution:

Do not suddenly stop taking your oral solution unless you have been told to do so by your doctor, as it can make you ill. When your doctor stops your steroid therapy, your doctor may choose to do this by lowering your dose gradually over a period of time.

- if you have been taking any steroids (this includes tablets, oral solutions or injections) for longer than 3 weeks.
- if you have taken repeated courses of any steroids.
- if you have stopped long term therapy of any steroids in the last 12 months.
- if you have a hormonal imbalance which causes a condition known as adrenal cortical insufficiency. If you are unsure, ask your doctor.
- if you have been taking high daily doses of steroids e.g. more than 40 mg of Loion 6 mg/ml oral solution.
- if you have usually been taking a steroid dose in the evening.
4. Possible side effects

Like all medicines Loion 6 mg/ml oral solution can have possible side effects. Most people taking this oral solution find it causes no problems if taken at the lowest effective dose for the shortest possible time.

A few people can be allergic to some medicines. If any of the following happens soon after taking your oral solution you may be having a serious allergic reaction. Stop taking it and tell your doctor immediately or go to the casualty at your nearest hospital if you notice any of the following:
- Sudden chest tightness or wheeziness
- Chest pain
- Heart pounding or beating irregularly
- Swelling of eye lids, face or lips
- Skin rash, red spots or hives (skin lumps)

These are all very serious side effects which are very rare (in less than 1 in 10,000 patients including single cases). If you have to take this oral solution for a long time your doctor will prescribe as small a dose as possible. High doses taken for a long time or repeated in short courses can lead to side effects such as bone thinning or damage (osteoporosis) or stomach ulcers.

If you have had a recent heart attack, further complications may occur.

In children high doses taken for a long time can stunt growth.

Tell your doctor immediately or go to the casualty at your nearest hospital if you notice any of the following:
- Skin thinning (stretch marks)
- Bruising
- Severe muscle weakness
- Eye problems (cataracts or glaucoma)
- Irregular monthly periods
- Mental upsets

These are all serious side effects. Serious side effects are rare (in less than 1 in 1,000 patients but more than 1 in 10,000 patients).

Tell your doctor if you notice any of the following mild side effects:
- Nausea
- General feeling of being unwell
- Hiccups

Treatment with steroids can make it easier for you to pick up infections and certain infections, such as chickenpox, can be made worse. Avoid contact with anyone suffering from these illnesses. Tell your doctor if you feel unwell or have any unusual discomfort you do not understand.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store Loion 6 mg/ml oral solution

Keep Loion 6 mg/ml oral solution out of the reach and sight of children. A child may be harmed by medicine prescribed for someone else.

Do not store above 25 °C. Store in the original package.

Use by date. Do not use Loion 6 mg/ml oral solution after the expiry date on the label or carton

What to do with unused oral solution

One bottle Loion 6 mg/ml oral solution is intended for single use only. Return unused oral solution to a pharmacist for safe disposal.
6. Further information

What Lioion 6 mg/ml oral solution contains

The active substance is prednisolone (as sodium phosphate). 1 ml of oral solution contains 6 mg prednisolone (as sodium phosphate).

Other ingredients are: Sorbitol, liquid (non-crystallising), E 420; glycerol (85 per cent); acesulfame potassium; disodium edetate; sodium dihydrogen phosphate dihydrate; sodium hydroxide; water, purified; cherry flavour

What Lioion 6 mg/ml oral solution looks like and contents of the pack

Lioion 6 mg/ml oral solution is a colourless, transparent, homogeneous and syrupy solution. It is available in brown bottles closed with a white child-proof screw cap and containing 10 or 20 ml oral solution.

Marketing authorisation holder and manufacturer:
Pharmapol Arzneimittelvertrieb-GmbH, Kaddenbusch 11, 25578 Dägeling, Germany

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist who has the information you need and will advise you.

You may be able to find out more about prescribed medicines from books in public libraries.

The information provided applies only to Lioion 6 mg/ml oral solution.

The leaflet was approved 217610025/1 7/7/2006
Loion® 6 mg/ml oral solution

Prednisolone (as sodium phosphate) 10 ml oral solution

The active ingredient of Loion® 6 mg/ml oral solution is prednisolone as the sodium phosphate ester. Each 1 ml oral solution contains 6 mg prednisolone (as sodium phosphate).

Excipients: Sorbitol, liquid (non-crystallising), E 420; Glycerol (85 per cent); Acesulfame potassium; Disodium edetate; Sodium dihydrogen phosphate dihydrate; Sodium hydroxide; Water, purified Cherry flavour

For oral use. Do not store above 25 °C. Store in the original package. Shake well before use. Keep all medicines out of the reach and sight of children.

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PL No:
Loion®
6mg/ml oral solution

Prednisolone
(as sodium phosphate)

20 ml oral solution for oral use

1 ml of the oral solution contains:
6 mg of prednisolone as prednisolone sodium phosphate,
Sorbitol, liquid (non-crystallising) E 420, Glycerol (85 per cent),
Acesulfame potassium, Disodium edetate, Sodium dihydrogen phosphate dihydrate, Sodium hydroxide, Water, purified,
Cherry flavour

Do not store above 25°C. Store in the original package.

Read enclosed leaflet before use.

Use only as directed by the physician.

The oral solution is best taken undiluted.
Shake well before use.

Keep all medicines out of the reach and sight of children.