Diater Laboratorio de Diagnóstico
y Aplicaciones Terapéuticas, S.A

Summary of Product characteristics

Diater Urpo®
Sublingual spray, suspension

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Diater Urpo® sublingual spray, suspension.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Diater Urpo® is a suspension of inactivated specific bacteria from the culture of urological specimens, diluted in phenolated and glycerinated physiological saline solution at a concentration of 10^9 CFU/mL (Colony Forming Units per mL) for sublingual use.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sublingual spray, suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Diater Urpo® is a product indicated for the specific and individual treatment of patients who have been previously diagnosed with urinary tract infections by a physician or who are predisposed to suffer from such infections, such as cystitis, urethritis, orchitis, prostatitis and pyelonephritis. The purpose of Diater Urpo® treatment is to induce a defensive immune response (production of antibodies) against the inactivated bacteria used in the production of the vaccine.

4.2 Posology and method of administration

Posology

The generally recommended dosage (although it may be modified by the doctor):

Diater Urpo® should be administered once daily for a period of at least three and a half months. The duration of treatment may be modified at the discretion of the physician. The usual dosage is two puffs of the delivery device (0.2 mL) under the tongue until the content of the container is used up.

The content of the vials may become slightly opaque after shaking.

Method of administration

Prior to the first use of the medicinal product, the device should be purged by two or three puffs on the air delivery mechanism to build up pressure in the nebulizer.

Prior to each administration, the vial should be shaken.

4.3 Contraindications

Hypersensitivity to any of the excipients listed in section 6.1.

Diater Urpo® is additionally contraindicated in the following cases:
- Severe disorders of the immune system.
- Diseases that severely affect autoimmunity.
- Pyrexia.

4.4 Special warnings and precautions for use

Diater Urpo® is a treatment for sublingual use.

Diater Urpo® should be administered with caution in patients with neurological impairments as the effect of Diater Urpo® in case of aspiration is unknown.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy and Breast-feeding:
Risk to the new-born/infants cannot be excluded. There is no information of safety of the medicine during pregnancy or lactation.

Fertility
There is no information concerning the safety of the medicine in regard to fertility.

4.7 Effects on ability to drive and use machines

There are no reports regarding the effect on the ability to drive and the use of tools or machinery, no special precautions are required.

4.8 Undesirable effects

Summary of safety profile

Local reactions
In general, local reactions are mild, consisting in the appearance of glossodynia, mucosal inflammation, hypogeusia, nausea, vomiting or abdominal pain. They usually resolve in short period of time, disappearing without treatment.

In rare cases diarrhoea may occur.

Moderate systemic reactions
Occasionally, moderate systemic reactions such as dizziness, general malaise and pyrexia may also be observed. In rare cases, eczema has been reported.

Rarely, urinary incontinence and tract infection may occur, usually associated with concurrent infections. In rare occasions rhinorrhoea associated with incorrect route of product administration may also be observed.

Tabulated summary of adverse reactions
The following table of adverse reactions is based on post-marketing experience data of specific bacterial immunotherapy.

Within each system organ class, adverse reactions identified during the marketing period are listed by frequency (number of patients who it is expected will experience the reaction), using the following category: frequency not known (cannot be estimated from the available data).

Classification by organs and systems	**Frequency**	**Adverse reaction to the medicine**
Infections and infestations	Not known	Urinary tract infection
Nervous system disorders	Not known	Dizziness, hypogeusia
Respiratory, thoracic and mediastinal disorders	Not known	Rhinorrhoea
Renal and urinary disorders	Not known	Urinary incontinence
Gastrointestinal disorders	Not known	Glossodynia, nausea, vomiting, abdominal pain. Diarrhoea.
Skin and subcutaneous tissue disorders	Not known	Eczema
General disorders and administration site conditions	Not known	Local reactions at the administration site (including mucosal inflammation) Malaise, pyrexia
Injury, poisoning and procedural complications	Not known	Incorrect route of product administration.

Description of adverse reactions

A doctor should be contacted immediately in case of severe systemic reactions. In these cases, treatment should be stopped permanently, or until recommended by the physician.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 via the national reporting system.

4.9 Overdose

No information is available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Grupo farmacoterapeútico: Other bacterial vaccines. ATC Code: J07AX.

The mechanism of action of bacterial vaccines via the mucosa involves direct stimulation of the organs present in the upper aerodigestive tract, specially Waldeyer's tonsillar ring. In addition, whole bacteria present all their antigenic determinant, activating the innate and adaptive immune response. Additionally, phagocytosis and the complement system are activated, together with the formation of secretory IgA antibodies and the synthesis of cytokines, interferon alpha and gamma and T-type cellular responses (López-Martín *et al.* 2019).

Animal models have demonstrated the protective effect of immunization with capsules, somatic antigens and outer membrane proteins and fimbriae of type 1 and P against urinary caused by bacteria expressing these types of virulence factors (López-Martín *et al.* 2019).

At the present time, the presence or absence of fimbriae/adhesins and the type to which they belong is considered to be the initial crucial factor in the development of urinary tract infection. They are common in most gram-negative bacteria and in particular in *Escherichia coli*, and the most studied are type 1 and P. Type 1 fimbriae are usually associated with lower urinary tract infection and type P with upper urinary trac infections. *Escherichia coli* (González-Lopez *et al.* 2012).

In a study with 21 patients with a mean of age 36.23 years ± 9.52, the number of infections dropped almost to zero fifteen days after the administration of the vaccine, remaining at this level in all patients until the end of the follow up (330 days) (López-Martín *et al.* 2019).

Literature references

- L. López-Martín, J. Alcover-Díaz, P. Charry-Gómina, R. Gonzáles-López, D. Rodríguez-Gil, R. Palacios-Peláez, C. González-Enguita "Prospective Observational Cohort Study of the Efficacy of Bacterial Immune Prophylacis in the Prevention of Uncomplicated, Recurrent Urinary Tract Infections". Uro. Int. 2019; 102(4): 449-455, DOI: 10.1159/000497107.
- F. González-Chamorro, R. Palacios, J. Alcover, J, Campos, F. Borrego, D. Dámaso "La infección urinaria y su prevención". Actas Urol Esp. 2012; 36(1):48-53, DOI: 10.1016/j.acuro.2011.05.002.

5.2 Pharmacokinetic properties

No information is available.

5.3 Preclinical safety data

No information is available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol.
Glycerine.
Sodium Chloride.
Sodium dihydrogen phosphate monohydrate.
Disodium Hydrogen Phosphate di-hydrate.
Water for injections.

6.2 Incompatibilities

No incompatibilities studies have been performed. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Do not use Diater Urpo® after the expiry date which is stated on the label.

6.4 Special precautions for storage

Store in a refrigerator (between 2-8°C). Do not freeze.

Store in the original packaging.

Do not use Diater Urpo® if the vial has lost some of its contents or if the packaging has been damaged.

6.5 Nature and contents of container

The container is a glass vial (type I) with a nebulizer.
Two vials with the same concentration (10^9 UFC/mL) and each vial contains 10.5 millilitres of Diater Urpo®.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

May 2021