ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG

UROFAST 3 g, granules for oral solution bag

2. Qualitative and quantitative composition

fosfomycin trometamol .....5.631 g

Amount corresponding to fosfomycin .....3.000 g

For a bag.

excipients: sucrose.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Granules for oral solution.

4. CLINICAL

4.1. Therapeutic indications

UROFAST 3 g, granules for oral solution bag is shown in adult women and the girl in the treatment of urinary tract infections (see sections 4.2, 4.4 and 5.1).

It should be given to official guidance on the appropriate use of antibacterial agents.

4.2. Dosage and administration

Dosage

Treatment recommendations should be followed.

In adult women and adolescent:

indications	Dosage
acute uncomplicated cystitis Urinary tract infections in pregnant women: - Cystitis of pregnancy - asymptomatic bacteriuria of pregnancy	1 3 g sachet in a single dose

Administration mode

Dissolve the pellet sachet in half a glass of water to be taken between meals (on an empty stomach or 2 to 3 hours before meals).

4.3. Cons-indications

Known hypersensitivity to fosfomycin.

4.4. Special warnings and precautions

Limits the scope of use of this specialty

Treatment with fosfomycin trometamol is not suitable for pyelonephritis or urinary tract infections in humans.

pediatric population

Pediatric clinical trials with fosfomycin trometamol are limited.

Some data on the use of trometamol fosfomycin in UTIs in children are available, but none was specifically conducted in adolescents. Given the target pathogens and pharmacodynamic-pharmacokinetic characteristics of trometamol fosfomycin, it is expected that the efficiency of this antibiotic is the same as in adult women and that the safety profile is no different.

The use of trometamol fosfomycin in adolescents in the treatment of urinary tract infections should follow official recommendations.

microbiological activity

Fosfomycin trometamol is very active vis-à-vis suspected or documented infections with Staphylococcus saprophyticus (see section 5.1).

persistent infections

In case of persistent infection, a thorough review is necessary because it is often complicated urinary tract infections.

hypersensitivity

sometimes hypersensitivity reactions including anaphylaxis may be life-threatening can be observed in patients treated with fosfomycin (see section 4.8). If such reactions occur, the fosfomycin trometamol should never be re-administered and appropriate treatment should be established.

pseudomembranous colitis

Cases of pseudomembranous colitis has been reported with the use of most antibiotics, including with fosfomycin. The severity of the diarrhea may range from mild diarrhea to fatal colitis in life-threatening.

Diarrhea, particularly severe, persistent and / or bloody, during or after treatment with fosfomycin trometamol (including several weeks after stopping treatment) may be symptomatic of Clostridium difficile-associated diarrhea. It is therefore important to consider this diagnosis in patients who develop severe diarrhea during or after treatment with fosfomycin trometamol. If a case of diarrhea associated with Clostridium difficile is discussed or confirmed, appropriate treatment should be initiated without delay (see section 4.8). In this case, any administration of inhibitors of peristalsis is to be avoided.

Excipient with known effect

This medicine contains sucrose. Its use is not recommended in patients with fructose intolerance, malabsorption of glucose and galactose or sucrase / isomaltase.

4.5. Interactions with other drugs and other forms of interaction

Concomitant use of metoclopramide slows absorption of fosfomycin.

Food intake can slow the absorption of UROFAST resulting from lower urinary concentrations; UROFAST should be administered on an empty stomach or 2 to 3 hours before meals.

Special problems of INR imbalance

Many cases of increased activity of oral anticoagulants have been reported in patients receiving antibiotics. The infectious and inflammatory context marked, age and the patient's general condition appear as risk factors. In these circumstances, it is difficult to distinguish between infectious disease and its treatment in the occurrence of imbalance of INR. However, some classes of antibiotics are more involved: these include fluoroquinolones, macrolides, tetracyclines, cotrimoxazole and some cephalosporins.

4.6. Pregnancy and breast feeding

Pregnancy

Studies in animals have not shown any toxic effect on reproduction. There are many data efficiency of fosfomycin used during pregnancy. However, only a limited number of safety data in pregnant women is available and indicates no malformative nor foetotoxic fosfomycin.

feeding

Fosfomycin administered by injection is excreted in small quantities in breast milk. Therefore, the fosfomycin trometamol administered orally in a single dose can be used during the lactation period.

Fertility

No effects on fertility were highlighted in studies conducted in animals. No clinical data are available in humans.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Side effects

The most common adverse reactions following administration of a single dose of fosfomycin trometamol concern the gastrointestinal tract, mainly diarrhea. These effects are usually short-lived and resolve spontaneously.

The following table presents adverse reactions that have been reported following the use of fosfomycin trometamol in clinical trials or post-marketing.

Rank the undesirable effects by frequency using the following convention: very common (≥ 1/10); common (≥ 1/100, <1/10); uncommon (≥ 1/1000, <1/100); rare (≥ 1/10 000, <1/1000); very rare (<1/10 000), not known (can not be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	**Side effects** **Frequency Category**		
	Frequent **(≥ 1/100, <1/10)**	**Rare** **(≥ 1/1000, <1/100)**	**Not known**
Infections and infestations	vulvovaginitis		
Immune system disorders			Anaphylactic reactions including anaphylactic shock Hypersensitivity *
Nervous system	Headache, dizziness		
Gastrointestinal disorders	Diarrhea, nausea	Abdominal pain, vomiting	pseudomembranous colitis
Skin and subcutaneous tissue		Rash, urticaria, pruritus	Angioedema *

* Some cases of anaphylaxis and angioedema have been reported since marketing of fosfomycin trometamol.

Declaration of suspected adverse reactions

The reporting of suspected adverse reactions after drug approval is important. It allows continuous monitoring of the benefit / risk ratio of the drug. Health professionals report any suspected adverse reactions via the national reporting system: National Agency drug safety and health products (ANSM) network of Regional Pharmacovigilance Centers. Website :www.ansm.sante.fr

4.9. Overdose

No adverse effects as a result of excessive dosage has been recorded so far.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: **OTHER ANTIBACTERIAL**

ATC code: **j01xx01**

Fosfomycin is an antibiotic derived from phosphonic acid. It exerts a bactericidal effect by destroying the bacteria by inhibiting the first step of the synthesis of the cell wall (inhibition of pyruvile transferase).

SPECTRUM OF ACTIVITY ANTI-BACTERIAL

Breakpoints separate susceptible strains of intermediate susceptibility strains and the latter from resistant:

Recommendations EUCAST (v.5.0, 2015-01-01)

Enterobacteriaceae: S≤ 32 mg / L and R> 32 mg / L

The prevalence of acquired resistance may vary depending on the geography and time for certain species. It is therefore useful to have information on the prevalence of local resistance, particularly when treating severe infections. If necessary, it is desirable to obtain expert advice when the interests of the drug in some infections can be questioned because of the level of prevalence of local resistance.

classes
Commonly susceptible species **Aerobic Gram-positive** *Staphylococcus aureus-sensitive, with the exception of Staphylococcus saprophyticus.* **Aerobic Gram-negative** *Citrobacter freundii* *Citrobacter koseri* *Escherichia coli* *Proteus vulgaris*
SPECIES FOR WHICH **(ACQUIRED RESISTANCE ≥ 10%)** **Aerobic Gram-positive** *Enterococcus faecalis* *Staphylococcus methicillin-resistant (1)* *Streptococcus sp.* **Aerobic Gram-negative** *Enterobacter sp.* *Klebsiella sp.* *Proteus mirabilis* *Providencia stuartii* *Pseudomonas aeruginosa (+)* *Serratia sp.*

classes
Inherently RESISTANT **Aerobic Gram-positive** *Corynebacterium sp.* *Enterococcus faecium* *Staphylococcus saprophyticus* **Aerobic Gram-negative** *Acinetobacter sp.* *Morganella morganii* **Other** *Chlamydia trachomatis* *Mycoplasma sp.*

(+) The prevalence of bacterial resistance is> 50% in France.

(1) The frequency of resistance to methicillin is about 20 to 50% of all staphylococci and occurs particularly in hospitals.

under treatment resistance acquisitions are possible, but are not crossed with other antibacterials.

5.2. pharmacokinetic properties

The fosfomycin trometamol salt is well absorbed after oral administration (about 50%).

Peak plasma concentrations (between 20 and 30 mcg / ml) are reached approximately 2 -2.5 hours after taking a dose of 50 mg / kg. The half-life of elimination is between 3 and 5 hours in healthy adults.

Fosfomycin is removed in active form mainly in the urine, where the maximum concentrations are reached 2-4 hours after taking the drug and remain effective for a bacteriological point of view up to 36-48 hours.

5.3. Preclinical safety data

Unspecified.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Flavor orange, tangerine flavor, sodium saccharin, sucrose.

6.2. incompatibility

Not applicable.

6.3. The duration of the conversation

3 years.

6.4. Special precautions for storage

No special storage conditions.

6.5. Nature and contents of container

8 g bag (Surlyn / Aluminum / PE / paper). Box 1.

6.6. Special precautions for disposal and handling

No special requirements.

7. OPERATOR AND MANUFACTURER

FRANCE :
LABORATOIRE NEITUM
104 BLD AUGUSTE BLANQUI
F-75013 PARIS

OPERATOR TO INTERNATIONAL :
LABORATOIERS FRILAB SA
17, RUE DES PIERRES DU NITON
1207 GENEVE – SUISSE

MANUFACTURER :
LABIANA PHARMACEUTICALS S.L.U.
CASANOVA, 27- 31
08757 -CORBERA DE LLOBREGAT (BARCELONA
ESPAGNE

8. NUMBER (S) AUTHORIZATION ON THE MARKET

34009 395 774 4 9: 8 g bag (Surlyn / Aluminum / PE / paper). Box 1.

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

[To be completed nationally]

10. DATE OF THE TEXT

[To be completed nationally]

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

CONDITIONS OF PRESCRIPTION AND DELIVERY

list I