APPENDIX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

POLYGYNAX, vaginal capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Neomycin sulfate ..... 35 000 I.U.
Polymyxin B sulfate ..... 35 000 I.U.
Nystatin ..... 100 000 I.U.

For one vaginal capsule

Excipient with known effect: Hydrogenated soybean oil.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Vaginal capsule.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Local treatment of vaginitis due to sensitive germs (bacterial vaginitis, vulvovaginitis due to *Candida albicans* and *Candida* non-*albicans*, mixed vaginitis) and bacterial vaginosis.

The official recommendations concerning appropriate use of antibacterial products must be taken into consideration.

4.2. Posology and method of administration

Posology
FOR ADULTS ONLY
One vaginal capsule in the evening for 12 days.

Method of administration
Introduce one capsule deep in the vagina, preferably in lying down position.

Practical advice:
- The treatment should be associated with hygiene advice (wearing cotton underwear, avoiding vaginal douches, avoiding the use of an internal tampon during treatment…) and, as far as possible, elimination of contributing factors.
- Treating the partner must be discussed on a case by case basis.
- Do not discontinue the treatment during menstruation periods.

4.3. Contraindications

This medicinal product is contraindicated in the following situations:

- Hypersensitivity to the active substances or to any excipients listed in section 6.1 (or group sensitivity),
- In case of use of diaphragms and latex condoms,
- In case of allergy to peanut or soya, due to the presence of soybean oil.

This medicinal product is generally not recommended in combination with spermicides.

4.4. Special warnings and precautions for use

Warnings

In the event of local intolerance or allergic reaction, the treatment must be interrupted.

The sensitisation to antibiotics by local route may compromise the later use of the same antibiotic or related antibiotics when administered by the systemic route.

Precautions for use

The duration of treatment should be limited because of the risk of selecting resistant germs and the risk of superinfection by these germs.

In the absence of data on the importance of neomycin and polymyxin B fractions resorbed by the mucosa, the risk of systemic effects, especially increased in case of renal insufficiency, cannot be excluded.

This medicinal product contains soybean oil and may cause hypersensitivity reactions (urticaria, anaphylactic shock).

4.5. Interaction with other medicinal products and other forms of interaction

Contraindicated combinations

+ Condoms and Diaphragms (latex)
Risk of rupture.

Combinations not recommended:

+ Spermicide
Any local vaginal treatment is likely to inactivate a local spermicidal contraception.

4.6. Fertility, pregnancy and lactation

Pregnancy

Due to the presence of an aminoside, neomycin, which can cause an ototoxic risk, and the possibility of its systemic absorption, the use of this medicinal product is not recommended during pregnancy.

Lactation

Due to the digestive immaturity of the newborn and the pharmacokinetic properties of this medicinal product, its prescription is not recommended during lactation.

4.7. Effects on ability to drive and use machines

Not relevant.

4.8. Undesirable effects

Undesirable effects are classified by system organ class.

For undesirable effects reported from spontaneous notifications, the frequency is not known (cannot be estimated from available data).

System organ class	Frequency	Undesirable effects
Immune system disorders	Not known	Hypersensitivity: rash, pruritus, urticaria and anaphylactic reaction
Reproductive system and breast disorders	Not known	Local reactions such as burning sensation, pruritus, irritation, redness and oedema

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 via the national reporting system: Agence nationale de sécurité du médicament et des produits de santé (ANSM - French Health Products Safety Agency) and Regional Pharmacovigilance Centers - Website: www.signalement-sante.gouv.fr

4.9. Overdose

An excessive and prolonged administration may produce systemic effects (auditory and renal), in particular in patients with renal insufficiency. A prolonged use also entails an increased risk of allergic eczema.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: ANTIINFECTIVES and ANTISEPTICS IN GYNECOLOGICAL USE (G. genitourinary system and sex hormones), ATC code: G01AA51.

Combination of neomycin, polymyxin B and nystatin.
Neomycin is an aminoside antibiotic.
Polymyxin B is a polypeptide antibiotic.
Nystatin is an antifungal with anticandida activity.

ANTIBACTERIAL ACTIVITY SPECTRUM OF POLYMYXIN B AND NEOMYCIN

POLYMYXIN **B**
Critical concentrations separate sensitive strains from strains with intermediate sensitivity and the latter from resistant strains:
S ≤ 2 mg/l and R > 2 mg/l
The prevalence of acquired resistance may vary with geographical location and time for certain species. It is therefore useful to have information on the prevalence of local resistance, in particular when treating severe infections. These data can only be used as an orientation for the probabilities of sensitivity of a bacterial strain to this antibiotic.

When the variability of the prevalence of resistance is known in France for a bacterial species, it is provided in the following table:

Categories	**Frequency of acquired resistance in France (> 10%) (limit values)**
SENSITIVE SPECIES **Aerobic Gram-negative bacteria** *Acinetobacter* *Aeromonas* *Alcaligenes* *Citrobacter freundii* *Citrobacter koseri* *Enterobacter* *Escherichia coli* *Klebsiella* *Moraxella* *Pseudomonas aeruginosa* *Salmonella* *Shigella* *Stenotrophomonas maltophilia*	**0 – 30%**
RESISTANT SPECIES **Aerobic Gram-positive bacteria** Cocci and bacilli **Aerobic Gram-negative bacteria** *Branhamella catarrhalis* *Brucella* *Burkholderia cepacia* *Burkholderia pseudomallei* *Campylobacter* *Chryseobacterium meningosepticum* *Legionella* *Morganella* *Neisseria* *Proteus* *Providencia*	

Serratia *Vibrio cholerae El Tor* **Anaerobic** Cocci and bacilli **Others** Mycobacteria	

NEOMYCIN

The prevalence of acquired resistance may vary with geographical location and time for certain species. It is therefore useful to have information on the prevalence of local resistance, in particular when treating severe infections. These data can only be used as an orientation for the probabilities of sensitivity of a bacterial strain to this antibiotic.

When the variability of the prevalence of resistance is known in France for a bacterial species, it is provided in the following table:

Categories	**Frequency of acquired resistance in France (> 10%) (limit values)**
SENSITIVE SPECIES	
Aerobic Gram-positive bacteria	
Corynebacterium	
Listeria monocytogenes	
Staphylococcus meti-S	
Aerobic Gram-negative bacteria	
Acinetobacter (essentially *Acinetobacter baumanii)*	50 – 75%
Branhamella catarrhalis	
Campylobacter	
Citrobacter freundii	20 – 25%
Citrobacter koseri	
Enterobacter aerogenes	?
Enterobacter cloacae	10 – 20%
Escherichia coli	15 – 25 %
Haemophilus influenzae	25 – 35 %
Klebsiella	10 – 15 %
Morganella morganii	10 – 20 %
Proteus mirabilis	20 – 50 %
Proteus vulgaris	?
Providencia rettgeri	?
Salmonella	?
Serratia	?
Shigella	?
Yersinia	?

MODERATELY SENSITIVE SPECIES (*in vitro* of intermediate sensitivity) **Aerobic Gram-negative bacteria** *Pasteurella*	

RESISTANT SPECIES **Aerobic Gram-positive bacteria** Enterococci *Nocardia asteroides* *Staphylococcus* meti-R* *Streptococcus*	

Aerobic Gram-negative bacteria *Alcaligenes denitrificans* *Burkholderia* *Flavobacterium sp.* *Providencia stuartii* *Pseudomonas aeruginosa* *Stenotrophomonas maltophilia* **Anaerobic** Strictly anaerobic bacteria **Others** *Chlamydia* Mycoplasmas Rickettsias	

* The frequency of resistance to methicillin is approximately 30 to 50% of all staphylococci and is mainly encountered in hospitals.

Remark: these spectra correspond to those of the systemic forms of these antibiotics. With local pharmaceutical presentations, concentrations obtained *in situ* are much higher than plasma concentrations. There is some remaining uncertainty concerning kinetics of *in situ* concentrations, local physicochemical conditions which can alter the antibiotic activity and product stability *in situ*.

5.2. Pharmacokinetic properties

Not provided.

5.3. Preclinical safety data

Not provided.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

PEG-6 stearate and glycol stearate and PEG-32 stearate (Tefose 63), hydrogenated soybean oil, dimeticone 1000.

Composition of the shell soft capsule: gelatine, glycerol, dimeticone 1000.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 years.

6.4. Special precautions for storage

Capsule under blister (PVC/PVDC/aluminium): Do not store above 25°C.
Capsule under blister (PVC/PE/PVDC/aluminium): Do not store above 30°C.

6.5. Nature and contents of container

6, 12 or 60 capsules under blister (PVC/PVDC/Aluminium) or (PVC/PE/PVDC/aluminium).

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

LABORATOIRE INNOTECH INTERNATIONAL

22 AVENUE ARISTIDE BRIAND
94110 ARCUEIL

8. MARKETING AUTHORISATION NUMBER(S)

- 34009 494 835 1 8: 6 capsules under blister PVC/PVDC/aluminium.
- 34009 494 836 8 6: 12 capsules under blister PVC/PVDC/aluminium.
- 34009 578 478 5 2: 60 capsules under blister PVC/PVDC/aluminium.
- 34009 301 719 7 4: 6 capsules under blister PVC/PE/PVDC/Aluminium.
- 34009 301 719 8 1: 12 capsules under blister PVC/PE/PVDC/Aluminium.
- 34009 550 625 0 9: 60 capsules under blister PVC/PE/PVDC/Aluminium.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 February 1997

Date of latest renewal: 11 February 2012

10. DATE OF REVISION OF THE TEXT

24 September 2019

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR THE PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

GENERAL CLASSIFICATION FOR SUPPLY

List I

Medicinal product subject to medical prescription.