**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

**GENOXYTAB F** 1 g intrauterine tablet for cows

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each intrauterine tablet contains:

**Active substance:**
Oxytetracycline hydrochloride 1 g

**Excipients:**
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Intrauterine tablet
Yellow oblong tablet.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Cattle (Cows).

### 4.2 Indications for use, specifying the target species

Prevention and minimising of development of metritis at its early stage, caused by selected pathogens (as *E.coli*, *Streptococcus uberis*, *Staphylococcus* spp.) susceptible to oxytetracycline associated with the post parturient disorders in cows, i.e. dystocia, retained fetal membranes, uterine prolapse, torsion, embryotomy or complicated parturitions, causing tissue injuries of the birth canal.

### 4.3 Contraindications

Do not use in case of known hypersensitivity to tetracyclines or to any of the excipients.
Do not use in case of infections caused by pathogens resistant to tetracyclines.
Do not use in case of kidney or liver damage.

### 4.4 Special warnings for each target species

None.

### 4.5 Special precautions for use

Special precautions for use in animals

The veterinary medicinal product is an intrauterine tablet, and should not be administered orally. Small silica gel tablet is used as dessicant - to control local humidity, and is not intended for use. When inserting intrauterine tablets, care should be taken not to cause additional infections. Therefore, before administration carefully wash hands. The use of clean obstetric gloves is recommended when administering the product. Before placing the tablet in the uterus, the vulva and perineal area of animal should be carefully washed, disinfected with a non-irritating solution and dried with disposable paper.

Proper care should be taken to ensure careful supervision of the health status of the animals and administration of the product either as prevention based on the thorough clinical investigation and/or just at an early stage of the infection.
As there has been proven great variability in the susceptibility of the main target pathogens both regionally and in time, the veterinary medicinal product should be used based on susceptibility testing, i.e. in accordance with history of determined susceptibility of uterine pathogens in the respective herd, taking into account rational use determined by official and national antimicrobial policies. The use of the product is not recommended in the herds where a high incidence of bacterial pathogens (especially *Trueperella pyogenes*, *Fusobacterium necrophorum* and *Prevotella melaninogenica*) with high rate of resistance to tetracycline has been proved previously.
All available tools based on the good clinical and good farmer practices should be used to prevent unnecessary use of the product.
Milk from treated cows should not be fed to calves due to potential for selection of resistance in intestinal flora of calves (sub-MIC concentrations within mutation selection window).

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Avoid direct contact to skin, eyes and mucosal membranes while handling the product.
People with known hypersensitivity to oxytetracycline should avoid contact with the veterinary medicinal product.
Protective gloves should be worn when handling the veterinary medicinal product.
In case of accidental contact in sensitised people, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

**4.6 Adverse reactions (frequency and seriousness)**

Allergic reactions are rare. In case of allergic or anaphylactic reactions, discontinue treatment immediately. In this case parenteral administration of corticosteroids and anti-histaminics is indicated.

**4.7 Use during pregnancy, lactation or lay**

The veterinary medicinal product is not indicated for use during pregnancy.
Primarily it should be used shortly after the calving, at the beginning of the lactation.

**4.8 Interaction with other medicinal products and other forms of interaction**

Other veterinary medicinal products should not be used by intrauterine route simultaneously.
If systemic antibiotic use is necessary, potential antagonism between tetracyclines and antibiotics with bactericidal action should be taken into account.

**4.9 Amounts to be administered and administration route**

For intrauterine use.
The tablet is to be inserted in the uterine cavity. The tablet should not be divided.

Therapeutic dose is 2 g of oxytetracycline hydrochloride per treatment (i.e. 2 - Genoxytab F intrauterine tablets, daily per cow). The dose should be administered for 3 consecutive days.

As Genoxytab F is foaming tablet and produces min. of 1500 mL of foam per tablet, presence of liquid is required to initiate production of foam. If the uterus does not contain or there is small amount of liquid content, before inserting the tablets, infuse with sterile catheter 200 to 400 mL of pure boiled water. In opposite, when the uterus is full of liquid it is recommended to remove part of the lochia by rectal massage before treatment.

### 4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Considering dosage form, method and route of administration, the risk of overdose is limited. In case of prolonged local antibiotic therapy, disturbance of regular genitourinary flora might lead to occurrence of super-infections with concurrent micro organisms (especially with yeasts – *Candida* spp.).

### 4.11 Withdrawal period(s)

Meat and offal: 7 days
Milk: 5 days (120 hours)

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiinfectives and antiseptics for intrauterine use, antibacterials, oxytetracycline
ATCvet code: QG51AA01

### 5.1 Pharmacodynamic properties

Oxytetracycline is a broad-spectrum bacteriostatic antibiotic. At concentrations higher then the therapeutic it acts as a bactericide. It inhibits the growth and proliferation of a large number of aerobic and anaerobic gram-positive and gram-negative bacteria, and is also effective against spirochetes, rickettsia, chlamydia and some protozoa. It is particularly effective in the treatment of puerperal infections. Oxytetracycline is concentrated in the bacterial cytoplasm, and in ribosomal 30S subunit it interferes with the binding of aminoacyl-tRNA on the acceptor location of the mRNA and ribosomes complex. In this way, the bacteria are effectively prevented to accept amino acids, i.e. lengthening of peptide chain, which inhibits the protein synthesis. Tetracyclines are more active at pH 6.0 to 6.5.

Five mechanisms of resistance, which first and second are most common, has been described yet:

1) Energy dependent efflux systems
2) Ribosomal protection proteins dissociating tetracyclines from their binding site near the ribosomal *AA-tRNA* docking site
3) Reduced uptake of tetracyclin, due to stress-induced down-regulation of the porins through which the drug crosses the outer cell wall of the gram-negative bacteria
4) Enzymatic inactivation- hydroxylation of carbon-11a, which disrupts the tetracyclines' β-keto-enol involved in ribosome binding
5) Ribosomal 16S RNA mutation at the primary binding site of tetracyclines

Different tetracycline resistance (*tet*) genes and oxytetracycline resistance (*otr*) genes have been characterized, when majority of known tet genes and one of the otr genes code for efflux pumps, some of the tet genes and gene *otr*A code for ribosomal protection proteins.

### 5.2 Pharmacokinetic particulars

The veterinary medicinal product is presented in the form of intrauterine tablet which is easily soluble and in contact with the uterus content cause a considerable amount of carbon dioxide foam. Carbon dioxide foam spreads the oxytetracycline throughout the uterine cavity, thus making oxytetracycline available to endometrial surface, which provides increased concentration in endometrium. In addition, carbon dioxide foam mechanically cleans the endometrial surface, evacuates present bacteria, tones the myometrium and stimulates contractions.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Maize starch
Tartaric acid
Sodium hydrogen carbonate
Gelatin
Polyoxyethylene cetyl ether
Cetostearyl alcohol
Magnesium stearate
Talc

### 6.2 Major incompatibilities

Not applicable.

### 6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 18 months.
Shelf life after first opening the immediate packaging: use immediately.

### 6.4. Special precautions for storage

Do not store above 25 °C.
Store in the original package in order to protect from light.

### 6.5 Nature and composition of immediate packaging

Each Genoxytab F intrauterine tablet is separately packaged in AL/PE foil. Silica gel tablet is added to each foil for moisture control (not to be used in animals). Inflated foil does not influence product´s quality.

Package size:
Cardboard box with 10 intrauterine tablets
Cardboard box with 40 intrauterine tablets
Cardboard box with 100 intrauterine tablets

Not all pack sizes may be marketed.

### 6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

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## 8. MARKETING AUTHORISATION NUMBER(S)

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

## 10 DATE OF REVISION OF THE TEXT

## PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

National issue (Czech Republic):
OTHER INFORMATION:

Veterinary medicinal product is supplied based on veterinary prescription only.