ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS
1. NAME OF VETERINARY MEDICINAL PRODUCT

HESKA PERIOceutic Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each unit dose contains:

2.1 Active substance  Doxycycline hyclate, Ph.Eur. 51 mg  
(Equivalent to 44 mg doxycycline; when reconstituted as recommended,  
the product contains 8.8% w/w doxycycline.)

2.2 Excipients  Poly(DL-lactide)  165 mg  
N-methyl-2-pyrrolidone  285 mg

3. PHARMACEUTICAL FORM

Powder and solvent for dental gel

4. PHARMACOLOGICAL PROPERTIES

Doxycycline is a semi-synthetic tetracycline derivative. Consistent with the tetracycline class of  
antibiotics, doxycycline is a bacteriostatic antibiotic with a wide range of antimicrobial activity. Upon contact with the aqueous environment (gingival crevicular fluid) the polymer will harden,  
resulting in the formation of a solid, pliable delivery system within the treated periodontal pocket(s). Doxycycline is released into the gingival crevicular fluid to provide a local effect on the  
microorganisms present, particularly gram-negative anaerobic bacteria, involved in periodontal  
disease. The extent and duration of release depends upon a large number of variables. Generally,  
concentrations of doxycycline in excess of relevant MIC (6 μg/ml) are maintained for at least 7 days,  
with concentrations in excess of the relevant MIC still being present at 28 days in most cases.

In a clinical trial, the highest plasma doxycycline concentration (0.7 μg/ml) was observed at 6 hours  
after treatment (2-4 affected teeth in each of 6 dogs). Plasma doxycycline concentrations observed at  
12 hours were at or below the limit of quantitation (0.1-0.4 μg/ml). Doxycycline was not detected in  
plasma samples taken at 24 hours after treatment or any time point thereafter. All detectable  
concentrations of doxycycline were well below levels associated with systemic activity or toxicity. A  
peak doxycycline concentration of 1749 μg/ml was observed in gingival crevicular fluid at 12 hours  
after treatment.

5. CLINICAL PARTICULARS

5.1 Target species

Dogs

5.2 Indications for use, specifying the target species

Treatment of periodontal disease in dogs.

Periodontal pocket probing depths ≥4 mm are evidence of disease that may be responsive to treatment  
with the HESKA PERIOceutic Gel. Use of this product as directed should result in attachment level  
gains, periodontal pocket depth reductions, local antimicrobial effect and improved gingival health. Noticeable improvements in these parameters should be evident within 2-4 weeks following  
treatment. The response in individual dogs is dependent on the severity of the condition and rigor of  
adjunctive therapy.
5.3 Contra-indications

Do not use in dogs less than 1 year of age as the use of tetracyclines during tooth development has been associated with permanent discoloration of the teeth. This product is not intended for use in oronasal fistulas, periapical abscesses, or severely compromised teeth.

5.4 Undesirable effects (frequency and seriousness)

None known

5.5 Special precaution(s) for use

None known

5.6 Use during pregnancy and lactation

Contra-indicated in pregnant or lactating bitches. The use of the product in breeding dogs has not been evaluated.

5.7 Interaction with other veterinary medicinal products and other forms of interaction

As doxycycline can bind with zinc, concurrent use of products containing zinc (e.g., chlorhexidine solutions formulated with zinc gluconate) is not recommended.

5.8 Posology and method of administration

Directions for Use: Apply subgingivally to periodontal pocket(s) of affected teeth.

Teeth should be cleaned and scaled prior to application of the product. If required, root planing and debridement of affected sites should be performed. The product is applied with the animal under sedation or anaesthesia. Use as many units as required to fill the periodontal pockets of affected teeth.

Each pouch contains 2 syringes and a blunt cannula. Syringe A contains the polymer delivery system and Syringe B contains doxycycline. Lock the syringes together. Beginning with Syringe A, use the plungers of Syringes A and B to exchange the material between the syringes approximately 100 times to achieve a homogeneous mixture. Fully deliver the mixture into Syringe A, separate the syringes, and lock the supplied blunt cannula onto Syringe A. The cannula may be bent to the desired angle. Gently place the cannula 1-2 mm below the gingival margin of an affected tooth. Express a small amount of the mixture into each periodontal pocket 4 mm or deeper. Ensure that the pockets are filled approximately to the gingival margin. The formulation will begin to solidify immediately upon application; however, lavage with a few drops of water or sodium chloride solution will facilitate the process. As the mixture hardens, the exposed surface of the product may be pressed into the pocket with the edge of a wax spatula or the back of a curette. Allow approximately 30-60 seconds for the polymer to harden before beginning to press it into the pocket. Pressure can be applied to the gingival margin to avoid dislodging the polymer inadvertently. As the product is biodegradable, removal at a subsequent visit is not required. Clients should be advised to suspend brushing treated teeth for approximately two weeks following application.

Treatment of periodontal disease requires a comprehensive program of routine scaling and cleaning, home care and dental hygiene (e.g., brushing, rinses or the use of chewing devices) in addition to application of this product. Severe cases may require surgical intervention.

The empty Syringe B should be placed in the resealable foil pouch to facilitate mixing if the reconstituted product is stored.

5.9 Overdose (symptoms, emergency procedures, antidotes)

Target animal studies have indicated a wide safety margin. Overdose is not likely to occur.
5.10 Special warnings for each target species
None known

5.11 Withdrawal period
Not applicable

5.12 Special precautions to be taken by the person administering the veterinary medicinal product to animals
Wash hands thoroughly after use.

As there is sustained release of doxycycline into the gingival crevicular fluid and saliva, dog owners sensitive to topically applied tetracyclines should avoid contact with saliva from treated dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 Incompatibilities (major)
None known

6.2 Shelf-life, when necessary after reconstitution of the veterinary medicinal product or when the container is opened for the first time
18 months
Reconstituted product: 3 days

6.3 Special precautions for storage
Store at 2°C-8°C.
Reconstituted product not used on the day of mixing should be stored at room temperature (≤25°C) in the resealable foil pouch and used within 3 days of mixing. Ten additional exchanges between syringes should be performed if reconstituted product has been stored.

6.4 Nature and contents of container
Each unit of HESKA PERIOceutic Gel contains two polypropylene syringes: Syringe A (450 mg polymer delivery system) and Syringe B (51 mg Doxycycline hyclate, Ph.Eur. which is equivalent to 44 mg doxycycline). When reconstituted as recommended, the product contains approximately 0.5 ml of a 8.8% w/w doxycycline gel). Syringe A is heat sealed in an inner foil pouch. The inner pouch, Syringe B and a blunt cannula are heat sealed in the outer foil pouch. Available as a 3 unit box (containing 1 additional blunt cannula) or a 10 unit box (containing 3 additional blunt cannulae).

6.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from such medicinal products, if appropriate
Any unused product or waste material should be disposed of in accordance with local requirements.

7. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER
Heska UK, Limited
P.O. Box 6, 5 George Street
Teignmouth, Devon TQ14 8AH UK

8. NUMBER IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCT
9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

10. DATE OF REVISION OF THE TEXT
ANNEX II
THE MANUFACTURING AUTHORISATION HOLDER(S)
RESPONSIBLE FOR IMPORT AND BATCH RELEASE AND CONDITIONS
OF THE MARKETING AUTHORISATION
A. MANUFACTURING AUTHORISATION HOLDER(S)

FATRO S.P.A
40064 Ozzano Emilia
Bologna
Via Emilia 285 Italy

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable

D. STATEMENT OF THE MRLs WHICH MAY BE ACCEPTED IN ACCORDANCE WITH COUNCIL REGULATION (EEC) No 2377/90

Not applicable
ANNEX III
LABELLING AND PACKAGE INSERT
A. LABELLING
Labelling for 3 unit outer box

1. **NAME OF THE VETERINARY MEDICINAL PRODUCT**  
HESKA PERIOceutic Gel

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**  
Active substance: Doxycycline hyclate, Ph.Eur. 51 mg (equivalent to 44 mg doxycycline). When reconstituted as recommended, the product contains 8.8% w/w doxycycline.

3. **PHARMACEUTICAL FORM**  
Powder and solvent for dental gel

4. **PACKAGE SIZE**  
3 units per box

5. **TARGET SPECIES**  
Dogs

6. **INDICATIONS**  
Treatment of periodontal disease in dogs. Use of this product as directed should result in attachment level gains, periodontal pocket depth reductions, local antimicrobial effect and improved gingival health.

7. **METHOD AND ROUTE OF ADMINISTRATION**  
For subgingival administration

8. **WITHDRAWAL PERIOD**  
Not applicable

9. **SPECIAL WARNING(S), IF NECESSARY**  
Wash hands thoroughly after use.

As there is sustained release of doxycycline into the gingival crevicular fluid and saliva, dog owners sensitive to topically applied tetracyclines should avoid contact with saliva from treated dogs.

10. **EXPIRY DATE**  
Exp. Date: month/year

11. **SPECIAL STORAGE CONDITIONS**  
Store at 2°C-8°C. Reconstituted product not used on the day of mixing should be stored at room temperature (≤25°C) in the resealable foil pouch and used within 3 days of mixing. Ten additional exchanges between syringes should be performed if reconstituted product has been stored.
12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED VETERINARY MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

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

13. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only

14. THE WORDS “KEEP OUT OF REACH OF CHILDREN”

Keep out of the reach of children

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing Authorisation Holder:

Heska UK, Limited
P.O. Box 6, 5 George Street
Teignmouth, Devon TQ14 8AH UK

Manufacturing Authorisation Holder:

FATRO S.P.A
40064 Ozzano Emilia
Bologna
Via Emilia 285 Italy

16. NUMBER(S) IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS

17. MANUFACTURER’S BATCH NUMBER

Lot number

18. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription

19. ADDITIONAL ITEMS
Labelling for 10 unit outer box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT
HESKA PERIOceutic Gel

2. STATEMENT OF ACTIVE SUBSTANCE(S)
Active substance: Doxycycline hyclate, Ph.Eur. 51 mg (equivalent to 44 mg doxycycline). When reconstituted as recommended, the product contains 8.8% w/w doxycycline.

3. PHARMACEUTICAL FORM
Powder and solvent for dental gel

4. PACKAGE SIZE
10 units per box

5. TARGET SPECIES
Dogs

6. INDICATIONS
Treatment of periodontal disease in dogs.
Use of this product as directed should result in attachment level gains, periodontal pocket depth reductions, local antimicrobial effect and improved gingival health.

7. METHOD AND ROUTE OF ADMINISTRATION
For subgingival administration

8. WITHDRAWAL PERIOD
Not applicable

9. SPECIAL WARNING(S), IF NECESSARY
Wash hands thoroughly after use.
As there is sustained release of doxycycline into the gingival crevicular fluid and saliva, dog owners sensitive to topically applied tetracyclines should avoid contact with saliva from treated dogs.

10. EXPIRY DATE
Exp. Date: month/year

11. SPECIAL STORAGE CONDITIONS
Store at 2°C –8°C.
Reconstituted product not used on the day of mixing should be stored at room temperature (≤25°C) in the resealable foil pouch and used within 3 days of mixing. Ten additional exchanges between syringes should be performed if reconstituted product has been stored.
12. **SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED VETERINARY MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

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

13. **THE WORDS “FOR ANIMAL TREATMENT ONLY”**

For animal treatment only

14. **THE WORDS “KEEP OUT OF REACH OF CHILDREN”**

Keep out of the reach of children


*Marketing Authorisation Holder:*

Heska UK, Limited  
P.O. Box 6, 5 George Street  
Teignmouth, Devon TQ14 8AH  UK

*Manufacturing Authorisation Holder:*

FATRO S.P.A  
40064 Ozzano Emilia  
Bologna  
Via Emilia 285  Italy

17. **NUMBER(S) IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS**

18. **MANUFACTURER’S BATCH NUMBER**

Lot number

19. **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Veterinary medicinal product subject to prescription

19. **ADDITIONAL ITEMS**
Labelling - Outer pouch of individual units

1. **NAME OF THE VETERINARY MEDICINAL PRODUCT**

HESKA PERIOceutic Gel

2. **QUANTITY OF THE ACTIVE SUBSTANCE(S)**

Active substance: Doxycycline hyclate, Ph.Eur. 51 mg (equivalent to 44 mg doxycycline). When reconstituted as recommended, the product contains 8.8% w/w doxycycline.

3. **ROUTE(S) OF ADMINISTRATION**

For subgingival administration

4. **BATCH NUMBER**

Lot number

5. **EXPIRY DATE**

Exp. Date: month/year

6. **THE WORDS “FOR ANIMAL TREATMENT ONLY”**

For animal treatment only

7. **ADDITIONAL ITEMS**

Read accompanying package insert carefully.
Reconstituted on:
Tear here to open
Store at 2 to 8°C
Reconstituted product not used on the day of mixing should be stored at room temperature (≤25°C) in the resealable foil pouch and used within 3 days of mixing. Ten additional exchanges between syringes should be performed if reconstituted product has been stored.

Labelling - Inner Pouch

Lot number:
Exp. Date:

Labelling - Syringe A

Syringe A
450 mg polymer delivery system
Lot number:
Exp. Date: month/year

Labelling - Syringe B

Syringe B
44 mg Doxycycline
Lot number:
Exp. Date: month/year
B. PACKAGE INSERT
1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HESKA PERIOceutic Gel

2. STATEMENT OF THE ACTIVE SUBSTANCE(S)

The active ingredient is doxycycline hyclate, Ph.Eur.

Each unit of the HESKA PERIOceutic Gel contains Syringe A (450 mg polymer delivery system) and Syringe B (44 mg doxycycline), which when mixed result in approximately 0.5 ml of doxycycline gel. Each unit also contains a blunt cannula. Available as a 3 unit box (containing 1 additional blunt cannula) or a 10 unit box (containing 3 additional blunt cannulae).

The HESKA PERIOceutic Gel is provided in a two syringe system requiring mixing prior to use. Syringe A contains the polymer delivery system and Syringe B contains the active ingredient (doxycycline). Once mixed, the product is a flowable solution of doxycycline hydrochloride equivalent to 8.8% doxycycline activity. The formulation is applied subgingivally to the periodontal pocket(s) of affected teeth, and doxycycline is slowly released from the polymer providing a local antimicrobial effect. The product is non-irritating and biodegradable.

3. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing Authorisation Holder:

Heska UK, Limited
P.O. Box 6, 5 George Street
Teignmouth, Devon TQ14 8AH   UK

Manufacturing Authorisation Holder:

FATRO S.P.A
40064 Ozzano Emilia
Bologna
Via Emilia 285   Italy

4. TARGET SPECIES

Dogs

5. INDICATIONS

Treatment of periodontal disease in dogs.

Use of this product as directed should result in attachment level gains, periodontal pocket depth reductions, local antimicrobial effect and improved gingival health. Periodontal pocket probing depths ≥4 mm are evidence of disease that may be responsive to treatment with the HESKA PERIOceutic Gel. Noticeable improvements in these parameters should be evident within 2-4 weeks following treatment. The response in individual dogs is dependent on the severity of the condition and rigor of adjunctive therapy.

6. DOSAGE FOR EACH SPECIES

Use as many units as are necessary to fill affected periodontal pocket(s).
7. **METHOD AND ROUTE OF ADMINISTRATION**

Apply subgingivally to periodontal pocket(s) of affected teeth.

Teeth should be cleaned and scaled prior to application of the product. If required, root planing and debridement of affected sites should be performed. The product is applied with the animal under sedation or anaesthesia. Use as many units as required to fill the periodontal pockets of affected teeth.

Each pouch contains 2 syringes and a blunt cannula. Syringe A contains the polymer delivery system and Syringe B contains doxycycline. Lock the syringes together. Beginning with Syringe A, use the plungers of Syringes A and B to exchange the material between the syringes approximately 100 times to achieve a homogeneous mixture. Fully deliver the mixture into Syringe A, separate the syringes, and lock the supplied blunt cannula onto Syringe A. The cannula may be bent to the desired angle. Gently place the cannula 1-2 mm below the gingival margin of an affected tooth. Express a small amount of the mixture into each periodontal pocket 4 mm or deeper. Ensure that the pockets are filled approximately to the gingival margin. The formulation will begin to solidify immediately upon application; however, lavage with a few drops of water or sodium chloride solution will facilitate the process. As the mixture hardens, the exposed surface of the product may be pressed into the pocket with the edge of a wax spatula or the back of a curette. Allow approximately 30-60 seconds for the polymer to harden before beginning to press it into the pocket. Pressure can be applied to the gingival margin to avoid dislodging the polymer inadvertently. As the product is biodegradable, removal at a subsequent visit is not required. Clients should be advised to suspend brushing treated teeth for approximately two weeks following application.

Treatment and control of periodontal disease requires a comprehensive program of routine scaling and cleaning, home care and dental hygiene (e.g., brushing, rinses or the use of chewing devices) in addition to application of this product. Severe cases may require surgical intervention.

The empty Syringe B should be placed in the resealable foil pouch to facilitate mixing if the reconstituted product is stored.

Wash hands thoroughly after use.

8. **ADVICE ON CORRECT ADMINISTRATION**

**CLINICAL PHARMACOLOGY:** Doxycycline is a semi-synthetic tetracycline derivative. Consistent with the tetracycline class of antibiotics, doxycycline is a bacteriostatic antibiotic with a wide range of antimicrobial activity. Upon contact with the aqueous environment (gingival crevicular fluid) the polymer will harden, resulting in the formation of a solid, pliable delivery system within the treated periodontal pocket(s). Doxycycline is released into the gingival crevicular fluid for up to 28 days to provide a local effect on the microorganisms present, particularly gram-negative anaerobic bacteria, involved in periodontal disease.

In a clinical trial, the highest plasma doxycycline concentration (0.7 mcg/ml) was observed at 6 hours after treatment (2-4 affected teeth in each of 6 dogs). Plasma doxycycline concentrations observed at 12 hours were at or below the limit of quantitation (0.1-0.4 mcg/ml). Doxycycline was not detected in plasma samples taken at 24 hours after treatment or any time point thereafter. All detectable concentrations of doxycycline were well below levels associated with systemic activity or toxicity. A peak doxycycline concentration of 1749 mcg/ml was observed in gingival crevicular fluid at 12 hours after treatment.

9. **CONTRA-INDICATIONS**

Do not use in dogs less than 1 year of age as the use of tetracyclines during tooth development has been associated with permanent discoloration of the teeth. Do not use in pregnant or lactating bitches. The use of the product in breeding dogs has not been evaluated. This product is not intended for use in oronasal fistulas, periapical abscesses, or severely compromised teeth.
10. UNDESIRABLE EFFECTS

None known

11. WITHDRAWAL PERIOD

Not applicable

12. SPECIAL STORAGE CONDITIONS, IF ANY

Store at 2°C -8°C. Reconstituted product not used on the day of mixing should be stored at room temperature (≤25°C) in the resealable foil pouch and used within 3 days of mixing. Ten additional exchanges between syringes should be performed if reconstituted product has been stored.

13. SPECIAL WARNING(S), IF NECESSARY

Wash hands thoroughly after use.

As there is sustained release of doxycycline into the gingival crevicular fluid and saliva, dog owners sensitive to topically applied tetracyclines should avoid contact with saliva from treated dogs.

Interactions: As doxycycline can bind with zinc, concurrent use of products containing zinc (e.g., chlorhexidine solutions formulated with zinc gluconate) is not recommended.

14. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED VETERINARY MEDICINAL PRODUCT OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

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

15. DATE ON WHICH THE PACKAGE INSERT WAS LAST REVISED

16. OTHER INFORMATION