ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cefenidex CA/DEX 2 mg/ml + 1 mg/ml eye drops, solution for dogs and cats (DE, HU, EL)
Cefenidex 2 mg/ml + 1 mg/ml eye drops, solution for dogs and cats (FR, IT, ES, PT, EE, LT, LV, DK, NO, SE, FI)
Cepfenidex 2 mg/ml + 1 mg/ml eye drops, solution for dogs and cats (AT, BE, IE, UK(NI), PL, NL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains:

Active substances:
Chloramphenicol: 2.0 mg
Dexamethasone: 1.0 mg
(equivalent to dexamethasone sodium phosphate: 1.32 mg)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzalkonium chloride	0.040 mg
Boric acid	
Borax	
Disodium edetate	
Polysorbate 20	
Water for injections	

Clear, colourless to slightly yellowish solution.

3. CLINICAL INFORMATION

3.1 Target species

Dog and cat

3.2 Indications for use for each target species

Treatment of inflammatory and allergic eye diseases such as conjunctivitis, keratitis, mild iritis and inflammation of the lacrimal sac associated with bacterial infections.

3.3 Contraindications

Do not use in cases of:
- hypersensitivity to the active substance or to any of the excipients;
- viral and fungal infections of the eye;
- corneal ulcers and corneal perforations.

3.4 Special warnings

Before starting treatment, it should be ensured that there are no mechanical or physical causes for the eye inflammation e.g. ectopic eyelash, entropion (inverted eyelids), foreign body, deficiency in tear secretion.
Cross-resistance has been shown between chloramphenicol and others phenicols. Use of the product should be carefully considered when susceptibility testing has shown resistance to phenicols because its effectiveness may be reduced.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Local application of glucocorticoids delays the healing of corneal injuries. Before starting treatment, it should be ensured that there are no corneal ulcers or mechanical causes of the eye inflammation.
Because of the possible systemic effects of corticosteroids and effects on cornea, a long-term use of the veterinary product is not recommended.
Long-term (several months) use of glucocorticoids makes the cornea susceptible to ulceration and can cause corneal and lens opacification.

Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Dexamethasone, chloramphenicol and benzalkonium chloride can cause allergic reactions. People with known hypersensitivity to dexamethasone, chloramphenicol and/or benzalkonium chloride should only administer the veterinary medicinal product with disposable gloves.
In humans, there is evidence that exposure to chloramphenicol may increase the risk of severe aplastic anaemia.
It is therefore essential to avoid skin and eye contact and wash hands after administration of the veterinary medicinal product. In case of accidental skin or eye contact, flush with plenty of water. In the event of hypersensitivity reactions, seek medical advice and show the package leaflet or the label to the physician.
Dexamethasone and chloramphenicol may cause serious harm to the unborn child and children who are breastfed. The veterinary medicinal product should therefore not be administered by pregnant and breastfeeding women.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dog and cat:

Rare (1 to 10 animals / 10,000 animals treated):	Allergic reaction, Corneal opacity[1]
Undetermined frequency (cannot be estimated from the available data)	Ocular burn[2], Increased intra-ocular pressure[3], Glaucoma[3], Cataract[3], Exopthalmia[3]

[1]superficial, temporarily
[2]when the drops are administered, temporarily.

[3]can occur after several weeks of treatment with dexamethasone. A glucocorticoid-induced increase in intraocular pressure is usually observed within the first 2 weeks after initiation of therapy.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Glucocorticoids and chloramphenicol can cross the placenta and pass into milk. The use is not recommended during pregnancy. Effects on suckling puppies and kittens are unlikely. Use only according to the benefit-risk assessment by the responsible veterinarian in lactating animals.

3.8 Interaction with other medicinal products and other forms of interaction

No data available.

3.9 Administration routes and dosage

Ocular use.
Put one drop (one drop contains 0.06 mg chloramphenicol and 0.03 mg dexamethasone) in the conjunctival sac of the affected eye, if necessary in both eyes; initially 6-8 times a day, then 4-6 times a day. Severe eye disease may require more frequent dosing (one drop every 1-2 hours) for the first 24-48 hours.
The veterinary medicinal product should only be used until the inflammatory symptoms have subsided. Subsequently, treatment should be continued with a monopreparation containing an antibiotic.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

In case of overdose, treatment should be discontinued and eyes should be flushed with water if irritation persists.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QS01CA01

4.2 Pharmacodynamics

Dexamethasone is a synthetic fluorinated glucocorticoid. Compared to hydrocortisone, its anti-inflammatory effectiveness is 25-30 times stronger. Dexamethasone has no noticeable mineralocorticoid effect. Glucocorticoid receptors are located in the cytoplasm of the target cells. Glucocorticoids have an antiallergic, anti-inflammatory and immunosuppressive effect. They prevent edema, fibrin coagulation, leukocyte migration, phagocytosis, collagen formation and proliferation of capillaries and fibroblasts. They also delay regeneration and repair in the epithelium and endothelium.

Chloramphenicol is a broad-spectrum antibiotic whose spectrum of activity includes gram-positive and gram-negative aerobic and anaerobic bacteria as well as chlamydia and mycoplasma. Chloramphenicol binds to the 50S subunit of the bacterial ribosome and prevents transpeptidation during bacterial protein synthesis. The action of chloramphenicol is primarily bacteriostatic. Chloramphenicol shows no significant activity against Pseudomonas aeruginosa.

The most commonly reported mechanism of resistance for chloramphenicol is enzymatic inactivation by chloramphenicol acetyltransferases (CATs). Acetylation prevents chloramphenicol from binding to the 50S subunit of the bacterial ribosome. Genes encoding CAT are often located on mobile elements such as plasmids, transposons or gene cassettes.
Several other resistance mechanisms through efflux systems, inactivating phosphotransferases and mutations in target sites are described.
There is cross-resistance between substances of the phenicol class. For instance, in gram-negative bacteria the *flo*R gene located on a plasmid promotes efflux of chloramphenicol and florfenicol. In gram-positive cocci, *fex*A has been found which encodes an efflux pump conferring resistance to florfenicol and chloramphenicol.
Additionally, a multi-resistance gene cfr has been identified that can be located on plasmids or transposons which confers resistance by the rRNA methyltransferase to pleuromutilins, oxazolidinones, phenicols, streptogramin A, and lincosamides.

4.3 Pharmacokinetics

Dexamethasone and chloramphenicol are fat-soluble substances. When applied topically, it is well absorbed into the mucous membrane and the aqueous humor. In the anterior segment of the eye, therapeutic concentrations of dexamethasone and chloramphenicol are achieved by topical application of the drops to the eye(s).
Topical application is not sufficient for treating the posterior segment of the eye.
Some of the medicinal substance topically administered into the eye may also be absorbed into the systemic circulation from the tear ducts, nasal mucosa, nasopharynx and alimentary tract, albeit measurable systemic concentrations have not been observed in connection with topical use.
Chloramphenicol is metabolized in the liver to inactive glucuronide and excreted primarily (80-90%) in the urine in humans. The elimination half-life in plasma is 2-4 hours.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Keep the container in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Colourless LDPE dropper container, and a white HDPE screw cap.

Pack size:
Cardboard box with 1x10 ml dropper container.

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

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.
Medicines should not be disposed of via wastewater or household waste.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

CP-Pharma Handelsgesellschaft mbH

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

MM/YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cefenidex CA/DEX 2 mg/ml + 1 mg/ml eye drops, solution

2. STATEMENT OF ACTIVE SUBSTANCES

Each mL contains:
Chloramphenicol: 2.0 mg
Dexamethasone: 1.0 mg
(equivalent to dexamethasone sodium phosphate: 1.32 mg)

3. PACKAGE SIZE

10 mL

4. TARGET SPECIES

Dog and cat

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Ocular use.
Eye drops

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. mm/yyyy

Once broached, use within 28 days – use by: _____.

9. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator.
Keep the container in the outer carton in order to protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

CP-Pharma Handelsgesellschaft mbH

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cefenidex

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Chloramphenicol 2.0 mg/ml
Dexamethasone 1.0 mg/ml
(equivalent to dexamethasone sodium phosphate: 1.32 mg)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 28 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Cefenidex CA/DEX 2 mg/ml + 1 mg/ml eye drops, solution for dogs and cats (DE, HU, EL)
Cefenidex 2 mg/ml + 1 mg/ml eye drops, solution for dogs and cats (FR, IT, ES, PT, EE, LT, LV, DK, NO, SE, FI)
Cepfenidex 2 mg/ml + 1 mg/ml eye drops, solution for dogs and cats (AT, BE, IE, UK(NI), PL, NL)

2. Composition

Each mL contains:

Active substances:
Chloramphenicol: 2.0 mg
Dexamethasone: 1.0 mg
(equivalent to dexamethasone sodium phosphate: 1.32 mg)

Excipient:
Benzalkonium chloride: 0.040 mg

Clear, colourless to slightly yellowish solution.

3. Target species

Dog and cat

4. Indications for use

Treatment of inflammatory and allergic eye diseases such as conjunctivitis, keratitis, mild iritis and inflammation of the lacrimal sac associated with bacterial infections.

5. Contraindications

Do not use in cases of:
- hypersensitivity to the active substance or to any of the excipients;
- viral and fungal infections of the eye;
- corneal ulcers and corneal perforations.

6. Special warnings

Special warnings:
Before starting treatment, it should be ensured that there are no mechanical or physical causes for the eye inflammation e.g. ectopic eyelash, entropion (inverted eyelids), foreign body, deficiency in tear secretion.
Cross-resistance has been shown between chloramphenicol and others phenicols. Use of the product should be carefully considered when susceptibility testing has shown resistance to phenicols because its effectiveness may be reduced.

Special precautions for safe use in the target species:

Local application of glucocorticoids delays the healing of corneal injuries. Before starting treatment, it should be ensured that there are no corneal ulcers or mechanical causes of the eye inflammation.
Because of the possible systemic effects of corticosteroids, and effects on cornea, a long-term use of the veterinary product is not recommended.
Long-term (several months) use of glucocorticoids makes the cornea susceptible to ulceration and can cause corneal and lens opacification.

Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Dexamethasone, chloramphenicol and benzalkonium chloride can cause allergic reactions. People with known hypersensitivity to dexamethasone, chloramphenicol and/or benzalkonium chloride should only administer the veterinary medicinal product with disposable gloves.
In humans, there is evidence that exposure to chloramphenicol may increase the risk of severe aplastic anaemia.
It is therefore essential to avoid skin and eye contact and wash hands after administration of the veterinary medicinal product. In case of accidental skin or eye contact, flush with plenty of water. In the event of hypersensitivity reactions, seek medical advice and show the package leaflet or the label to the physician.
Dexamethasone and chloramphenicol may cause serious harm to the unborn child and children who are breastfed. The veterinary medicinal product should therefore not be administered by pregnant and breastfeeding women.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Glucocorticoids and chloramphenicol can cross the placenta and pass into milk. The use is not recommended during pregnancy. Effects on suckling puppies and kittens are unlikely. Use only according to the benefit-risk assessment by the responsible veterinarian in lactating animals.

Interaction with other medicinal products and other forms of interaction:
No data available.

Overdose:
In case of overdose, treatment should be discontinued, and eyes should be flushed with water if irritation persists.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Dog and cat:

Rare (1 to 10 animals / 10,000 animals treated):	Allergic reaction, Corneal opacity[1]

Undetermined frequency (cannot be estimated from the available data)	Ocular burn[2], Increased intra-ocular pressure[3] Glaucoma[3], Cataract[3], Exopthalmia[3]

[1]superficial, temporarily
[2]when the drops are administered, temporarily.
[3]can occur after several weeks of treatment with dexamethasone. A glucocorticoid-induced increase in intraocular pressure is usually observed within the first 2 weeks after initiation of therapy.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

Ocular use.
Put one drop (one drop contains 0.06 mg chloramphenicol and 0.03 mg dexamethasone) in the conjunctival sac of the affected eye, if necessary in both eyes; initially 6-8 times a day, then 4-6 times a day. Severe eye disease may require more frequent dosing (one drop every 1-2 hours) for the first 24-48 hours. The veterinary medicinal product should only be used until the inflammatory symptoms have subsided. Subsequently, treatment should be continued with a monopreparation containing an antibiotic.

9. Advice on correct administration

See section: “Dosage for each species, routes and method of administration”

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Store in a refrigerator (2°C – 8°C).
Keep the container in the outer carton in order to protect from light.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after "Exp.". The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Cardboard box with 1x 10 ml dropper container.

15. Date on which the package leaflet was last revised

MM/YYYY

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release:
CP-Pharma Handelsgesellschaft mbH
Ostlandring 13
31303 Burgdorf

Local representatives and contact details to report suspected adverse reactions:

{To be completed nationally.}

17. Other information