1. NAME OF THE VETERINARY MEDICINAL PRODUCT

UpCard 0.75 mg tablets for dogs
UpCard 3 mg tablets for dogs
UpCard 7.5 mg tablets for dogs
UpCard 18 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

UpCard 0.75 mg tablets
Torasemide 0.75 mg

UpCard 3 mg tablets
Torasemide 3 mg

UpCard 7.5 mg tablets
Torasemide 7.5 mg

UpCard 18 mg tablets
Torasemide 18 mg

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate
Povidone
Sodium laurilsulfate
Crospovidone
Microcrystalline cellulose
Sodium stearyl fumarate
Bacon flavour

UpCard 0.75 mg tablets: oblong white to off-white tablets with 1 break-line on each side. The tablets can be divided into equal halves.

UpCard 3 mg, 7.5 mg and 18 mg tablets: oblong white to off-white tablets with 3 break-lines on each side. The tablets can be divided into equal quarters.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For treatment of clinical signs, including oedema and effusion, related to congestive heart failure.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in cases of renal failure.
Do not use in cases of severe dehydration, hypovolaemia or hypotension.
Do not use concomitantly with other loop diuretics.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In dogs presenting in acute crisis with pulmonary oedema, pleural effusion and/or ascites requiring emergency treatment, the use of injectable drugs should be considered first before commencing oral diuretic therapy.

Renal function, hydration status and serum electrolytes status should be monitored:
- at treatment initiation
- from 24 hours to 48 hours after treatment initiation
- from 24 hours to 48 hours after dose change
- in case of adverse events.

While the animal is on treatment, these parameters should be monitored at very regular intervals according to the benefit-risk assessment performed by the responsible veterinarian (see sections 3.3 and 3.6 of the SPC).

Torasemide should be used with caution in cases of diabetes mellitus, and in dogs with previously prescribed high doses of an alternative loop diuretic. In dogs with pre-existing electrolyte and/or water imbalance, this should be corrected prior to treatment with torasemide.

Torasemide treatment should not be initiated in dogs already clinically stable on an alternative diuretic for treatment of the signs of congestive heart failure, except where this has been justified taking into account the risk of de-stabilising the clinical condition and of adverse reactions as indicated in section 3.6.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to torasemide or other sulphonamides should administer the veterinary medicinal product with caution.

This veterinary medicinal product may cause increased urination and/or gastrointestinal disturbances if ingested.

Keep tablets in the blister packs until required and keep the blisters in the outer carton.

In case of accidental ingestion, particularly in the case of children, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Elevated renal parameters, Renal insufficiency Haemoconcentration, Polyuria, Polydipsia
Rare (1 to 10 animals / 10,000 animals treated):	Soft stool[2]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Electrolyte disorder[1] (e.g. hypokalaemia, hypochloraemia, hypomagnesaemia) Dehydration[1] Digestive tract disorders (e.g. emesis, constipation, reduced faecal output) Pinnal erythema[3]

[1] In cases of prolonged treatment
[2] Transient, mild, and does not necessitate the withdrawal of the treatment
[3] Inner

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

The safety of the veterinary medicinal product has not been established during pregnancy or lactation in dogs.

The use is not recommended during pregnancy, lactation and in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

Co-administration of loop diuretics and non-steroidal anti-inflammatory drugs (NSAIDs) can result in a decreased natriuretic response.

Concomitant use with veterinary medicinal products affecting electrolyte balance (corticosteroids, amphotericin B, cardiac glycosides, other diuretics) requires careful monitoring.

Concurrent use of veterinary medicinal products that increase the risk of renal injury or renal insufficiency should be avoided. Concomitant use with aminoglycosides or cephalosporins may increase the risk of nephrotoxicity and ototoxicity.

Torasemide may increase the risk of sulfonamide allergy.

Torasemide can reduce the renal excretion of salicylates, leading to an increased risk of toxicity. Care should be exercised when administering torasemide with other highly plasma protein-bound drugs. Since protein binding facilitates the renal secretion of torasemide, a decrease in binding due to displacement by another drug may be a cause of diuretic resistance.

Concomitant administration of torasemide with other veterinary medicinal products metabolised by cytochrome P450 isoforms such as 3A4 (e.g. enalapril, buprenorphine, doxycycline, cyclosporine) and 2E1 (isoflurane, sevoflurane, theophylline) may decrease their clearance from the systemic circulation.

The effect of antihypertensive medicinal products, especially angiotensin-converting enzyme (ACE) inhibitors, may be potentiated when co-administered with torasemide.

When used in combination with cardiac treatments (e.g. ACE-inhibitors, digoxin), the dose regimen may need to be modified depending upon the animal's response to therapy.

3.9 Administration routes and dosage

Oral use.

This veterinary medicinal product can be administered with or without food.

The recommended dose of torasemide is 0.1 to 0.6 mg/kg bodyweight, once daily. The majority of dogs are stabilised at a dose of torasemide less than or equal to 0.3 mg/kg bodyweight, once daily. The dosage should be titrated to maintain patient comfort with attention to renal function and electrolyte status. If the level of diuresis requires alteration, the dose may be increased or decreased within the recommended dose range by increments of 0.1 mg/kg bodyweight. Once signs of congestive heart failure have been controlled and the patient is stable, if long term diuretic therapy with this product is required it should be continued at the lowest effective dose.

Frequent re-examinations of the dog will enhance the establishment of an appropriate diuretic dose.

The daily schedule of administration can be timed to control the period of micturition according to need.

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

Doses greater than 0.8 mg/kg/day have not been evaluated in the target animal safety or controlled clinical studies. However, it is anticipated that overdose increases the risk of dehydration, electrolyte imbalance, renal insufficiency, anorexia, weight loss and cardiovascular collapse. Treatment should be symptomatic.

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:
QC03CA04.

4.2 Pharmacodynamics

Torasemide is a loop diuretic of the pyridyl sulfonylurea class. Torasemide is secreted into the tubule lumen via the probenecid-sensitive organic acid transport system. The main site of action is the medullary portion of the ascending limb of the loop of Henle. Loop diuretics mainly inhibit the $Na^+/2Cl^-/K^+$carrier from the luminal side of the cell.

Inhibition of sodium and chloride ion reabsorption not only results in saluresis but also in a decrease in interstitial osmolarity within the renal medulla. This in turn decreases free water reabsorption resulting in increased water excretion/urine production.
In healthy dogs and after once daily administration for 5 days, the mean percentage of increase in excreted urine over 24 hours ranged between 33% and 50% at 0.15 mg/kg, between 181% and 328%

at 0.4 mg/kg and between 264% and 418% at 0.75 mg/kg.

Based on a pharmacodynamics modelling study conducted in healthy dogs at doses of 0.1 and 0.6 mg torasemide/kg, a single dose of torasemide had approximately 20 times the diuretic effect of a single dose of furosemide. Refer to section 3.5.

4.3. Pharmacokinetics

In dogs, after a single intravenous dose of 0.1 mg/kg, the total body clearance was 0.017 L/h·kg, the volume of distribution was 0.14 L/kg and the terminal half-life was 7.0 hours. After a single oral dose of 0.1 mg/kg, the oral absolute bioavailability corresponded to about 90%. The oral absorption was fast with mean T_{max} at 0.93 hours after administration of 0.1 mg/kg. The maximum plasma concentrations C_{max} corresponded to 1.1 mcg/mL after a single oral dose of 0.1 mg/kg and to 19 mcg/mL after a single oral dose of 1.6 mg/kg. The AUC_{inf} corresponded to 6.3 mcg·h/mL after a single oral dose of 0.1mg/kg and to 153.6 mcg·h/mL after a single oral dose of 1.6 mg/kg. The plasma protein binding was > 98%. A large proportion of the dose (between 61% and 70%) is excreted in the urine as unchanged parent drug. Two metabolites (a dealkylated and a hydroxylated metabolite) were also identified in urine. The parent drug is metabolised by the hepatic cytochrome P450 family isoforms 3A4 and 2E1, and to a lesser extent by 2C9. Dose proportionality for C_{max} and AUC_{inf} was demonstrated between 0.2 and 1.6 mg/kg.

Feeding significantly increased torasemide AUC_{last} by 36% on average and slightly delayed T_{max} but no significant impact on C_{max} was detected. After repeated administration to dogs at 0.2 mg/kg daily for 14 days, no plasma accumulation of torasemide was detected.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Any remaining tablet part should be discarded after 7 days.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Any part tablet should be stored in the blister pack or in a closed container for a maximum of 7 days.

5.4 Nature and composition of immediate packaging

Polychlorotrifluoroethylene-PVC/aluminium blister pack.

Pack sizes:

Cardboard box containing 30 or 100 tablets. Each blister pack contains 10 tablets.

Not all pack sizes may be marketed.

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

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 national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetoquinol SA

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/15/184/001–008

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 31/07/2015

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

{DD/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*).