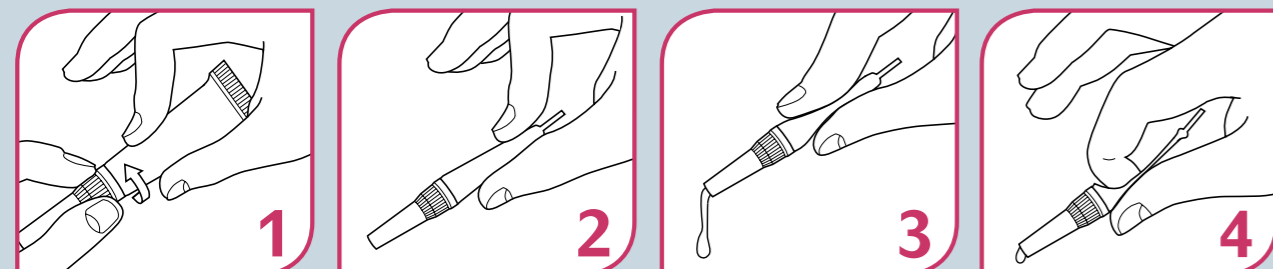


Take back control of your canine otitis externa cases

Innovative Gel Formulation:

- Colourless gel squeezes out of the tube and the lipophilic formulation spreads through the ear canal
- This then dissolves into the ear wax and is slowly eliminated from the ear.¹ Therapeutic concentrations in the ear canals are therefore achieved and maintained²
- Harder for dogs to shake out of their ears meaning less mess, and drives enhanced compliance

Clean the ear just once



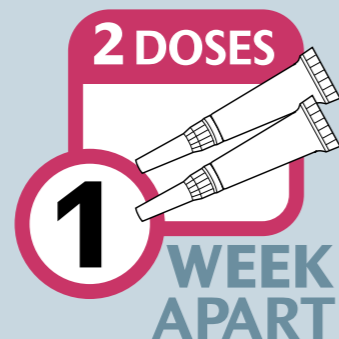
1. Open the tube till you hear a 'click' by twisting the soft tip.

2. Place the tube between the thumb and index finger of your dominant hand. Make sure your fingers cover the length of the tube.

3. To empty the tube, squeeze it once with a continuous back to front motion down the length of the tube.

4. The tube is empty when your fingertips are compressing the front end of the tube, just below the tip.

1 week later apply second dose



Get it right first time

Elanco

Best New Veterinary Product of 2015 as Voted by Vets**

Elanco

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT
OSURNIA ear gel for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:
1 dose (1.2 g) contains:
Terbinafine: 10 mg
Florfenicol: 10 mg
Betamethasone acetate: 1 mg
equivalent to Betamethasone base 0.9 mg

Excipient:
Butylhydroxytoluene (E321): 1 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ear gel.
Off-white to slightly yellow translucent gel.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of acute otitis externa and acute exacerbation of recurrent otitis externa associated with *Staphylococcus pseudintermedius* and *Malassezia pachydermatis*.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substances, to other corticosteroids or to any of the excipients.
Do not use if the eardrum is perforated.
Do not use in dogs with generalised demodicosis.
Do not use in pregnant or breeding animals.

4.4 Special warnings for each target species

Bacterial and fungal otitis is often secondary to other conditions. Appropriate diagnosis should be used and therapy of causative conditions should be investigated before antimicrobial treatment is considered.

Clean the ears before the initial treatment is applied. Ear cleaning should not be repeated until 21 days after the second administration. In clinical trials, saline only was used for ear cleaning.

Transient wetness of the inner and outer pinna can be observed. This observation is attributed to presence of product and is not of clinical concern.

4.5 Special precautions for use

Special precautions for use in animals

If hypersensitivity to any of the components occurs, the ear should be thoroughly washed.

The safety of the product has not been established in dogs less than 2 months of age or weighing less than 1.4 kg.

Whenever possible the use of the veterinary medicinal product should be based on identification of infecting organisms and susceptibility testing.

Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to florfenicol and fungi resistant to terbinafine and may decrease the effectiveness of treatment with other antibiotics and antifungal agents.

In case of parasitic otitis, an appropriate acaricidal treatment should be implemented.

Before the veterinary medicinal product is applied, the external auditory canal must be examined thoroughly to ensure that the ear drum is not perforated. Prolonged and intensive use of topical corticosteroids preparation is known to trigger systemic effects, including suppression of adrenal function. (see section 4.10).

Decreased cortisol levels were observed after product instillation in tolerance studies (before and after ACTH stimulation), indicating that betamethasone is absorbed and enters the systemic circulation. The finding was not correlated with pathological or clinical signs and was reversible.

Additional corticosteroid treatments should be avoided.
Use with precaution in dogs with suspected or confirmed endocrine disorder (e.g. diabetes mellitus; hypo- or hyper-thyroid disease, etc.).

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

In case of accidental eye contact, rinse thoroughly with water.
In case of accidental skin contact wash exposed skin thoroughly with water.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

No adverse reactions that could be related to the veterinary medicinal product were observed in dogs with otitis externa under field conditions when administered as indicated in section 4.9.

4.7 Use during pregnancy, lactation or lay

Betamethasone is known to be teratogenic in laboratory species. The safety of the veterinary medicinal product has not been established in pregnant and lactating bitches; therefore, the product should not be used during pregnancy and lactation.

4.8 Fertility

Do not use in breeding animals.

4.9 Interaction with other medicinal products and other forms of interaction

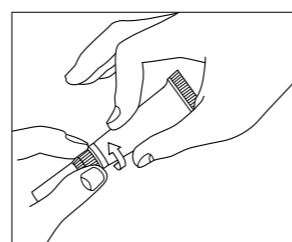
Compatibility with ear cleaners, other than saline, has not been demonstrated.

4.9 Amounts to be administered and administration route

Auricular use.
Administer one tube per infected ear. Repeat the administration after 7 days. The maximum clinical response may not be seen until 21 days after the second administration.

Instructions for proper use:

It is recommended to clean and dry the external ear canal before the first administration of the product. It is recommended not to repeat ear cleaning until 21 days after the second administration of the product. If treatment with this product is discontinued, the ear canals should be cleaned before treatment with an alternative product is initiated.



1. Open the tube by twisting the soft tip.
2. Introduce the flexible soft tip into the ear canal.
3. Apply the product into the ear canal by pressing it between two fingers.
4. After application, the base of the ear may be massaged briefly and gently to facilitate even distribution of the veterinary medicinal product into the ear canal. Keep out of the sight and reach of children.

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

Auricular administration of five times the recommended dose, one week apart, for 5 consecutive weeks (a total six administrations of 5 tubes per ear or 10 tubes per dog) to mixed breed dogs weighing 10 to 14 kg resulted in clinical signs of wetness of the inner and outer pinna (attributed to presence of the product). There were no clinical signs associated with unilateral vesicle formation within the epithelium of the tympanic membrane (also observed after six administrations, one week apart, of 1 tube per ear or 2 tubes per dog), unilateral mucosal ulceration in the lining of the middle ear cavity, or decrease in serum cortisol response below normal reference range in ACTH stimulation testing. The decreased adrenal and thymus weights accompanied by atrophy of the adrenal cortex and lymphoid depletion of the thymus correlated with the decreased cortisol levels, and were consistent with the pharmacologic effects of betamethasone. These findings are considered reversible. Reversibility of the epithelial tympanic membrane blistering is also likely through epithelial migration, a natural self-cleaning and self-repair mechanism for the tympanic membrane and ear canal. Additionally, dogs showed slightly elevated red blood cell count, haematocrit, total protein, albumin and alanine aminotransferase. These findings were not associated with clinical signs.

4.11 Withdrawal period(s)
Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Otiologics – Corticosteroids and anti-infectives in combination.
ATC-vet code: QS02CA90.

5.1 Pharmacodynamic properties

The veterinary medicinal product is a fixed combination of three active substances (corticosteroid, antifungal and antibiotic).
Betamethasone acetate belongs to the diesters class of the glucocorticosteroids with a potent intrinsic glucocorticoid activity which relieves both inflammation and pruritus leading to an improvement of clinical signs observed in otitis externa.

Terbinafine is an allylamine with a pronounced fungicidal activity. It selectively inhibits the early synthesis of ergosterol, which is an essential component of the

membrane of yeasts and fungi including *Malassezia pachydermatis* (MIC₅₀ of 2 µg/ml). Terbinafine has a different mode of action than azole antifungals, therefore there is no cross resistance with azole antifungals.

Florfenicol is a bacteriostatic antibiotic which acts by inhibiting protein synthesis. Its spectrum of activity includes Gram-positive and Gram-negative bacteria including *Staphylococcus pseudintermedius* (MIC₅₀ of 8 µg/ml). Due to the high antimicrobial concentrations achieved in the ear canal and the multifactorial nature of otitis externa, *in vitro* susceptibility may not be directly correlated with clinical success.

5.2 Pharmacokinetic particulars

The formulation dissolves in ear wax and is slowly eliminated from the ear mechanically.
Systemic absorption of all active substances was determined in multiple-dose studies after placing the veterinary medicinal product into both ear canals of healthy mixed breed dogs. Absorption occurred primarily during the first two to four days after administration, with low plasma concentrations (1 to 42 ng/ml) of active substances.

The extent of percutaneous absorption of topical medications is determined by many factors including the integrity of the epidermal barrier. Inflammation can increase the percutaneous absorption of veterinary medicinal products.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E 321)
Hypromellose
Locthin
Oleic acid
Propylene carbonate
Glycerol formal

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).

6.5 Nature and composition of immediate packaging

Single-use multi-layered aluminium and polyethylene tube with a polypropylene thermoplastic elastomer tip.
Cardboard box containing 2, 12, 20 or 40 tubes (each containing 2.05 g).
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

Elanco Europe Ltd,
Lilly House, Priestley Road
Basingstoke
RG24 9NL
UNITED KINGDOM

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/14/170/0001 (2 tubes)
EU/2/14/170/0002 (12 tubes)
EU/2/14/170/0003 (20 tubes)
EU/2/14/170/0004 (40 tubes)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31/07/2014

10 DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

Osurnia

¹For the treatment of acute otitis externa and acute exacerbation of recurrent otitis externa associated with *Staphylococcus pseudintermedius* and *Malassezia pachydermatis*

²Online survey conducted on 290 small animal vets in March 2016, conducted by CM Research

³Over 20% of owners have difficulty complying with once daily dosing and 80% of owners have difficulty complying with twice daily dosing

References 1. EU Pivotal Study, INT-11-011 2. Nuttal and Forster Abstract BVDSG Spring Meeting 2015 3. ANGUS J.C.: Otic cytology in health and disease. Vet. Clin. Small. Anim., 2004, 34, 411-424. 4. Veterinary Practice News 2015.04.15 12:24 PM VPI Reveals Top 10 Pet Disorders. 5. Gauging interest in a new otitis externa treatment – quantitative result, Kadence International, September 2013. 6. Oliveira L. et al. Comparative study of the microbial profile from bilateral canine otitis externa. Can Vet J 2008;49:785-788.

Osurnia ear gel for dogs contains terbinafine, florfenicol and betamethasone acetate. Legal category [POM.V] UK [POM] IE. Information regarding the side effects, precautions, warnings and contra-indications can be found in product packaging and leaflets; further information can also be found in the Summary of Product Characteristics. For further information call Elanco Animal Health on +44 (0)1256 353131 or write to Elanco Animal Health, Lilly House, Priestley Road, Basingstoke, Hampshire, RG24 9NL. Use medicines responsibly www.roah.co.uk/responsible. Osurnia is a registered trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates. 2016; UKCACOSJ00094

Osurnia

Otitis externa is a common challenge for vets and pet owners

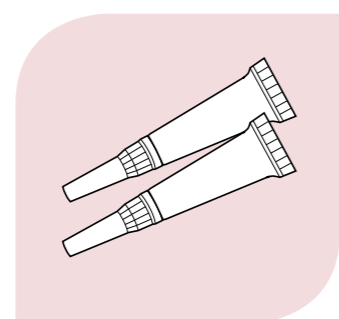
- Ear infections are among the **ten most frequent reasons** for dogs to be presented to vets, affecting up to 20% of dogs^{3,4}
- Vets consider poor treatment compliance by pet owners as the most challenging aspect of managing otitis externa cases⁵

Up to **80%†** of owners administer the **incorrect dose of ear product to their pet.**

Up to 28 applications vs 2
What would pet owners choose?



2 weeks of twice daily ear medications



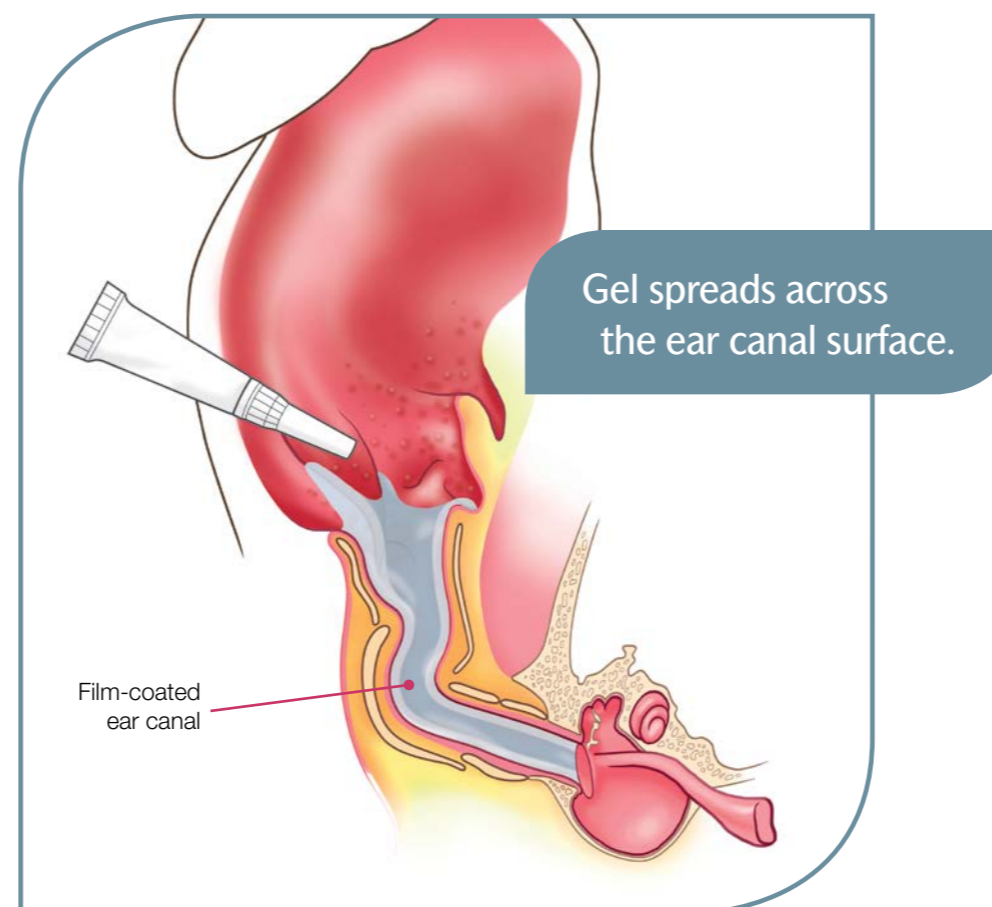
Osrurnia

Osrurnia

Treating Otitis Externa* just got easier!

Osrurnia is **easy to use** and supports **maximum compliance ... done!**

- With just **2 doses, 1 week apart**, you can take control of canine otitis externa treatment and help improve the clinical outcome
- Innovative adaptable gel formulation enabling optimal distribution through the ear canal and less mess



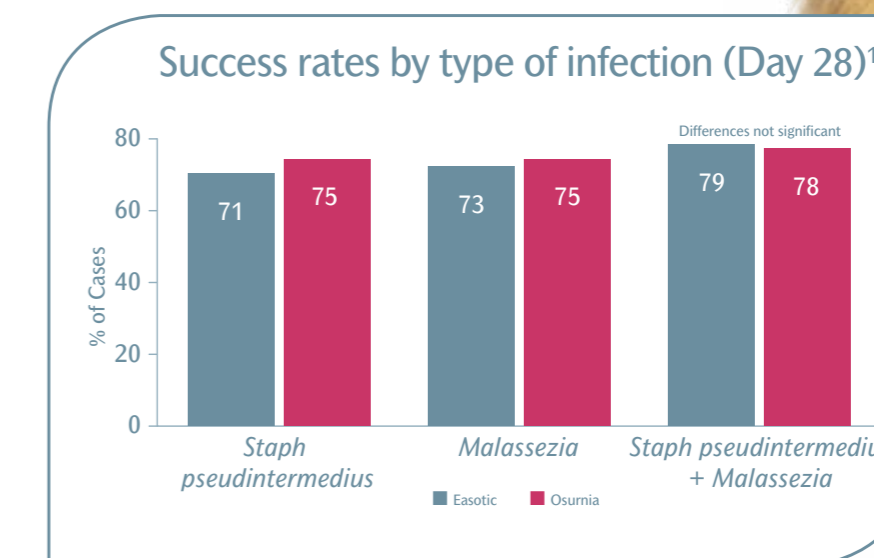
- Same dose for any dog, regardless of their size and weight
- Pre-measured, single-use tubes for the right dose every time

A **first line treatment** that you can prescribe with confidence for your Otitis Externa* cases ... **done!**

- Osrurnia is a unique sustained release gel:

<p>Antibacterial</p> <p>Contains florfenicol</p> <ul style="list-style-type: none"> • 1st line spectrum of activity 	<p>Antifungal</p> <p>Contains terbinafine</p> <ul style="list-style-type: none"> • Effective against <i>Malassezia</i> spp. 	<p>Anti-inflammatory</p> <p>Contains betamethasone acetate</p> <ul style="list-style-type: none"> • Helps to relieve discomfort
--	--	--

- Field trials prove that just 2 doses of Osrurnia treats otitis externa effectively



The most common pathogens associated with otitis are *Staphylococcus pseudintermedius* and *Malassezia pachydermatis*⁶

Comfortable dogs and peace of mind for owners brought through innovation ... done!

- Flexible soft tip gentle for a dog's ears that makes otitis externa treatment a comfortable experience for the dog
- You take control of treatment and remove product administration from the owners' hands making everybody's life easier

For more comfortable dogs and happier owners, choose enhanced compliance with Osrurnia