

Otodine®



Otodine®

(Tris-EDTA – Chlorhexidine 0.15%)
for bacterial otitis in dogs



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Otodine®

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Properties

Otodine®, is a new concept in otological solutions: it combines two molecules (chlorhexidine digluconate 0.15% and Tris-EDTA)¹, both effective against bacteria. In particular, the association has a synergic effect: the efficacy of chlorhexidine can be increased up to 100 times with a bactericide effect not only on Gram-positive (Staphylococcus and Streptococcus), but also and especially on Gram-negative bacteria (Escherichia, Pseudomonas and Proteus).

Additionally, chlorhexidine 0.20%, used in the ear canal with perforated tympanic membrane in dogs, did not induce cochlear or vestibular neurotoxicity².

TRIS-EDTA
+
chlorhexidine 0,15%

PCT/IT2004/000627

Chlorhexidine digluconate

Tris-EDTA has a synergic effect in association with antiseptics-disinfectants. In particular, chlorhexidine digluconate is the most indicated molecule for this association: it is not irritant and is not deactivated by organic debris. Chlorhexidine digluconate has bactericide action provided by acting on the bacterial cell membrane, causing the precipitation of the intracellular molecules, and the inhibition of ATP.



Chronic Purulent otitis caused by *Proteus mirabilis*



Notes

- 1 - EDTA increases the activity of chlorhexidine digluconate against bacteria
"The increased bactericide activity was obtained with the addition of a chelating agent (EDTA) and a buffer solution (Tris) which, at low concentrations of chlorhexidine (0.01%), are effective against *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis* and *Streptococcus faecalis*". Harper WE, 1983. Simple additives to increase the activity of chlorhexidine digluconate against urinary pathogens. *Paraplegia* Apr; 21 (2), 86-93
- 2 - Chlorhexidine digluconate 0.20%, is not ototoxic
Merchant SR, Neer TM, Tedford BL, et al. Ototoxicity assessment of a chlorhexidine otic preparation in dogs. Prog Vet Neurol 1993; 4_72-75



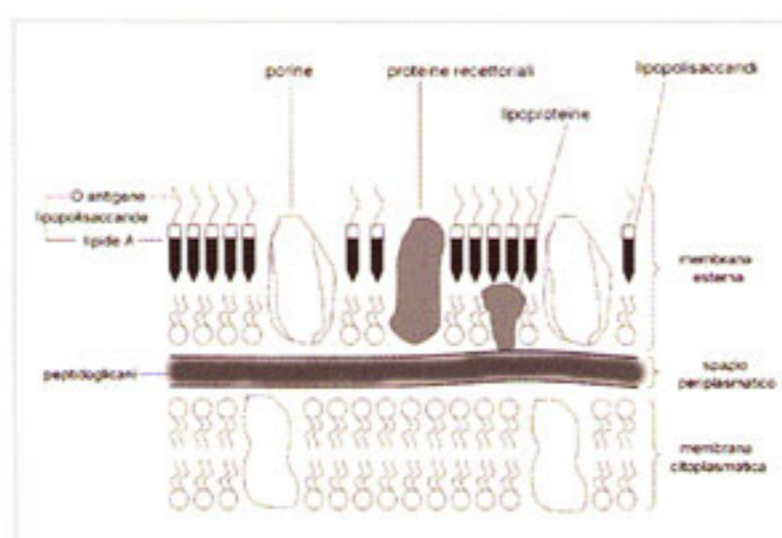
Tris EDTA

Ethylenediaminetetraacetic acid (EDTA) has a direct bactericide action against various bacteria. This action is due to its capacity³ to chelate metallic ions important for the integrity of the bacterial cell membrane; in addition, EDTA stimulates the release of proteins and lipopolysaccharides from the same cell membrane and activates autolysins, which destroy the bacterial cell. Buffer solutions containing tromethamine (Tris) have been used to increase the effectiveness of EDTA against *Pseudomonas aeruginosa*. For the best efficacy, it is important to buffer the EDTA solution to pH8 and compound it with tromethamine (Tris).

Recent studies have demonstrated that Tris-EDTA can reduce the minimum inhibitory concentration⁴ (MIC) of enrofloxacin against ciprofloxacin resistant *Pseudomonas aeruginosa*. Various in-vitro works have demonstrated the effectiveness of Tris-EDTA against Gram-negative bacteria (*P. aeruginosa*, *E. Coli*, *Proteus spp.*). Tris-EDTA has been demonstrated to be effective in cases of chronic bacterial otitis resistant to antibiotics⁵.

Cases of MRSA (Methicillin-resistant *Staphylococcus aureus*) have been reported in dogs. These bacteria have probably been selected by an excessive use of antibiotics and could be transferred between the owners and their animals. With its bactericide properties, Otodine can also be seen as an "antibiotic saver", and help in decreasing the use of antibiotics⁶.

Graphic representation of the cellular wall of Gram-negative bacteria



Note

3 - Action of Tris EDTA in potentiating the antibiotic activity

"Tris EDTA binds the metallic ions (Mg^{2+} , Ca^{2+}), which compete with the aminoglycosides for the cellular membrane receptors, these receptors allow the antibiotics to enter the bacteria." Sparks TA, Kemp DT, Wooley RE, Gibbs PS. Antimicrobial effect of combinations of EDTA-Tris and amikacin or neomycin on the microorganisms associated with otitis externa in dogs. *Vet Res Commun.* 1994 18(4):241-9

4 - Tris EDTA reduces MIC of enrofloxacin in resistant bacteria

Gotthelf L.N. Evaluation of the in vitro effect of Tris-EDTA on the minimum inhibitory concentration of enrofloxacin against ciprofloxacin resistant *Pseudomonas aeruginosa* Proceedings 19th Annual Congress of ESVD-ECVD, Tenerife 2003 145.

5 - Tris EDTA and antibiotic resistance

"When the same antibiotics (enrofloxacin, kanamycin and cefaloridine) are administered together with Tris-EDTA, the clinical signs (pain, edema, inflammation and purulent material) disappear in the span of a couple of weeks and in the culture examination, no bacterial growth is found." Farca AM; Promalli G; Re G.; Potentiation of antibiotic activity by EDTA-Tris on the activity of antibiotics against resistant bacteria associated with otitis, dermatitis and cystitis. *J Small Animal Practice*; 38: 243-5, 1997.

6 - Risk of abuse in the excessive use of antibiotics

"Staphylococcal pyoderma: an emerging problem" ?? KA, May E. *Compend Contin Educ Pract Vet.* 26 560-568.2004.



Otodine®

Clinical Study

Evaluation of the in vivo efficacy of a solution containing Tris-EDTA and chlorhexidine digluconate 0.15% (Otodine®) in chronic external bacterial otitis in dogs: 11 cases.

Ghibaudo G.; Comegliani L.; Martino P.: Poster at the 5th World Congress of Veterinary Dermatology Vienna 2004 Veterinary Dermatology 2004, 15 (Supplement 1), 65

Inclusion

11 dogs with chronic external bacterial otitis were included in the study:
 3 mixed breed, 3 German Shepherds
 2 Italian Bloodhounds, 1 English Setter
 1 Spinone, 1 Maremma Sheepdog
 6 spayed females, 5 intact males, 1 to 14 years old.

Protocol

Day 0

Evaluation of 3 clinical parameters:

- exudation, erythema, pain

Evaluation of 3 cytological parameters:

- malassezia, round-shaped bacteria, rod-shaped bacteria (scale 0-4)

Otoscopic examination

Culture.

Administration of **Otodine®** once daily for 2 weeks.

Day 14

Otoscopic examination

Cytological examination of the exudate

Culture

If not cured administration of **Otodine®** and after 10 minutes administration of injectable 2,5% enrofloxacin (1:4 in saline solution) daily for 2 weeks.

Day 28

Otoscopic examination

Cytological examination

Culture

if cured: ok

if not cured: exclusion from the study

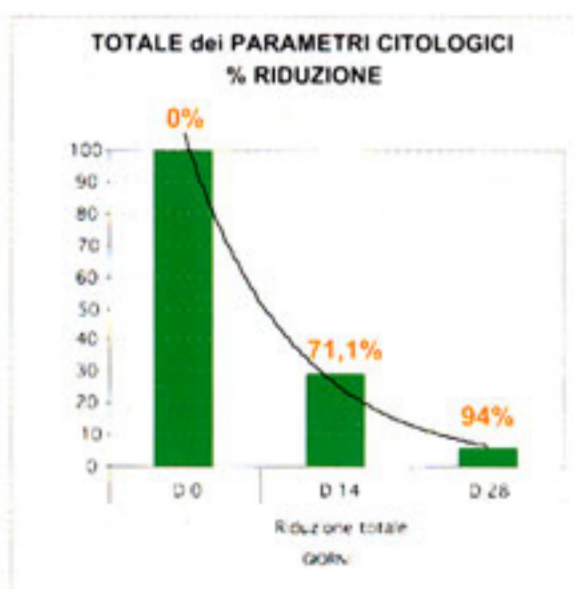
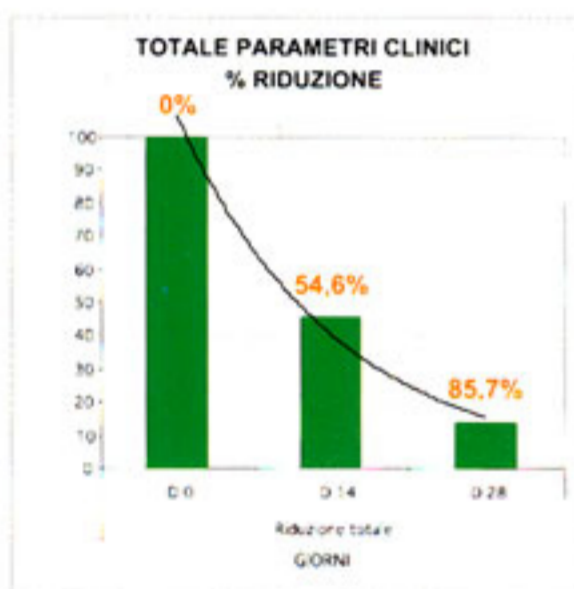
6 cases: *Proteus m.* and *Staphy intermedius*

2 cases: *Proteus m.*

1 case: *Proteus m.* *Klebsiella spp.*

1 case: *Pseudomonas aeruginosa*

1 case: *Pseudomonas & Streptoc. beta-lyticus*



Results

10/11 cured
 6/11 cured at Day 14
 4/11 cured at Day 28
 1/11 not cured (due to stenosis of the auricular canal)

At the end of the study period, 95% of the ears showed clinical and microbial improvement.
 100% tolerance to the product (no side effect) - 91% cure rate.

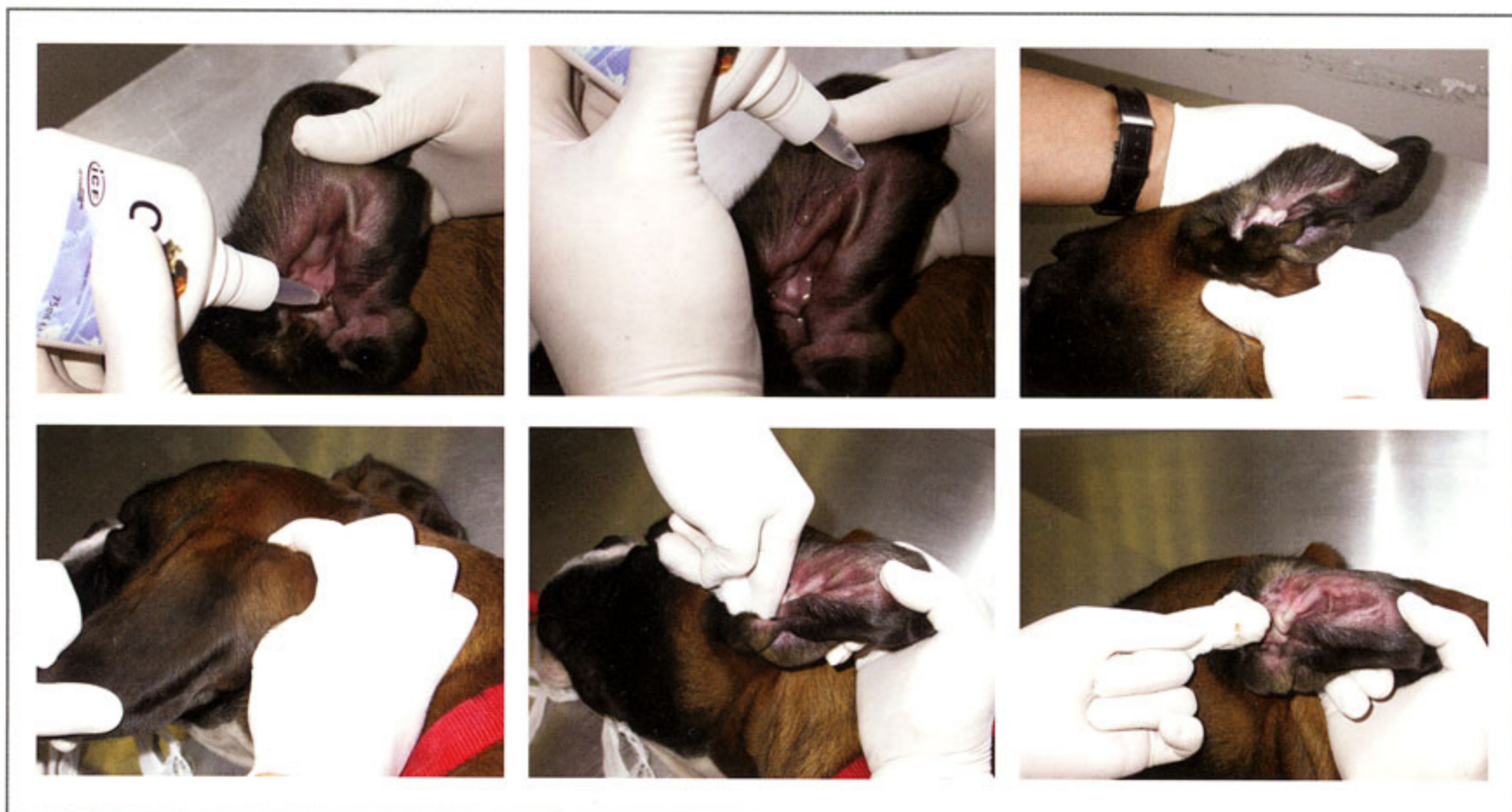
70% clinical and microbial improvement in 2 weeks shows that this solution helps in the management of chronic external bacterial otitis in dogs.




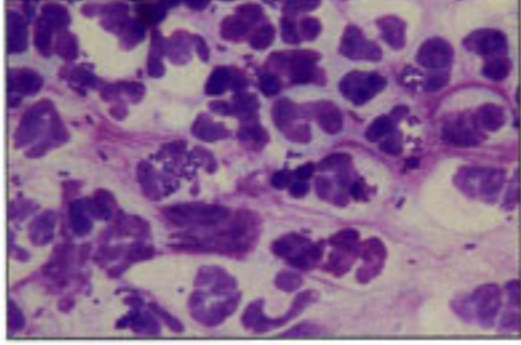

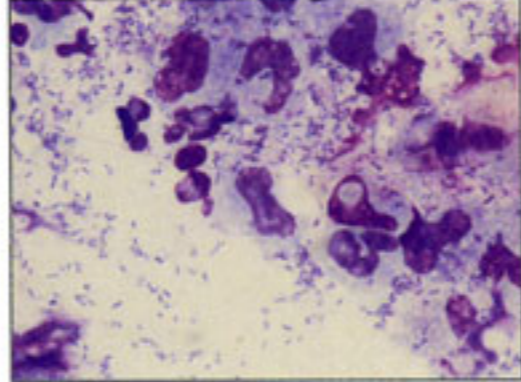

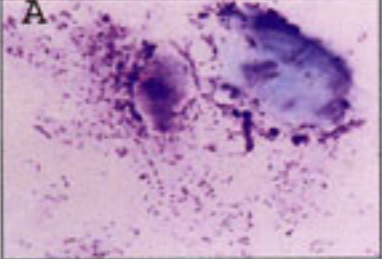
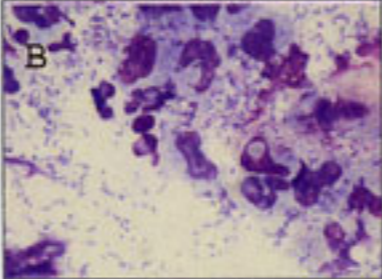
Use

Protocol for bacterial otitis

- 2 times a day for at least 14 days.
- Wash and clean the auricular canal and pinna with **Otodine**[®]; NEVER touch the skin with the tip of the bottle!
- Pour **Otodine**[®] in the auricular canal until completely filled (again NEVER touch the skin with the tip of the bottle!).
- Massage the base of the external ear canal (cartilage) for at least one minute to allow the solution to reach the bottom of the canal. Allow it to work for 10 minutes.
- Dry with a finger wrapped in a cotton ball or gauze and completely remove the residual debris.
- If necessary, in the case of recurring chronic otitis, a topical antibiotic may also be applied in the ear, one hour after the application of **Otodine**[®].



Otitis Atlas - A clinical and therapeutic approach

Clinical Picture	Cytological Picture	Products used
		<p>Clorexiderm® Oto for deep cleaning of the canal and pinna. Indicated in acute forms and with cocci.</p> <p><i>2 times a day for at least 10-15 days.</i></p>
		<p>Clorexiderm® Oto For initial deep cleaning of the canal and pinna.</p> <p>Otodine® Indicated for sub-acute and chronic otitis, in particular in those with the presence of rod-shaped and/or antibiotic-resistant bacteria.</p> <p><i>2 times a day for at least 10-15 days.</i></p>
	<p>A) Malassezias and bacteria</p>  <p>Otoprof® Clorexiderm® Oto</p>  <p>B) Bacteria</p> <p>DR. GHIBAUO</p>	<p>Spot Gel® After cleaning and removal of cerumen with OtoProf. Indicated for mixed ceruminous otitis.</p> <p><i>2 times a day for at least 15-20 days.</i></p> <p>Otodine® 12 hours after cleaning and removal of cerumen. Indicated for sub-acute and chronic otitis, in particular those with the presence of rod bacteria and antibiotic-resistant bacteria.</p> <p><i>2 times a day for at least 10-15 days.</i></p>





Clinical Picture



Parasitic otitis.
DR. LEONE



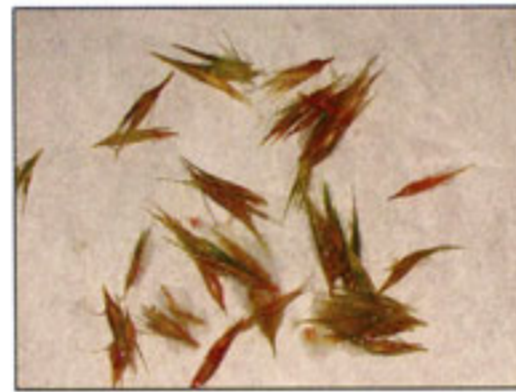
Otitis due to a foreign body
DR. LEONE

Cytological Picture

Otoprof®



Presence of mites: *Otodectes cynotis*
DR. GHIBAUDO



Presence of a grass awn
DR. LEONE

Products used

Otoprof®

Zekout®
for deep acaricide action in the ear canal and pinna, apply also in the peri-auricular skin, neck, tail and distal extremities.

Once a week for 4 consecutive weeks.



Removal of the C.E.

Cloxyderm® Oto
For deep cleaning of the canal and pinna. Evaluate possible bacterial or yeast complications with a cytological examination.

Twice a day.



1

Always properly and completely clean the external ear canal and remove all material present.

2

Use gloves and cotton or gauze for cleaning the ear and avoid touching the skin with the tip of the product bottle as much as possible.

3

ALWAYS investigate and treat the primary, predisposing and perpetuating causes of the otitis.

4

OTODINE A new product indicated for sub-acute and chronic bacterial otitis. Association of tris-EDTA and chlorhexidine – The association has a synergistic bactericide effect against bacteria and especially Gram negative microorganisms.





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