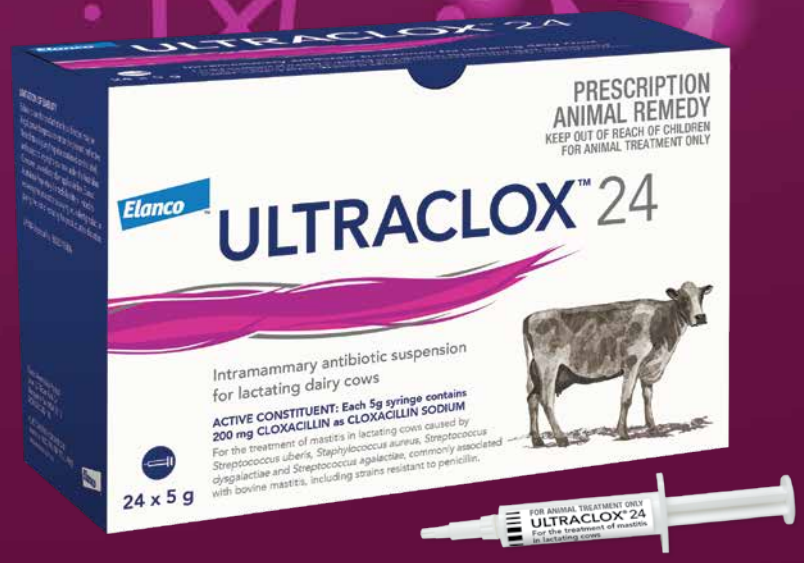
ULTRACLOX™ 24

For the treatment of mastitis in lactating cows



ACTIVE CONSTITUENT:
Each 5g syringe contains 200mg CLOXACILLIN as CLOXACILLIN SODIUM

Elanco™

ULTRACLOX™ 24

For the treatment of mastitis in lactating cows

DESCRIPTION:

Ultraclox™ 24 is a white to off-white oily suspension for intramammary injection. Each 5g syringe contains 200mg cloxacillin.

ACTION:

Ultraclox™ 24 contains cloxacillin, which is highly effective against Gram-positive bacteria, such as *Staphylococci* and *Streptococci*. Cloxacillin cannot be broken down by ß-lactamase hence Ultraclox™ 24 is also effective against ß-lactamase producing *Staphylococci*. Ultraclox™ 24 is indicated when sustained bactericidal action against both penicillin resistant and sensitive bacteria is considered necessary by the prescribing veterinarian.

INDICATIONS:

For the treatment of mastitis in lactating cows caused by *Streptococcus uberis, Staphylococcus aureus, Streptococcus dysgalactiae* and *Streptococcus agalactiae*, commonly associated with bovine mastitis, including strains resistant to penicillin.

DOSING REGIME:

Infuse the entire contents of the syringe into the teat canal of each infected quarter immediately after milking and repeat every 24 hours for 3 treatments. The teat may be gently massaged to disperse the suspension upwards into the quarter. Three syringes provide a full course of treatment. For extended therapy, if required, infuse the entire contents of one syringe per infected quarter every 24 hours for 6 treatments.

WITHHOLDING PERIODS:

MILK: 5 days (10 milkings for cows milked twice per day).

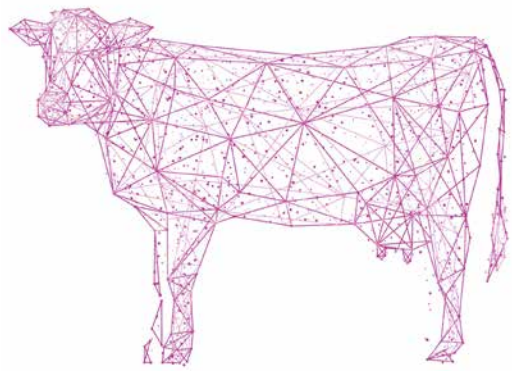
MEAT: 3 days.

Always read and follow the label directions.

FEATURES AND BENEFITS

- Intramammary treatment for mastitis during the lactation.
- Cloxacillin 200mg/5ml Injector.
- Unique patented formulation.
- 24 hour treatment interval – 3 or 6 day treatment regimes.
- Milk WHP – 5 days (10 milkings for cows milked twice per day).

  Meat WHP – 3 days.
- Cows milk returns to the vat sooner using Ultraclox compared to using Noroclox® LC (24 hours sooner) or Orbenin® L.A. (48 hours sooner) based on twice per day milkings (based on a 3 day treatment).

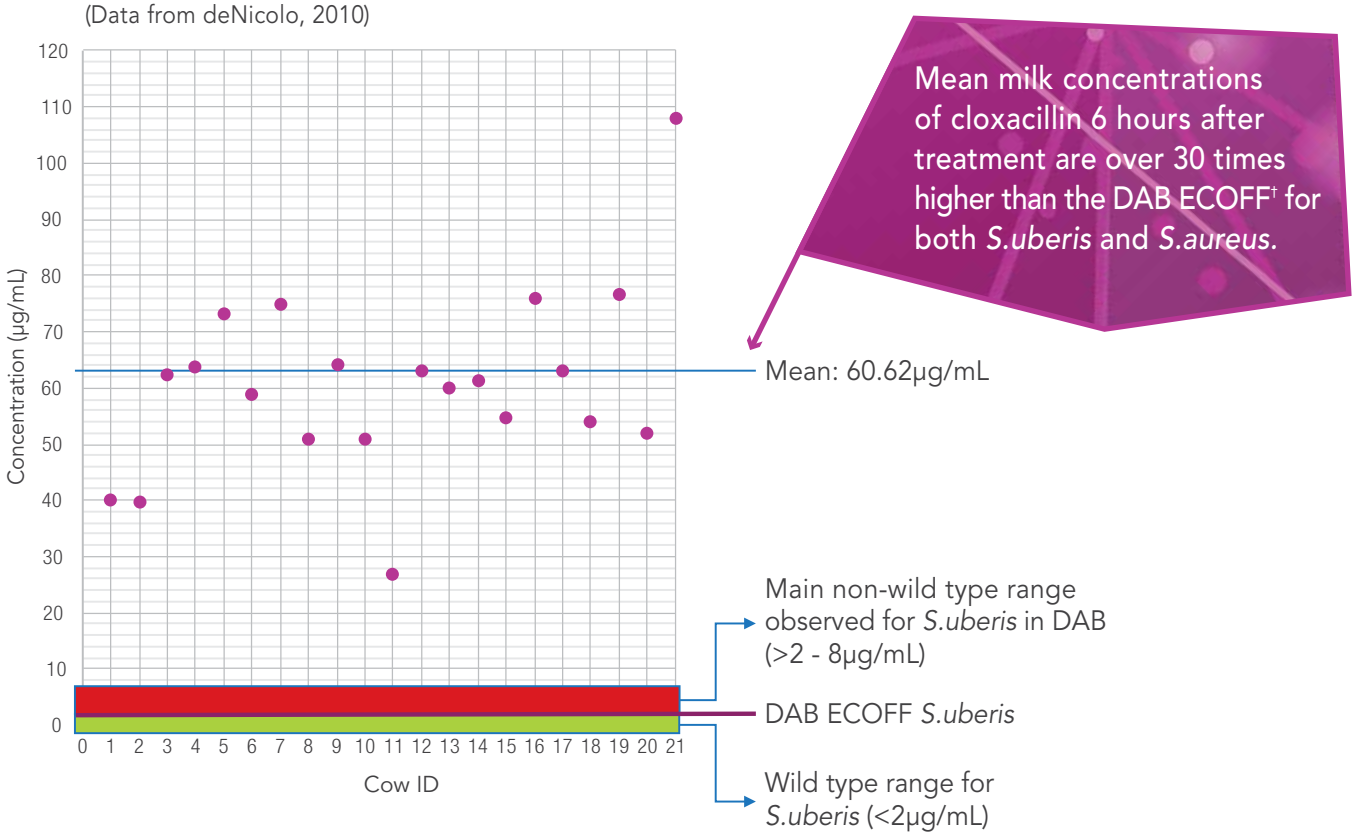


High Concentrations of Antibiotic Achieved in the Milk

With ß-lactam antibiotics, it is important to maintain a free drug concentration above the MIC of the organism for a portion of the dosing interval. The magnitude of this time period varies by ß-lactam subclass. For maximal bactericidal effect this period is reported to be >50% of the dosing interval for the penicillins, and >60-70% of the dosing interval for cephalosporins. (Onufrak et al 2016).

Concentration of Cloxacillin in Milk 6 hours after the 3rd and final dose with Ultraclox 24®. Individual Cow Samples from 21 cows.*

(Data from deNicolo, 2010)



As the dosing interval for Ultraclox™ 24 is 24 hourly, we therefore need to have free cloxacillin concentrations above the relevant MIC for at least 12 hours. Samples taken 22 hours (over 90% of the dosing interval) after the last treatment shows that the average concentration of cloxacillin was 4.47ug/mL (deNicolo, 2010). This is still above the DAB MIC for over 85% of the DAB *S.uberis* antibiograms to date, and 100% of the DAB *S.aureus* antibiograms.#

†DAB = DAIRYANTIBIOGRAM; ECOFF = Epidemiological Cut Off Value
*Based on 3 day treatment protocol
#New Zealand DAB MIC data for *S.Uberus* and *S.Aureus*

Ultraclox™ 24 vs Orbenin® L.A.

KEY POINTS

Ultraclox™ 24
(3 treatments, once per day)

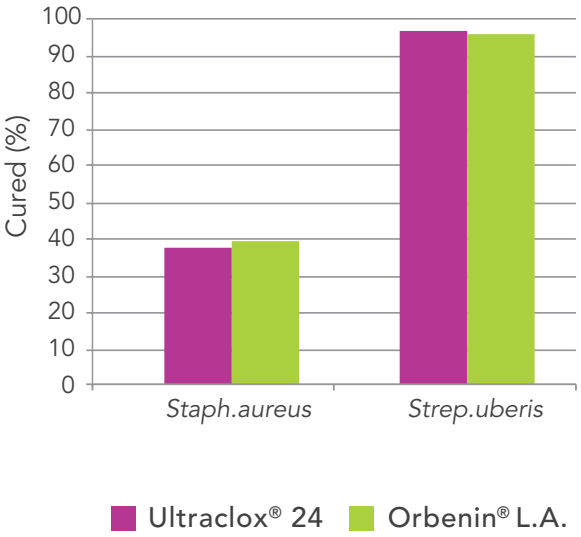
VS

Orbenin® L.A.
(3 treatments, every 48hours)

1017 quarter cases of clinical mastitis enrolled from 44 farms in the Otago regions, New Zealand.

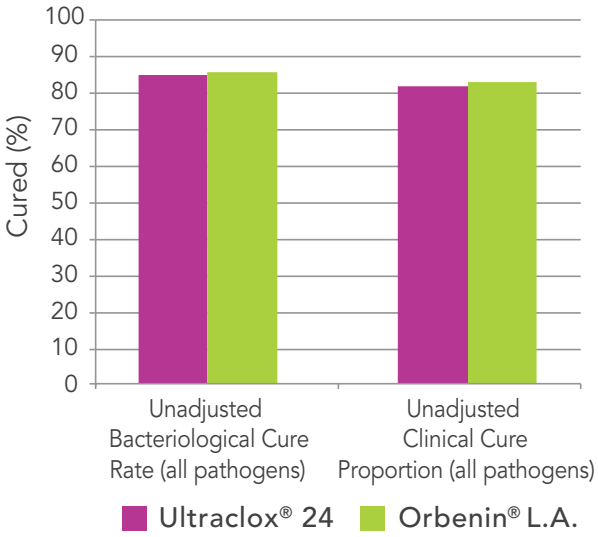
RESULTS

Bacteriological Cure Rate by Pathogen



(Bryan, 2017)

Bacteriological and Clinical Cure Rates



(Bryan, 2017)

CONCLUSIONS

Ultraclox™ 24 was non-inferior to Orbenin® L.A. for both clinical cure proportion, and for bacteriological cure proportion for clinical mastitis in commercial dairy herds.

Ultraclox™ 24 achieved this with a shorter treatment period than Orbenin® L.A. (3 x 24 hours versus 3 x 48 hours respectively). This was found for all major pathogens.

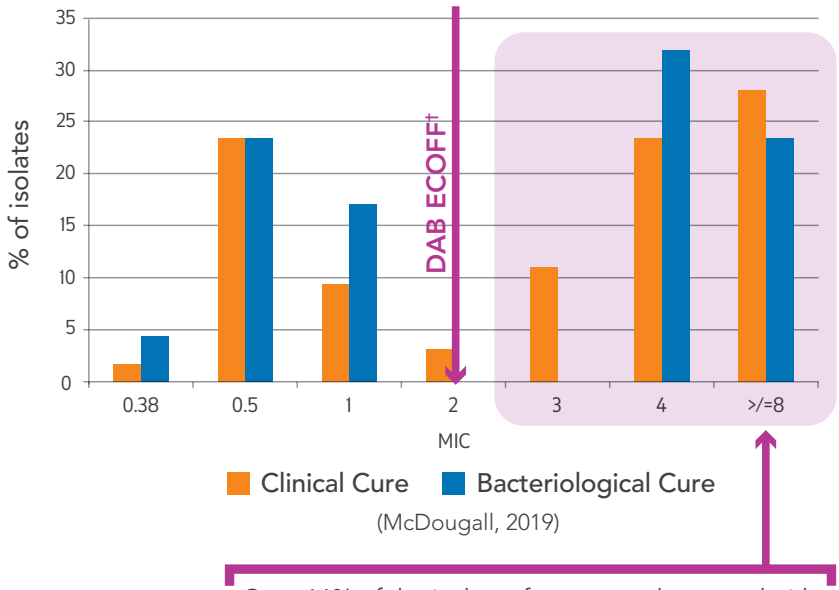
Bryan M, 2017. Demonstration of non-inferiority between a cloxacillin based intramammary suspension for lactating cows and an existing commercially available cloxacillin intramammary, for the treatment of clinical mastitis in dairy cows. Final Study Report. Data on File.

NEW FOLLOW UP MIC DATA

A follow up study was performed to analyse the MICs of *S.uberis* isolates from the Ultraclox™ 24 vs Orbenin® L.A. study.

In this study, it was found that cloxacillin treatment achieved high cure rates amongst populations which contained a significant proportion of non-wild type *S.*uberis (MIC 4 and MIC >/= 8µg/mL).

MIC distribution of a sample of 111 *S.*uberis isolates from mastitis cases that cured with cloxacillin treatment (either Ultraclox® 24 or Orbenin® L.A.).



(McDougall, 2019)

Over 66% of the isolates from cases that *cured* with cloxacillin treatment were actually above the DAB ECOFF, and therefore non-wild type.

DAB = DAIRYANTIBIOGRAM;
ECOFF = Epidemiological Cut Off Value

MULTI OR MONOTHERAPY?

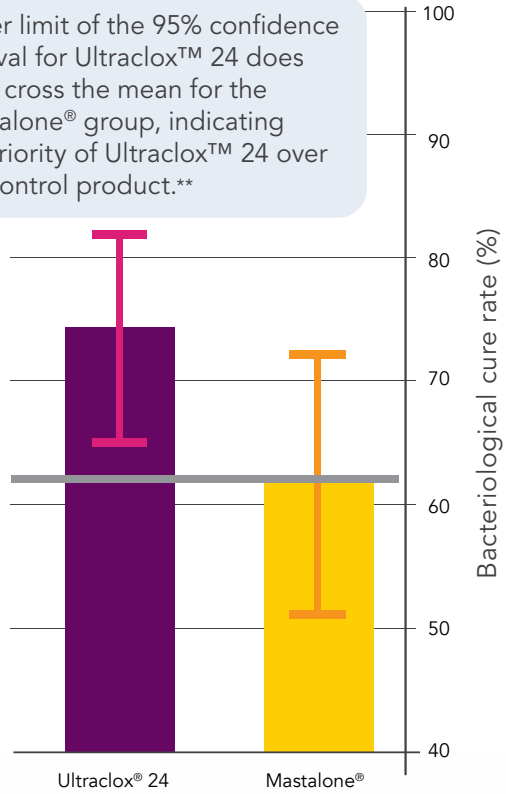
Ultraclox™ 24 showed superior bacteriological cure rate compared to Mastalone®† in New Zealand dairy herds.

In this trial, Ultraclox™ 24 demonstrated superior bacteriological cure and responsible antimicrobial use by selecting a **single antimicrobial ingredient product** which out-perfomed the combination therapy.

Products with more than one antimicrobial active may lead to unnecessary exposure of bacteria to one or more of the actives – which may contribute to the selection of resistant bacteria.

†*Mastalone NZ includes prednisolone.

Lower limit of the 95% confidence interval for Ultraclox™ 24 does NOT cross the mean for the Mastalone® group, indicating superiority of Ultraclox™ 24 over the control product.**



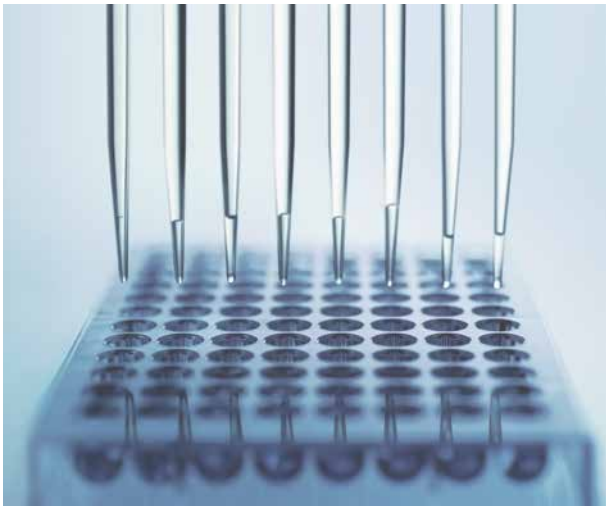
**In this trial, Ultraclox™ 24 (3 x 24hr treatments) demonstrated superior bacteriological cure and responsible antimicrobial use by selecting a single antimicrobial ingredient product which out-performed the combination therapy.

Bryan M. Demonstration of non-inferiority or of superiority of a novel intra-mammary cloxacillin compared to existing intramammary therapy in the treatment of clinical mastitis. Final Study Report, 2013, data on File.

*Mastalone® registered in NZ and AU both contain multiple antimicrobials, but are different formulations.

Make the right choice with the DAIRY**ANTIBIOGRAM**

DairyAntibiogram is a Elanco initiative which uses an automated microbroth dilution system to provide economical MIC data unique to the farm, on antimicrobial susceptibility to the common actives available for mastitis therapy in Australia. The DairyAntibiogram can help facilitate targeted antimicrobial selection, thereby promoting antimicrobial stewardship.



To find out more contact us on **1800 995 709** or visit **www.farmanimal.elanco.com/au**

REFERENCES

1. Bryan M, 2013. Demonstration of non-inferiority or of superiority of a novel intramammary cloxacillin compared to existing intramammary therapy in the treatment of clinical mastitis. Final Study Report. Data on File.
2. Bryan M, 2017. Demonstration of non-inferiority between a cloxacillin based intramammary suspension for lactating cows and an existing commercially available cloxacillin intramammary, for the treatment of clinical mastitis in dairy cows. Final Study Report. Data on File.
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4. McDougall S. 2019. Association between minimum inhibitory concentration of cloxacillin and bacteriological cure of clinical *Streptococcus uberis mastitis*. Final Study Report. Data on file.
5. deNicolo G. 2010. A regulatory study to determine the residue depletion profile of cloxacillin in a developmental intramammary antibiotic to be used in lactating dairy cattle. Final Study Report. Data on file.