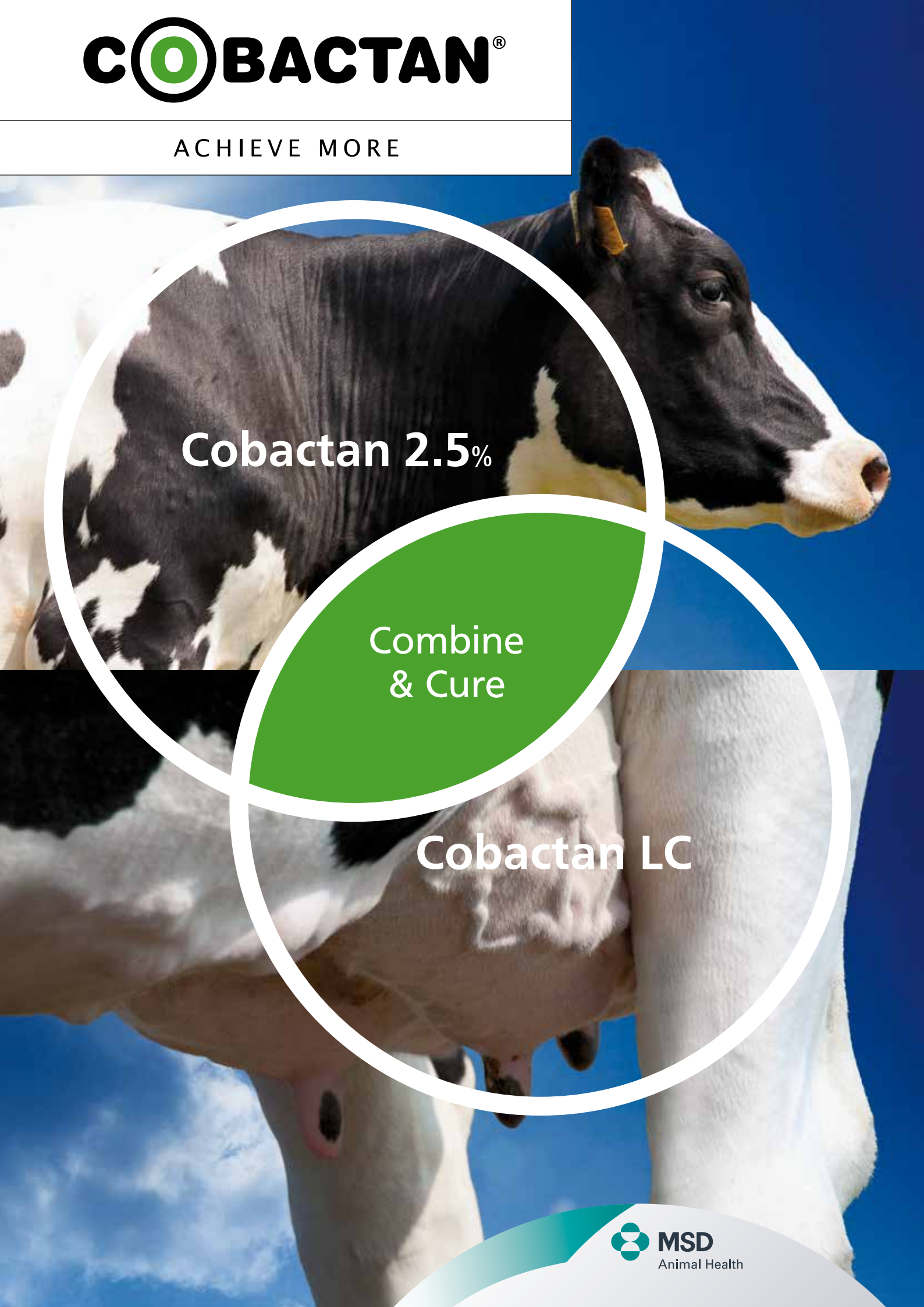
COBACTAN®

ACHIEVE MORE



MSD
Animal Health

Mastitis: a guessing game with deadly consequences

Mastitis is a major problem confronting dairy producers. Often, treatment decisions must be made without the luxury of identifying the specific pathogens infecting the animal. Getting mastitis treatment right and right from the start will play a critical role in ensuring cure rates, milk productivity and even survival. But how can it be more than a guessing game?

The first 100 days are critical

Mastitis can take many forms representing a range of pathogens. It isn't always easy or convenient to determine exactly which pathogens are behind a case of mastitis. What is clear is that mastitis requires fast and effective action if the cow is to return to the production of good quality milk. Cows are particularly vulnerable in the first 100 days of lactation. High production, negative energy balance and low immunity are frequent factors precipitating the infection.

Mild or severe... It's not written on the ear tag...

Unfortunately! There is a great deal of variability when it comes to how individual animals react to mastitis pathogens. Some cows are able to overcome the onset of the disease with their own defenses while others see a rapid evolution from mild to severe in an extremely short time frame.

Incidence of mastitis pathogens % of sample[1, 2]

Streptococcus dysgalactiae	4 - 13%
Streptococcus uberis	6 - 7%
Staphylococcus aureus	10 - 19%
Escherichia coli	8 - 20%
Negative	15 - 44%

Research shows that guessing is not a good option

It is notoriously difficult to predict the specific pathogens involved in mastitis. White et al., 1986, determined that the accuracy rate of clinical diagnosis of *E. coli* mastitis was only 62%. That means that in nearly 40% of cases, clinical mastitis was misdiagnosed.

Accuracy of clinical diagnosis, E. coli mastitis[3]

100% of severe mastitis cases begin as mild mastitis

The fact is, you can't know which case will develop into severe mastitis. With severe coliform mastitis comes a high risk of blood poisoning (bacteraemia). Blood poisoning is caused by the presence of bacteria in the blood and may also be accompanied by toxins leading to severe illness and death. The risk of blood poisoning is one of the principle reasons why additional, broad spectrum parenteral treatment is recommended.

42% of cows with severe mastitis have blood poisoning!

If there is *E. coli* in the milk, then there is a high probability that the same bacterium will be found in the blood.

Bacteraemia in coliform mastitis[4]

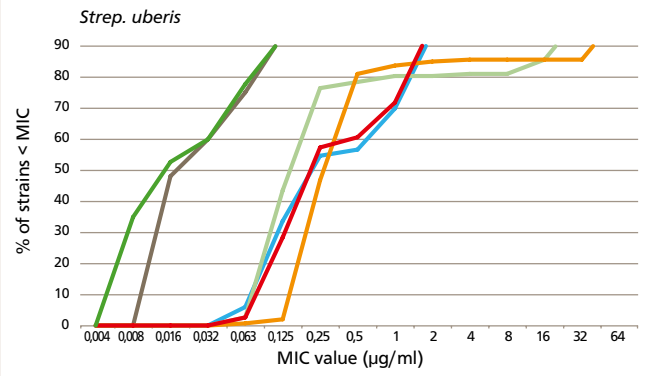
144 cows, *E. coli* (n=122) or *Klebsiella* (n=19) or both isolated (n=3) in milk

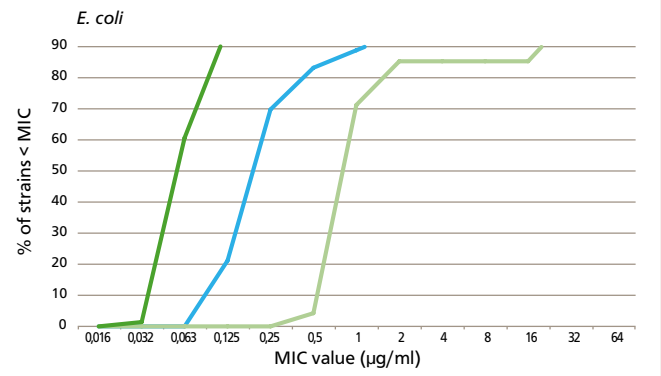
	number of cows	number of positive milk samples	number of postive blood samples	% of positive blood samples
Healthy	156	0	0	0
Coliform mastitis	144	144	20 [a]	14 [a]
Mild		69	3	4,3
Moderate		44	4	9,1
Severe		31	13	42

[a] significantly different from healthy cows, p< 0.001

A need for early, broad-spectrum treatment.

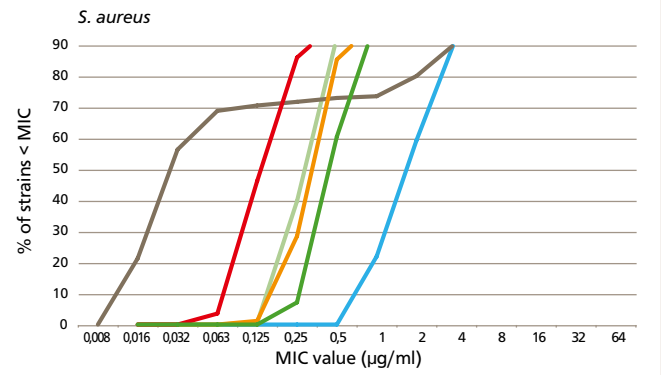
Cobactan's exceptionally broad spectrum of activity covers both the gram positive and gram negative organisms involved in mastitis. The MIC of cefquinome against the main mastitis germs throughout Europe are regularly monitored. The intensive screening scheme gives the following results:[5]





% of *Strep. uberis* strains (n=152), % of *S. aureus* strains (n=168) and % of *E. coli* strains (n=142) < Minimum Inhibitory Concentration (MIC). The bacterial strains were isolated from clinical mastitis cases in different European countries between 2000-2005.[5]

- cefquinome
- oxytetracyclin
- penicillin
- tylosin
- cloxacillin
- cefoperazone



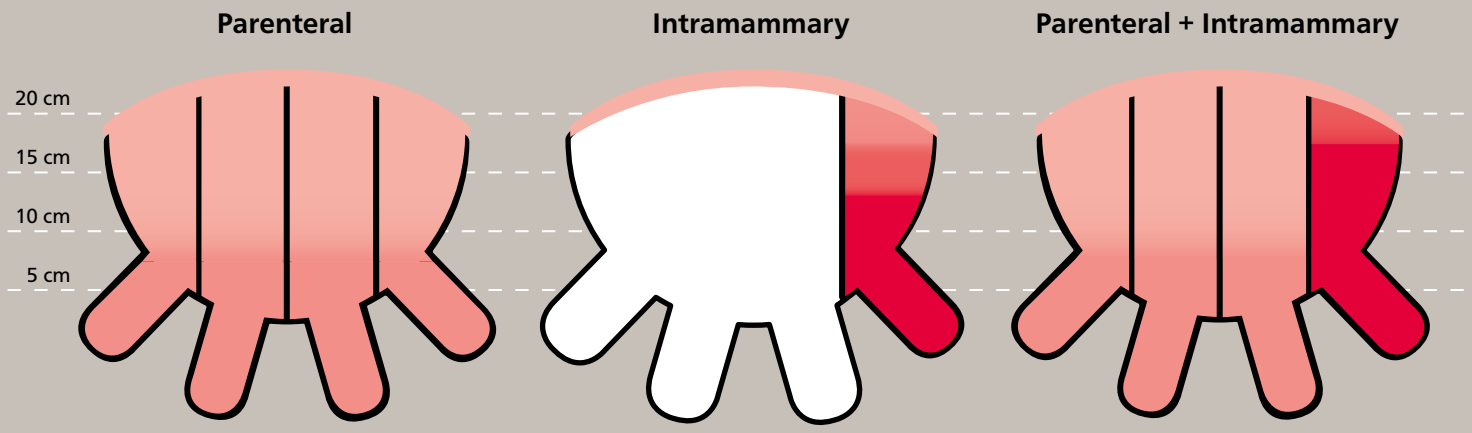
Isolates of *E.coli* are resistant to penicillin, tylosin and cloxacillin.

The injection is tailored to the tube

Not all antibiotic combinations are effective due to their specific pharmacokinetics or pharmacodynamics. For example, quinolones become inhibited by milk components while macrolides, whose activity is bacteriostatic, are counteractive when combined with bactericidal antibiotics. Cobactan combination therapy ensures peace of mind thanks to the same active ingredient (cefquinome) in the intramammary and parenteral application.

Better distribution and higher concentrations in udder tissue

Experimental study, cefquinome treatment[6]

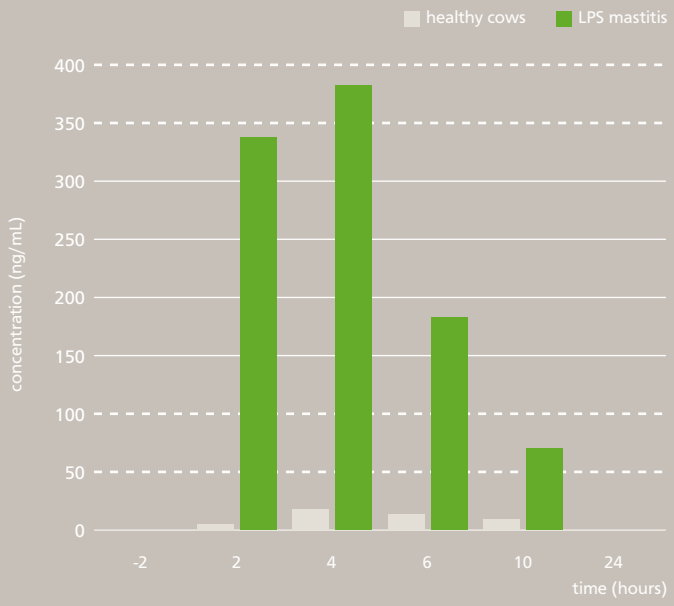


Parenteral treatment by itself provides good distribution of cefquinome throughout the udder.

Cefquinome delivered via local injection delivers a high dose in the infected quarter... the basis of effective mastitis treatment.

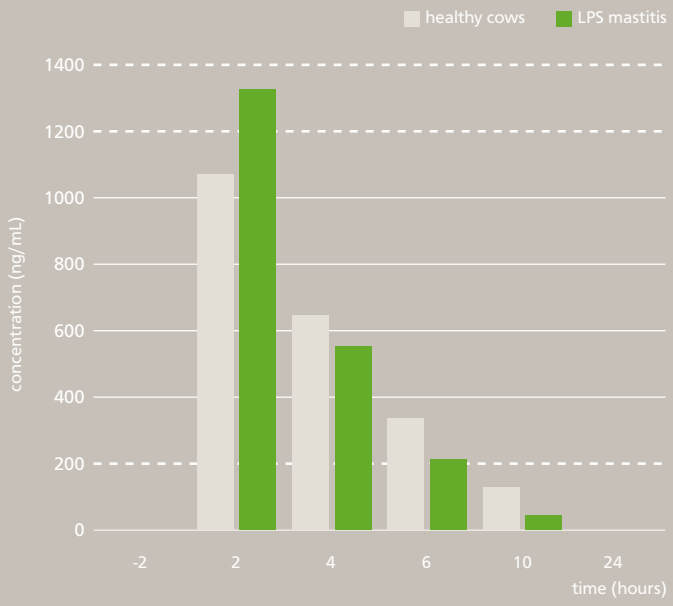
Combining parenteral and local injections ensures the highest concentrations of cefquinome in the infected quarter while treating the entire udder and eliminating pathogens in the blood.

Cefquinome concentrations in milk [ng/mL]7



In healthy cows cefquinome penetration in the milk is low, but in mastitis cows, changes in the milk pH cause cefquinome to penetrate the milk in therapeutic concentrations.

Cefquinome concentrations in blood plasma [ng/mL]7



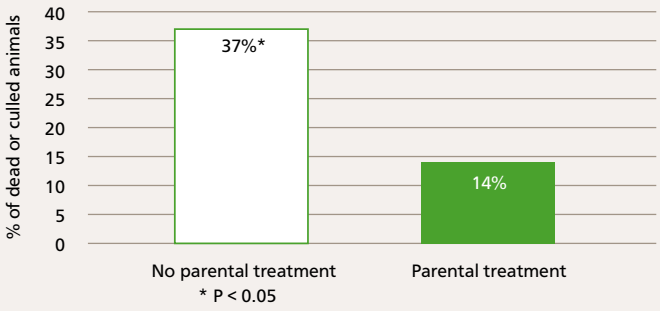
In both healthy cows and mastitis cows, cefquinome concentrations are in therapeutic levels in the blood plasma.

Cobactan combination therapy has clear benefits

Cefquinome, delivered as a parenteral antibiotic treatment and in intramammary application, yields clear benefits including higher survival, higher cure and higher milk production. This combination achieves more thanks to better antibiotic distribution throughout the whole udder, higher concentrations in the infected quarter and therapeutic levels in the blood plasma.

Higher survival rate

Additional parenteral treatment of coliform mastitis[8]



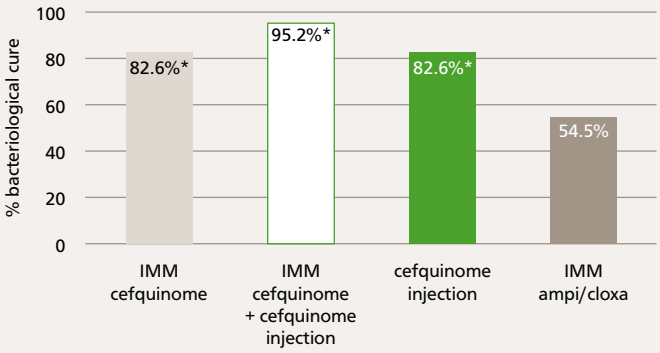
Higher cure rate

Experimental *E. coli* mastitis trial[9]

E coli mastitis model
4 groups of 12 cows
1. IMM cefquinome
2. IMM cefquinome + Injection cefquinome
3. Injection cefquinome
4. IMM ampicillin / cloxacillin
Treatment at onset of clinical signs

Bacteriological cure[9]

7 and 14 days after infection

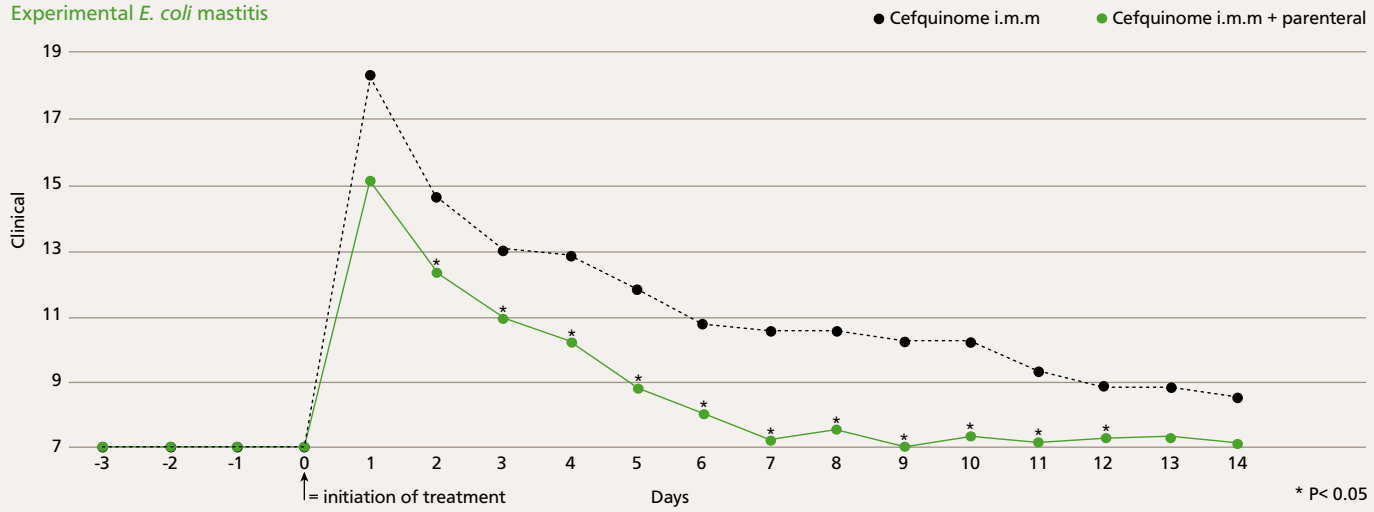


* Significantly different from Ampi-Cloxa treatment, P < 0.05

Higher cure rate (continued...)

Clinical mastitis score[9]

Experimental *E. coli* mastitis

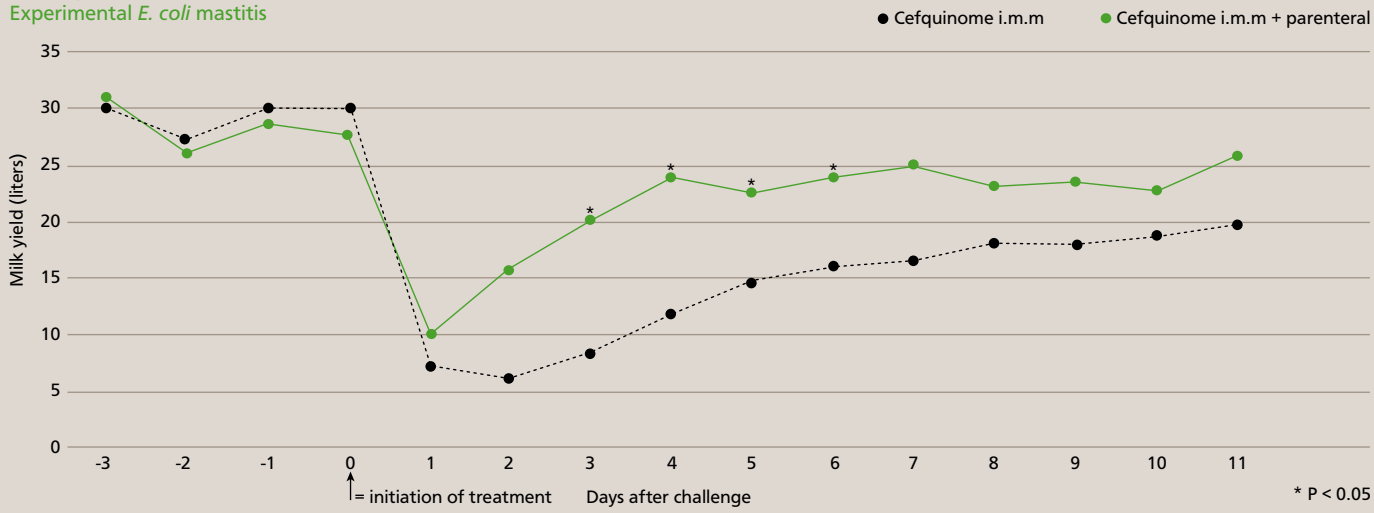


Clinical mastitis score; A 7-35 scale of attitude, appetite, milk appearance, clinical mastitis quarter size, edema, pain and temperature (Anderson et al.,1986)

Higher milk production

Milk yield[9]

Experimental *E. coli* mastitis



Combination therapy with a single, short withhold

You can count on short, reliable withholding periods with Cobactan combination therapy. You get the extended effect of cefquinome in the milk and blood plasma without extending the withholding period. In fact, in the United Kingdom, a single license for the combination has been awarded featuring a 4 day withhold for milk and a 5 day withhold for meat.

Dose		
Cobactan 2.5%	1 ml/25 kg	2 days with an interval of 24 hrs
Cobactan LC	1 injector per infected quarter	repeat twice with an interval of 12 hrs

Example 650 kg dairy cow:
- Begin: 26 ml Cobactan 2.5% and 1 injector of Cobactan LC
- 12 hrs later 1 injector of Cobactan LC
- 24 hrs later: 26 ml Cobactan 2.5% and 1 injector of Cobactan LC

Withhold		
Cobactan 2.5%	milk 1 day	meat 5 days
Cobactan LC	milk 5 days	meat 4 days

Withhold of the Combination
• Regulatory approval in the UK for the combination therapy: withhold Cobactan 2.5% + LC: milk 4 days, meat 5 days


COBACTAN 2.5%
COBACTAN 2.5%
Cefquinome
SUSPENSION INJECTABLE
BOVINS, PORCINS
Flacon de 100 ml
COBACTAN 2.5%
100 ml


COBACTAN LC
COBACTAN LC
COBACTAN LC
cefquinome

COBACTAN®

ACHIEVE MORE

Combination therapy:
Powerful benefits in the fight against mastitis

- Broad spectrum activity for peace of mind against unidentified pathogens
- Eliminates mastitis pathogens throughout the udder and blood leading to higher survival, cure and milk production
- The injection is tailored to the tube for cumulative efficacy
- Short and reliable milk and meat withhold

REFERENCES: [1] Barkema et al., J Dairy Sci. 81:411-9, 1998 • [2] Olde Riekerink et al., J. Dairy Sci. 91:1366–1377, 2008 • [3] White et al., Cornell Vet. 76:342-347, 1986 • [4] Wenz et al., JAVMA, 219, 7, 976-981. • [5] Intervet/Schering-Plough AH, data on file • [6] Ehinger et al., The Veterinary Journal 172 147–153, 2006 • [7] Intervet/Schering-Plough AH, Data on file • [8] Erskine et al., J. Dairy Sci. 85:2571–2575, 2002 • [9] Shpigel et al., J. Dairy Sci. 80:318–323, 1997.

SUMMARY OF PRODUCT CHARACTERISTICS

Name: Cobactan 2.5%, Suspension for injection. **Active ingredient:** cefquinome (as sulphate): 25 mg/ml **Indications for use:** For the treatment of bacterial infections in cattle caused by the Gram positive and Gram negative micro-organisms sensitive to cefquinome such as: I. Respiratory disease caused by *Pasteurella haemolytica* and *Pasteurella multocida*. 2. Acute *E. coli* mastitis with signs of systemic involvement. 3. *E. coli* septicaemia in calves. 4. Digital dermatitis, infectious bulbar necrosis and acute interdigital necrobacillosis (foul in the foot). **Amounts to be administered for Acute *E. coli* mastitis:** Two intramuscular injections of 1 mg cefquinome / kg bodyweight (equivalent to 2 ml/50 kg bodyweight) with a 24 hour interval. **Amounts to be administered for BRD and Digital Dermatitis:** 3-5 Intramuscular injections of 1 mg cefquinome / kg bodyweight (equivalent to 2 ml/50 kg bodyweight) with a 24 hour interval. **Amounts to be administered for *E. coli* septicaemia in calves:** 3-5 Intramuscular injections of 2 mg cefquinome / kg bodyweight (equivalent to 4 ml/50 kg bodyweight) with a 24 hour interval. **Withdrawal period Cattle:** Milk: 1 day; Meat 5 days. **Contraindications:** Not to be administered to animals which are known to be hypersensitive to cephalosporin antibiotics or other ß-lactam antibiotics.

Name: Cobactan LC for lactating cows. **Active ingredient:** cefquinome (as cefquinome sulphate) 75 mg per 8 g syringe. **Indications for use:** For the treatment of clinical mastitis in the lactating dairy cow caused by the following cefquinome sensitive organisms: *Streptococcus uberis, Streptococcus dysgalactiae, Streptococcus agalactiae, Staphylococcus aureus* and *Escherichia coli*. **Contraindications:** Not to be administered to animals which are known to be hypersensitive to cephalosporin antibiotics and other betalactam antibiotics. **Undesirable effects:** None known. **Use during pregnancy and lactation:** Cobactan LC is intended for use during lactation. There is no available information indicating reproductive toxicity (inc. teratogenicity) in cattle. In reproductive toxicity studies in laboratory animals cefquinome did not reveal any effect on reproduction or teratogenic potential. Interactions with other medicaments and other forms of interaction: It is known that a cross sensitivity to cephalosporins exist for bacteria sensitive to the cephalosporin group. **Posology and Method of Administration:** The content of one syringe should be infused gently into the teat of the infected quarter every 12 hours after each of three successive milkings. Milk out the affected quarter(s). After thoroughly cleaning and disinfecting the teat and teat orifice, gently infuse the contents of one syringe into each affected quarter. Disperse the product by gently massaging the teat and udder of the affected animal. **Overdose:** No symptoms expected or emergency procedures required. **Special warnings:** None. **Withdrawal periods:** Meat=4 days, Milk=5 days. (National regulations should be observed).

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