



# MIC Test Strip Technical Sheet **Ceftobiprole**

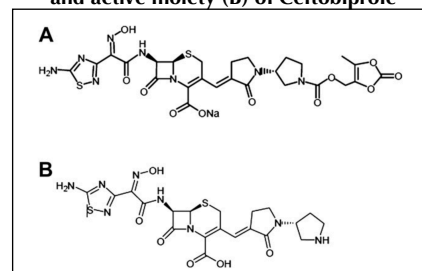
## INTRODUCTION

Ceftobiprole medocaril (BAL5788, formerly Ro-65-5788) is the prodrug form of ceftobiprole (BAL9141, formerly Ro-63-9141), which is an extended-spectrum anti-methicillin-resistant *Staphylococcus aureus* (anti-MRSA) parenteral cephalosporin with potent activity against Gram-positive and -negative bacterial pathogens.

Ceftobiprole demonstrates *in vitro* activity against Gram-positive cocci, including methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *S. epidermidis*, penicillin-resistant *Streptococcus pneumoniae*, *Enterococcus faecalis*, Gram-negative bacilli including AmpC-producing *Escherichia coli* and *Pseudomonas aeruginosa*, but excluding extended-spectrum  $\beta$ -lactamase-producing strains. Like cefotaxime, ceftriaxone, ceftazidime, and cefepime, ceftobiprole demonstrates limited activity against anaerobes such as *Bacteroides fragilis* and non-fragilis *Bacteroides* spp. In addition, ceftobiprole has demonstrated activity against *Haemophilus influenzae*, *Moraxella catarrhalis*.

These characteristics make ceftobiprole an attractive therapeutic candidate, given its broad spectrum and its potent bactericidal action.

### Structures of the prodrug form (A) and active moiety (B) of Ceftobiprole



## TEST PROCEDURE

Before using MIC Test Strip Ceftobiprole from an unopened package, visually inspect to ensure the package is intact. Do not use the strips if the package has been damaged.

When removed from the refrigerator, allow the package or storage container to reach room temperature for about 30 minutes.

Moisture condensing on the outer surface must evaporate completely before opening the package.

### Materials required but not provided:

- Mueller Hinton II Agar plates (ref. 10031)
- Sterile saline (0.85% NaCl) (ref. 20095)
- Sterile loops, swabs (not too tightly spun), test tubes, pipettes and scissors
- Forceps
- 0.5 McFarland turbidity standard (ref. 80400)
- Incubator ( $35 \pm 2^\circ\text{C}$ )
- Quality control organisms
- Additional technical information from [www.liofilchem.net](http://www.liofilchem.net)

### Inoculum preparation

Suspend well-isolated colonies from an overnight agar plate into saline to achieve a 0.5 McFarland standard turbidity.

A confluent or almost confluent lawn of growth will be obtained after incubation, if the inoculum is correct.

In order to verify that your procedure gives the correct inoculum density in terms of CFU/mL, performing regular colony counts is recommended.

### Inoculation

Dip a sterile swab in the broth culture or in a diluted form thereof and squeeze it on the wall of the test tube to eliminate excess liquid.

Alternatively, use a rotation plater to efficiently streak the inoculum over the agar surface. Allow excess moisture to be absorbed so that the surface is completely dry before applying MIC Test Strip.

### Application

Apply the strip to the agar surface with the scale facing upwards and code of the strip to the outside of the plate, pressing it with a sterile forceps on the surface of the agar and ensure that whole length of the antibiotic gradient is in complete contact with the agar surface. Once applied, do not move the strip.

### Incubation

Incubate the agar plates in an inverted position at  $35 \pm 2^\circ\text{C}$  for 16-20 hours in ambient atmosphere. Extend the incubation for up to 48 hours in case of slow growing organisms.

## EVALUATING THE RESULTS

### Reading

Observe where the relevant inhibition ellipse intersects the strip and read the MIC at complete inhibition. Growth along the entire gradient i.e. no inhibition ellipse indicates that the value is greater than or equal to ( $\geq$ ) the highest value on the scale. An inhibition ellipse that intersects below the lower end of the scale is read as less than ( $<$ ) the lowest value.

See page 2 for example of results. Also consult the MIC Test Strip Photographic Guide.

### Interpretation

Use EUCAST breakpoints shown below. Always round up MIC Test Strip half dilution values to the next upper two-fold value before categorization.

## QUALITY CONTROL

The following CLSI-recommended quality control strains are used as outlined under TEST PROCEDURE:

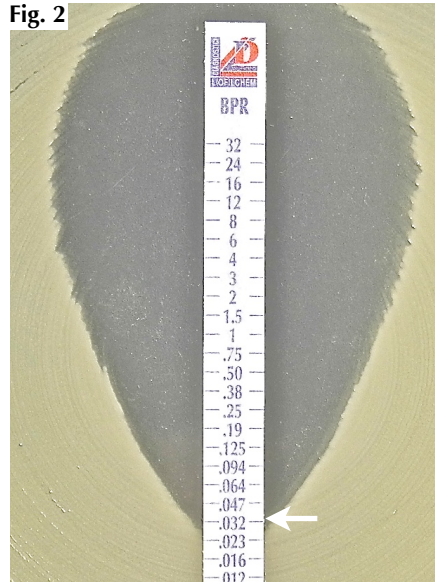
*S. aureus* ATCC® 29213, *E. faecalis* ATCC® 29212, *E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853, *H. influenzae* ATCC® 49247, *H. influenzae* ATCC® 49766, *S. pneumoniae* ATCC® 49619.

Organism group	Breakpoint ( $\mu\text{g/mL}$ )		Quality Control MIC Range ( $\mu\text{g/mL}$ )		
	S $\leq$	R $>$			
Enterobacteriaceae	0.25	0.25	<i>S. aureus</i>	ATCC® 29213	0.12-1
<i>Staphylococcus aureus</i>	2	2	<i>E. faecalis</i>	ATCC® 29212	0.06-0.5
<i>Streptococcus pneumoniae</i>	0.5	0.5	<i>E. coli</i>	ATCC® 25922	0.03-0.12
PK/PD (Non-species related) breakpoints	4	4	<i>P. aeruginosa</i>	ATCC® 27853	1-4
			<i>H. influenzae</i>	ATCC® 49247	0.12-1
			<i>H. influenzae</i>	ATCC® 49766	0.016-0.06
			<i>S. pneumoniae</i>	ATCC® 49619	0.004-0.03

## MIC Test Strip Ceftobiprole Reading Guide



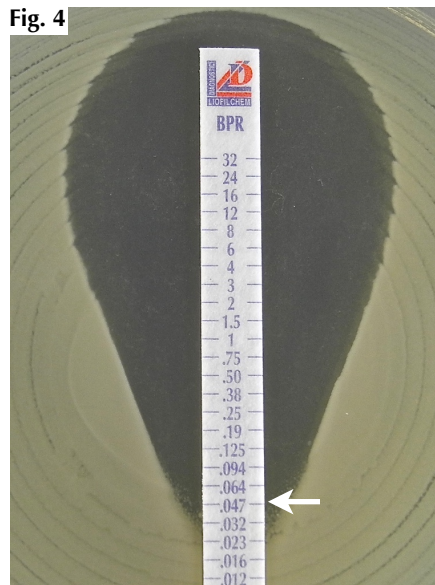
MIC 0.38 µg/mL.



MIC 0.032 µg/mL.



MIC 0.094 µg/mL.



MIC 0.047 µg/mL.

### REFERENCES

- CLSI M07-A10 (2015) Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard – Tenth Edition.
- CLSI M100-S25 (2015) Performance Standards for Antimicrobial Susceptibility Testing.
- Farrell D.J. et al (2014) Ceftobiprole activity against over 60,000 clinical bacterial pathogens isolated in Europe, Turkey, and Israel from 2005 to 2010. *Antimicrob Agents Chemother.* 58(7):3882-8
- Chahine E.B. and A.O. Nornoo (2011) Ceftobiprole: The First Broad-Spectrum Anti-methicillin-resistant *Staphylococcus aureus* Beta-Lactam. *J Exp Clin Med.* 3(1):9-16.
- Zhanel G.G. et al (2008) Ceftobiprole: a review of a broad-spectrum and anti-MRSA cephalosporin. *Am J Clin Dermatol.* 9(4):245-54.

PRESENTATION	µg/mL	Code	Packaging	Ref.
MIC Test Strip Ceftobiprole	0.002-32	BPR	10 30 100	921401 92140 921400

MIC Test Strip, Patent No. 1395483

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