

# ACTIVITY OF CEFTAROLINE AND CEFTOBIPROLE AGAINST STAPHYLOCOCCI AND STREPTOCOCCUS PNEUMONIAE IN THE UK AND IRELAND

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Public Health  
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RESISTANCE  
SURVEILLANCE  
PROGRAMME

## INTRODUCTION

- Ceftaroline (Pfizer)<sup>1</sup> and ceftobiprole (Correvio)<sup>2</sup> are cephalosporins active against Gram-positive bacteria, including MRSA. Indications and clinical breakpoints differ (Table 1).
- There are few direct comparisons of their activity published.
- We reviewed comparative data for both agents vs.
  - staphylococci and pneumococci causing clinically-significant bacteraemia
  - pneumococci causing community-acquired pneumonia (CAP)

	Ceftaroline	Ceftobiprole		
Licensed Indications (UK/EU)	Acute skin and skin structure infections. CAP	CAP Hospital-acquired pneumonia (excl. ventilator-associated)		
Breakpoint	S	R	S	R
<i>S. aureus</i>	≤1mg/L	>2mg/L	≤2mg/L	>2mg/L
<i>S. pneumoniae</i>	≤0.25mg/L	>0.25mg/L	≤0.5mg/L	>0.5mg/L

TABLE 1. Licensed indications and EUCAST breakpoints<sup>6</sup> for ceftaroline and ceftobiprole.

## METHODS

- The BSAC Resistance Surveillance Programme<sup>3</sup> has collected *S. aureus*, CoNS (coagulase-negative staphylococci) and *S. pneumoniae* causing clinically-significant bacteraemia between 2001 and 2017, and respiratory *S. pneumoniae* since 1999, from 22-39 hospitals throughout the UK and Ireland.
- Ceftaroline and ceftobiprole were tested in parallel by agar dilution<sup>4</sup> in 2008, 2013 and 2017 for bloodstream isolates (all species) and in 2016/17 for respiratory *S. pneumoniae* only.
- CoNS were identified to species level in 2013 and 2017 by MALDI-ToF, but not in 2008.
- mecA* was sought by PCR.<sup>5</sup>
- Current EUCAST *S. aureus* breakpoints were assumed for CoNS (Table 1).

## TO REQUEST ISOLATES

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## RESULTS

- 3029 isolates were tested with both agents in the 3 non-consecutive years (Table 2).
- Modal and geometric mean MICs did not change significantly between years, except for CoNS tested with ceftobiprole where MICs rose for MR-CoNS and fell for MS-CoNS (Table 2).
- The geometric mean MICs of ceftobiprole varied by MR-CoNS species:
  - MR-*S. epidermidis* (215/291: 0.77)
  - MR-*S. haemolyticus* (33/36: 1.31)
  - MR-CoNS (other species) (53/105: 0.98)

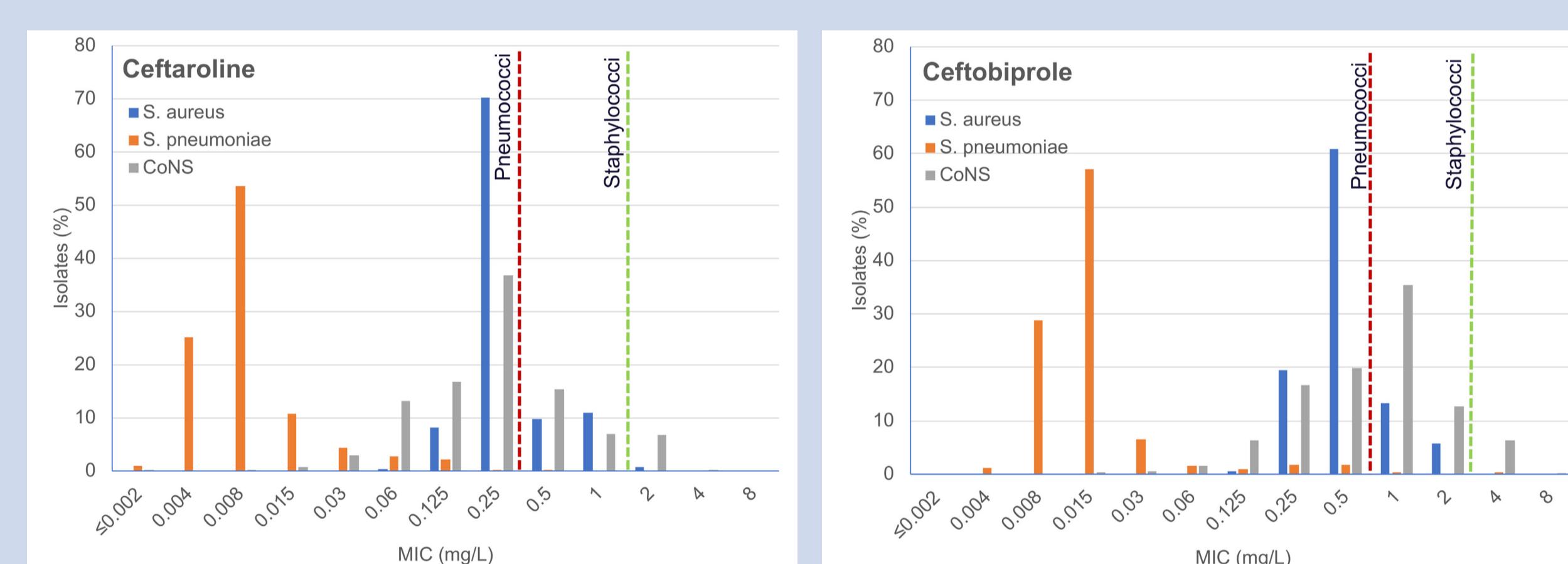


FIGURE 1. MIC distributions among staphylococci and pneumococci tested against ceftaroline and ceftobiprole. Dashed lines indicate EUCAST breakpoints.

	Ceftaroline MIC (mg/L)					Ceftobiprole MIC (mg/L)							
	2008		2013		2017		2008		2013		2017		
	Total (n)	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean	Mode	Geo. mean
<i>S. aureus</i>	1428	0.25	0.4	0.25	0.25	0.25	0.27	0.5	0.7	0.5	0.4	0.5	0.51
MRSA	210	1	0.4	0.5	0.25	0.5	0.27	2	0.7	1	0.4	1	0.52
MSSA	1218	0.25	0.4	0.25	0.25	0.25	0.27	0.5	0.7	0.5	0.4	0.5	0.51
CoNS	612	0.25	0.24	0.25	0.22	0.25	0.23	<b>1</b>	0.67	<b>0.5</b>	0.64	<b>0.25</b>	0.66
MR-CoNS	431	0.25	0.24	0.25	0.28	0.25	0.35	1	<b>0.67</b>	0.5-1	<b>0.8</b>	1	<b>1.03</b>
MS-CoNS	181	0.06	0.24	0.06	0.14	0.06	0.1	0.25	<b>0.69</b>	0.25	<b>0.41</b>	0.25	<b>0.27</b>
<i>S. pneumoniae</i>	989	0.008	0.01	0.004	0.01	0.008	0.01	0.015	0.02	0.008	0.01	0.015	0.02

TABLE 2. Modal and geometric mean MICs of ceftaroline and ceftobiprole against staphylococci and pneumococci. MR: methicillin-resistant; MS: methicillin-susceptible.  
**Bold text:** change in modal MIC or geometric mean.

## CONCLUSIONS

- Ceftaroline and ceftobiprole have similarly good activity against both staphylococci and pneumococci.
- Modal ceftaroline MICs for staphylococci tended to be c. 2-fold lower than ceftobiprole, but ceftobiprole has a 2-fold higher breakpoint.
- There were no changes in susceptibility of ceftaroline and ceftobiprole among *S. aureus* and pneumococci across the 10 years (2008-17).
- Changes in ceftobiprole MICs in CoNS were not due to changes in species distribution.
- Ceftobiprole MICs for MR-*S. haemolyticus* were >2mg/L in 22/33 (67%) cases compared with 2/215 (0.9%) MR-*S. epidermidis*.
- Ceftaroline MICs were also raised for MR-*S. haemolyticus* at 2mg/L.
- Choices regarding which agent to prefer should be predicated on other differentiating factors, e.g. licensed indications, reported clinical experience, and breadth of Gram-negative coverage.
- Continued collection of surveillance data is crucial for our understanding of antibiotic resistance trends in the UK and Ireland.

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- 6) [http://www.eucast.org/clinical\\_breakpoints](http://www.eucast.org/clinical_breakpoints).