## Multidrug-Resistant *Streptococcus* pneumoniae Infections

## **Current and Future Therapeutic Options**

Françoise Van Bambeke,<sup>1</sup> René R. Reinert,<sup>2</sup> Peter C. Appelbaum,<sup>3</sup> Paul M. Tulkens,<sup>1</sup> and Willy E. Peetermans<sup>4</sup>

1 Unité de Pharmacologie Cellulaire et Moléculaire, Université Catholique de Louvain, Brussels, Belgium

2 Institute for Medical Microbiology, National Reference Center for Streptococci, University Hospital (RWTH), Aachen, Germany

3 Department of Pathology, Hershey Medical Center, Hershey, Pennsylvania, USA

4 Department of Internal Medicine-Infectious Diseases, Katholieke Universiteit Leuven, University Hospital Gasthuisberg, Leuven, Belgium

## **Supplementary Material**

This supplementary material contains the figures referred to in the full version of this article, which can be found at http://drugs.adisonline.com.

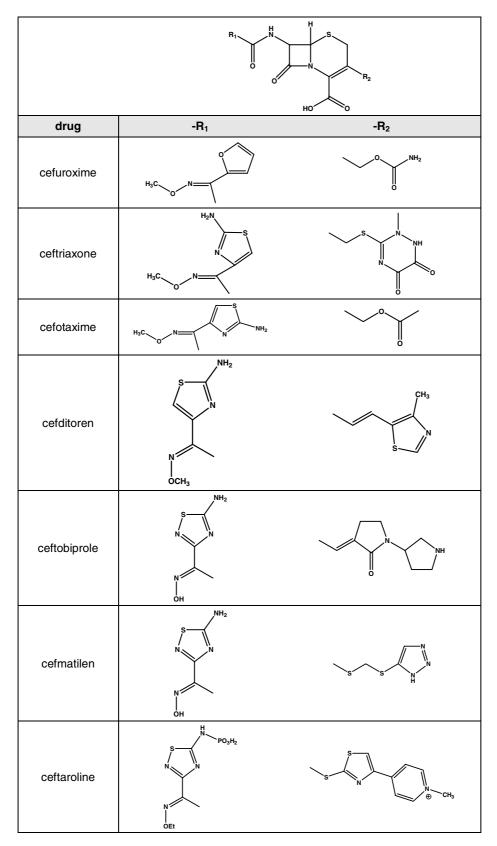
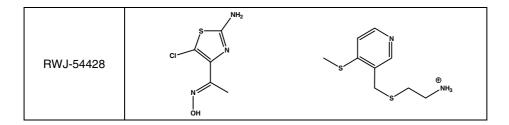


Figure 1. Chemical structures of reference cephalosporins and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae*.



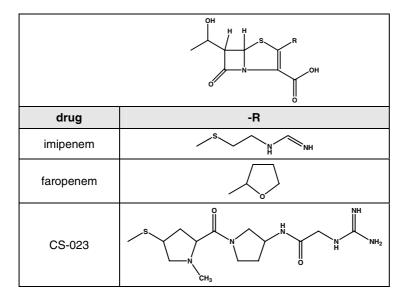


Figure 2. Chemical structures of a reference carbapenem and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae*.

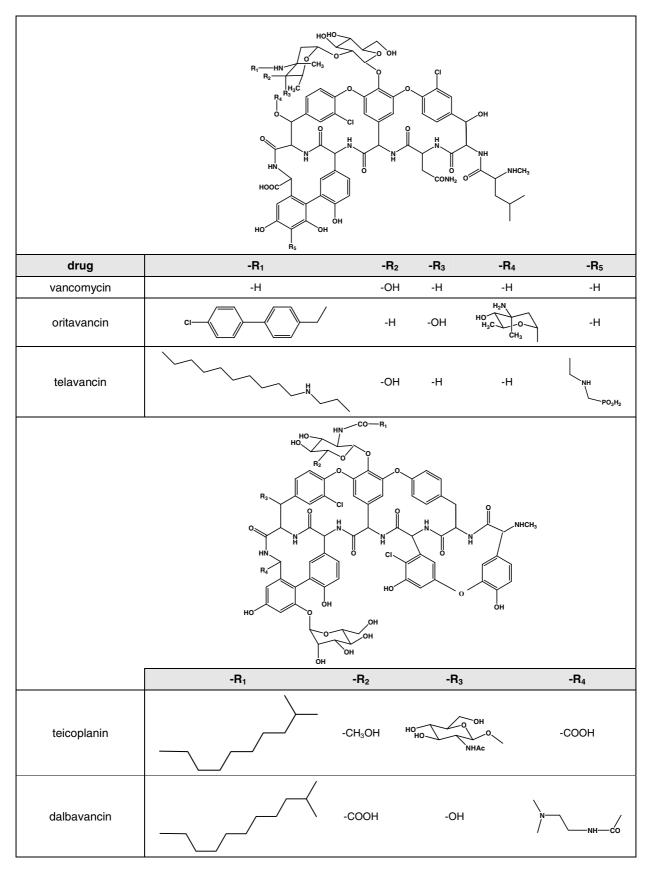


Figure 3. Chemical structures of reference glycopeptides and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae*.

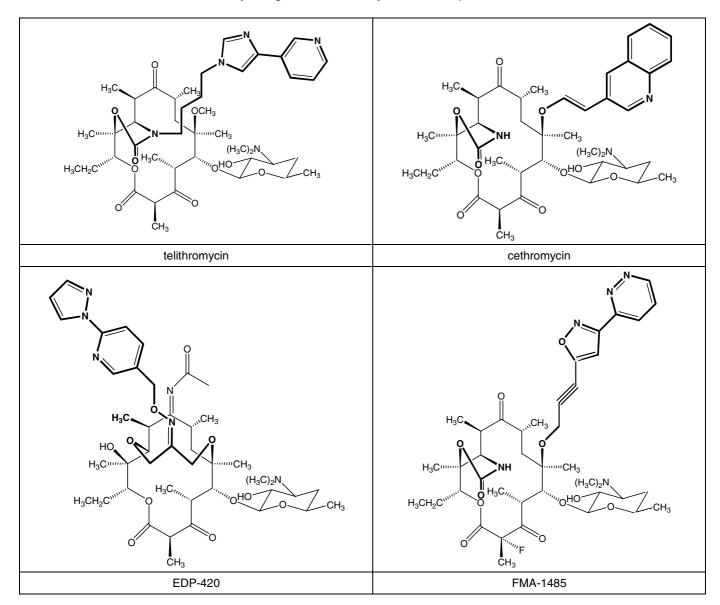
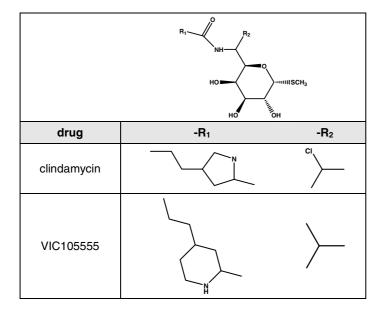


Figure 4. Chemical structures of a reference ketolide and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae.* 

Figure 5. Chemical structures of a reference lincosamide and of a derivative in development that is characterised by a high *in vitro* activity towards *S. pneumoniae*.



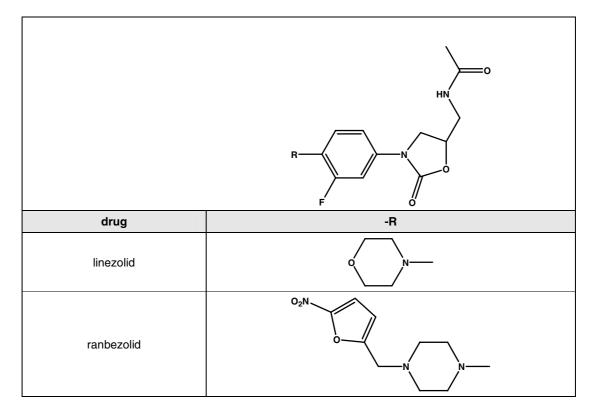


Figure 6. Chemical structures of a reference oxazolidinone and of a derivative in development that is characterised by a high *in vitro* activity towards *S. pneumoniae*.

$\begin{array}{ c c c c c c c c c c c c c c c c c c c$								
drug	-R4	-R3	-R2	-R1				
tetracycline	-H	-OH	-H	-H				
doxycycline	-H	$-CH_3$	-H	-OH				
tigecycline		-H	-N(CH <sub>3</sub> ) <sub>2</sub>	-CH₃				
PTK-0796		-H	-N(CH <sub>3</sub> ) <sub>2</sub>	-CH₃				

Figure 7. Chemical structures of reference tetracyclines and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae*.

			R <sub>5</sub> R <sub>7</sub> K <sub>8</sub>		соон	
drug	Х	-R <sub>8</sub>	-R <sub>1</sub>	-R₅	-R <sub>6</sub>	- <b>R</b> <sub>7</sub>
levofloxacin		C CH3		-H	-F	N
moxifloxacin	С	-O-CH₃	$\downarrow$	-H	-F	H H
gemifloxacin	Ν		$\downarrow$	-H	-F	NH <sub>2</sub>
garenoxacin	С	-O-CHF <sub>2</sub>	$\square$	-H	-H	HN
sitafloxacin	С	-Cl	F	-H	-F	H <sub>2</sub> N
WCK-771		CC N CC CH <sub>3</sub>		-H	-F	HO-NN
WCK-1152	С	-O-CH₃	$\downarrow$	-H	-F	
WCK-1153	С	-O-CH₃	${\frown}$	-H	-F	H <sub>3</sub> C H <sub>3</sub> H <sub>2</sub> N N
DX-619	С	-O-CH <sub>3</sub>	F	-H	-F	NH <sub>2</sub>
DK-507k	С	-O-CH₃	F	-H	-F	H <sub>2</sub> N
DC-159a	С	-O-CH₃	F	-H	-F	NH2 NH2

Figure 8. Chemical structures of reference quinolones and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae.* 

DW-224a	N		$\land$	-H	-F	HN
PGE 9262932	С	-O-CH₃	$\land$	-H	-F	H H
olamufloxacin	С	-CH <sub>3</sub>	$\downarrow$	-NH₂	-F	H <sub>2</sub> N

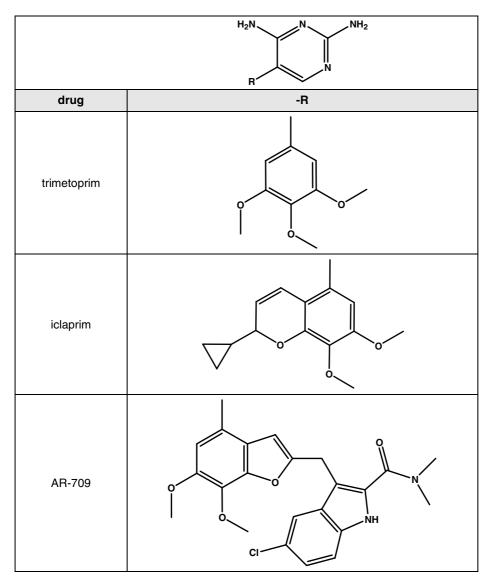


Figure 9. Chemical structures of a reference diaminopyridine and of derivatives in development that are characterised by a high *in vitro* activity towards *S. pneumoniae*.