

Rule No.	Organism(s)	Indicator Agent	Agents Affected	Rule	Remarks	Grade	References
<b>Beta-lactams</b>							
1	<i>Haemophilus influenzae</i>	benzylpenicillin (disk diffusion) screening test	other beta-lactams	IF susceptible in the benzylpenicillin screening test THEN report all indicated beta-lactams susceptible;  IF resistant in the benzylpenicillin screening test THEN follow the <i>H. influenzae</i> flow chart in breakpoint table.	Resistance to benzylpenicillin will detect all relevant resistance mechanisms to beta-lactam agents in <i>Haemophilus influenzae</i> , it does not, however, distinguish between resistance caused by PBP mutations and/or beta-lactamase	A	Skaare et al., 2015
<b>Fluoroquinolones</b>							
2	<i>Haemophilus influenzae</i>	nalidixic acid screening test	all fluoroquinolones	IF susceptible in the nalidixic acid screening test THEN report susceptible to all indicated fluoroquinolones;  IF resistant in the nalidixic acid screening test, THEN report resistant to ciprofloxacin, levofloxacin and moxifloxacin, OR determine the susceptibility of the agent to be used in therapy AND if susceptible add a cautionary remark that resistance may develop during therapy.	Decreased susceptibility to fluoroquinolones in <i>H. influenzae</i> due to target topoisomerase mutations can be more reliably detected in tests with nalidixic acid. First step mutants show MICs between 0.125 and 1mg/L. High-level fluoroquinolone resistance in this organism has rarely been described. Until there is evidence of clinical significance of these isolates they should be reported as resistant	C	Puig et al., 2015; Shoji et al., 2014
<b>Tetracyclines</b>							
3	<i>Haemophilus influenzae</i>	Tetracycline	doxycycline minocycline	IF susceptible to tetracycline THEN report doxycycline and minocycline susceptible.  IF resistant to tetracycline THEN report doxycycline and minocycline resistant OR determine the susceptibility of the agent to be used in therapy.	Implicit rule from breakpoint table	C	

**References**

- Puig C, Tirado-Vélez JM, Calatayud L, Tubau F, Garmendia J, Ardanuy C, et al. Molecular characterization of fluoroquinolone resistance in nontypeable *Haemophilus influenzae* clinical isolates. *Antimicrob Agents Chemother*. 2015; 59(1):461-6. DOI: 10.1128/AAC.04005-14
- Shoji H, Shirakura T, Fukuchi K, Takuma T, Hanaki H, Tanaka K, et al. A molecular analysis of quinolone-resistant *Haemophilus influenzae*: validation of the mutations in Quinolone Resistance-Determining Regions. *J Infect Chemother*. 2014; 20(4):250-5. DOI: 10.1016/j.jiac.2013.22.007.
- Skaare D, Lia A, Hannisdal A, Tveten Y, Matuschek E, Kahlmeter G, et al. *Haemophilus influenzae* with Non-Beta-Lactamase-Mediated Beta-Lactam Resistance: Easy To Find but Hard To Categorize. *J Clin Microbiol*. 2015; 53(11):3589-95. DOI: 10.1128/JCM.01630-15
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