

THE LABORATORY SUSCEPTIBILITY TESTING LEAFLET

ANTIBIOTIC SUSCEPTIBILITY TESTING WITH DACI

INTRODUCTION

Daci is indicated for the treatment of the following infections.

- Adult and pediatric (1 to 17 years of age) patients with complicated skin and soft-tissue infections (cSSTI).

- Adult patients with right-sided infective endocarditis (RIE) due to *Staphylococcus aureus*. It is recommended that the decision to use daptomycin should take into account the antibacterial susceptibility of the organism and should be based on expert advice.

Adult and pediatric (1 to 17 years of age) patients with *Staphylococcus aureus* bacteraemia (SAB)

In adults, use in bacteraemia should be associated with RIE or with cSSTI, while in pediatric patients, use in bacteraemia should be associated with cSSTI.

Daptomycin is active against Gram-positive bacteria only. In mixed infections where Gram-negative and/or certain types of anaerobic bacteria are suspected, Daptomycin should be co-administered with appropriate antibacterial agent(s).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

THE EFFECT OF Ca²⁺ ON SUSCEPTIBILITY TESTING

Daci activity is dependent on the physiological Ca²⁺ concentration.

Other divalent and monovalent cations have negligible effect on Daci activity.

A Ca²⁺ concentration of 50 µg /ml (1.1 mM) in growth media provides the optimal determination of the Daptomycin minimum inhibitory concentration (MIC) and correlates with the physiological levels of free Ca²⁺ in human plasma (1.15 – 1.31 mM)

Reliable in vitro susceptibility testing of Daptomycin will therefore require the appropriate standardisation of the test media to 50 µg/ml Ca²⁺

SUMMARY OF DAPTOMYCIN SUSCEPTIBILITY TESTING METHODS

RECOMMENDED METHODS FOR DAPTOMYCIN SUSCEPTIBILITY TESTING

<p>Broth Microdilution (BMD)</p>	<p>The BMD method is the Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommended method for determining MIC and susceptibility of pathogens to Daptomycin</p> <p>Follow CLSI-approved method using Mueller-Hinton broth (with or without 2-5% lysed horse blood) adjusted to 50 µg /ml Ca²⁺</p> <p>MIC determination using broths other than Mueller-Hinton broth have not been validated</p>
<p>fE test *</p>	<p>Daptomycin e-test strips (BioMerieux SA) which contain a constant Ca²⁺ level throughout the Daptomycin gradient are also a recommended method.</p> <p>Ca²⁺ content in the agar is essential and should be in the range 25-40 µg/ml</p> <p>The Daptomycin e-test strips are suitable for use on Mueller-Hinton agar (note BBLTM Mueller-Hinton agar is recommended because the Ca²⁺ concentration is consistently within the required range)</p>

* For further information and local distributor contact details go to www.biomerieux-diagnostics.com/etest

NON-RECOMMENDED METHODS FOR SUSCEPTIBILITY TESTING

Agar dilution	<p>This method is not recommended because there is no agar with consistent Ca²⁺ concentrations that is also appropriate for Daptomycin testing. Supplementation of agar with Ca²⁺ is problematical and not recommended</p> <p>The variability in Ca²⁺ concentrations of agar between different batches and manufacturers makes this method unpredictable</p>
Disc diffusion	<p>A 30 µg disc was withdrawn from the US market due to problems in distinguishing resistant isolates from susceptible strains</p> <p>This method is currently not recommended</p>

EU-CAST APPROVED INTERPRETATIVE CRITERIA

Gram-positive organism	Susceptible	Resistant
Staphylococcus spp.	≤ 1 µg /ml	> 1 µg/ml
Streptococcus spp. Groups A,B,C and G(excluding S. pneumoniae)	≤ 1 µg /ml	> 1 µg/ml

Susceptibility to Daptomycin – of 2977 European Gram-positive isolates tested in a 2011 European surveillance programme 99.9% were susceptible to Daptomycin.

FURTHER INFORMATION BEFORE PRESCRIBING DACI PLEASE ENSURE THAT YOU REFER TO THE SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Reporting of suspected adverse reactions

Please continue to report suspected adverse drug reactions (ADRs) including medication errors (any errors while prescribing, preparing or administering the drug).

Please report all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

When making a report please provide us with as much information as possible, including the method of dilution, the dose administered and any side effects, medical history, concomitant medications etc.

References

2- Medicines.org.uk. (2019). Cubicin (daptomycin): Important safety information to minimise the risk of reduced susceptibility of S.aureus to daptomycin-The Laboratory Susceptibility Testing Leaflet. [online] Available at: <https://www.medicines.org.uk/emc/rmm/629/Document> [Accessed 27 Jun. 2019]

FOR MORE INFORMATION AND FOR ADVERSE EVENT REPORTING YOU CAN CONTACT US*

Pharmacovigilance department / MS Pharma Saudi
King Abdulaziz road - Alrabaa District - Grand Center 1st floor – Front of Kingdom Hospital
P.O Box 47315 Riyadh, 13456 Saudi Arabia
Phone: + 966112790122 Ext. 6013 - Fax: +966112471323 - Mobile : + 966548933555

The National Pharmacovigilance Centre (NPC) Saudi Food and Drug Authority (SFDA)
SFDA call center: 19999
Toll free phone: 8002490000 - Fax: +966-11-2057662
E-mail: npc.drug@sfd.gov.sa - Website: <http://ade.sfd.gov.sa/>

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