

!" #&/
4;O <548G=>3> 70AB>AC20==O ;V:0@AL:>3> 70A>1C

" !
(ZITHROX)

!::04:

4VNG0 @5G>28=0: Ozithromycin;

1 B01;5B:0 078B@>

4>?>28=8: :0;LFVN 3V4@>D>AD0B, :@>E<0;L ?@565;0B8=V7>20=89, :@>A?>2V4=>, ?>;VA>@10B 80,
:@5<=VN 4V>:A84 :>;>W4=89 1572>4=89, F5;N;>70 :@8AB0;VG=0, =0B@VN ;0C@8;AC;LD0B, B0;L.;
<03=VN AB50@0B, 3V?@><5;>70, B8B0=C 4V>:A84 (171), ?>;V5B8;5=3;V:>;L 400.

V:0@AL:0 D>@<0. "01;5B:8, 2:@8BV >1>;>=:>N.

A=>2=V DV78:>-EVABV:

B01;5B:8 ?> 250 <3: 1V;V, 42>>?C;;V B01;5B:8, :0?AC;>?>4V1=>W D>@<8, 2:@8BV >1>;>=:>N,
3;045=L:V 7 >1>E 1>:V2;

B01;5B:8 ?> 500 <3: 1V;V, 42>>?C;;V B01;5B:8, :0?AC;>?>4V1=>W D>@<8, 2:@8BV >1>;>=:>N, 7
;V=VTN @>7;>4=>3> 1>:C B0 3;045=L:V 7 V=H>3>.

\$0@<0:>B5@0?52B8G=0 3@C?0.

=B810:B5@V0;L=V 70A>18 4;O A8AB5<=>3> 70AB>AC20==O. 0:@>;V48, ;V=:>703@04 "% J01F A10.

\$0@<0:>;>3VG=V 2;0AB82>ABV.

\$0@<0:>48=0

78B@>CB2>@NTBLAO C @57C;LB0BV 22545==O 0B><0 07>BC 2 ;0:B>=>25 :V;LF5 5@8B@>;O30T 2
V=3V1C20==V A8=B57C 10:B5@V0;L=>3> 1V;:0 70 @0EC=>: 72'O7C20==O 7 50 S-AC1>48=8F5N
@81>A>< V ?@83=VG5==O B@0=A;>:0FVW ?5?B84V2.

5E0=V7< @578AB5=B=>ABV.

>2=0 ?5@5E@5A=0 @578AB5=B=VABL VA=CT A5@54Streptococcus pneumoniae, 15B0-35<>;VB8G=>3>

AB@5?B>:>:C 3@C?8 , Enterococcus faecalisB0 Staphylococcus aureus, 2;;NG0NG8 <5B8F8;V=-

@578AB5=B=89 7;>;>B8AB89 AB0DV;>:>: (MRSA), 4> 5@8B@>

>H8@5=VABL =01CB>W @578AB5=B=>ABV<>65 1CB8 @V7=>N 70;56=> 2V4 ABV V G0AC 4;O

284V;5=8E 284V2, B>:0;L=0 V=D>@<0FVO ?@> @578AB5=B=VABL =5>1EV4=0 >A>1;82> ?@8

;V:C20==V BO6:8E V=D5:FV9. # @07V =5>1EV4=>ABV<>6=0 725@=CB8AO 70 :20;VDV:>20=>N

?>@04>N, O:I> H8@5=VABL @578AB5=B=>ABV T B0:>N, :>;8 5D5:B82=VABL ?@5?0@0BC ?@8

;V:C20==V ?@8=09<=V 450:8E B8?V2 V=D5:FV9 T AC<=V2=>N.

!?:B@ 0=B81=>W 4VW 078B@>

0728G09 GCB;82V 2848
5@>1=V 3@078B82=V 10:B5@VW
Staphylococcus aureus<5B8F8;V=-GCB;8289
Streptococcus pneumoniae?5=VF8;V=-GCB;8289
Streptococcus pyogenes
5@>1=V 3@0<=530B82=V 10:B5@VW
Haemophilus influenzae
Haemophilus parainfluenzae
Legionella pneumophila
Moraxella catarrhalis
Pasteurella multocida
=05@>1=V 10:B5@VW
Clostridium perfringens
Fusobacterium spp.

<i>Prevotella spp.</i>
<i>Porphyriomonas spp.</i>
=HV >@30=V7<8
<i>Chlamydia trachomatis</i>
<i>Chlamydia pneumoniae</i>
<i>Mycoplasma pneumoniae</i>
848, 4;O O:8E =01CB0 @578AB5=B=VABL <>65 1CB8 ?@>1;5<>N
5@>1=V 3@078B82=V 10:B5@VW
<i>Streptococcus pneumoniae</i> 7 ?@>N GCB;82VABN 4> ?5=VF8;V=C V ?5=VF8;V=- @578AB5=B=89
@>465=>@578AB5=B=V >@30=V7<8
5@>1=V 3@078B82=V 10:B5@VW
<i>Enterococcus faecalis</i>
!B0DV;>:>:8 MRSA, MRSE*
=05@>1=V 10:B5@VW
@C?0 10:B5@>W4V2 Bacteroides fragilis

*5B8F8;V=-@578AB5=B=89 7>;>B8AB89 AB0DV;>:>:<0T 4C65 28A>:C ?>H8@5=VABL =01CB>W ABV9:>ABV
4> <0:@>;V4V2 V 1C2 707=0G5=89 BCB G5@57 @V4:VA=C GCB;82VABL 4> 078B@>

\$0@<0:>:V=5B8:0.

V>4>ABC?=VABL ?VA;O ?5@>@0;L=>3> ?@89>28BL ?@81;87=> 37 %. 0:A8<0;L=0 :>=F5=B@0FVO C
A8@>20BFV :@>2V 4>AO30TBLAO G5@57 2-3 3>48=8 ?VA;O ?@89>

@8 2=CB@VH=L>7?>4V;OTBLAO ?> 2AL>@30=V7 28IO (2 50 @07V2), =V6 C ?;072V, I> A2V4G8BL
?@> A8;L=5 72'07C20==O ?@5?0@0BC 7 B:0=8=0<8.

2'07C20==O 7 1V;;<8 A8@>20B:8 :@>2V 20@VNT 70;56=> 2V4 ?;07<>28E :>=F5=B@0FV9 V
AB0=>28BL 2V4 12 % ?@8 0,5 ss) AB0=>282 31,1 ;/:3.

V=F5289 ?5@V>4 ?;07<>2>3> =0?V2282545==O ?>2=VABN 2V4>1@060T ?5@V>4 =0?V2282545==O 7
B:0=8= C?@>4>26 2-4 4=V2.

@81;87=> 12 % 2=CB@VH=L>25==>W 4>78 078B@>3> 078B@>2GV ;N48=8. "0:>6 C 6>2GV 1C;8
28O2;5=V 10 <5B01>;VBV2, O:V CB2>@N20;8AL 70 4>?<>3>N N- B0 O-45<5B8;N20==O,

3V4@>:A8;N20==O :V;5FL 457>70=C V @>7I5?;5==O ;:04V=>78 :>='N30BC. >@V2=O==O

@57C;LB0BV2 @V48==>W E@><0B>3@0DVW B0 1V>;>3VG=8E 0=0;V7V2 ?>:070;>, I> <5B01>;VB8
078B@>1V>;>3VG=> 0:B82=8<8.

;V=VG=V E0@0:B5@8AB8:8.

>:070==O.

=D5:FVW, A?@8G8=5=V>@30=V7<0<8, GCB;828<8 4> 078B@>

V=D5:FVW ->@30=V2 (10:B5@V0;L=89 D0@8=3VB/B=>78;VB, A8=CA8B, A5@54=V9 >B8B);

V=D5:FVW 48E0;L=8E H;OEV2 (10:B5@V0;L=89 1@>=EVB, =53>A?VB0;L=0 ?=52<>=VO);

V=D5:FVW H:V@8 B0 <O:8E B:0=8=: @8==V ?V>45@<0B>78; 0:=5 2C;L30@VA (2C3@V 728G09=V)

A5@54=L>3> ABC?5=O BO6:>ABV;

V=D5:FVW, I> ?5@540NBLAO AB0B528< H;OE>*Chlamydia trachomatis*.

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> 078B@>4> 1C4L-O:>3> <0:@>;V4=>3> 01> :5B>;V4=>3> 0=B81V>B8:0, 01>
4> 1C4L-O:>3> V=H>3> :>=5=B0 ?@5?0@0BC.

'5@57 B5>@5B8G=C <>6;82VABL 5@3>B874=>G0A=> 7 ?>EV4=8<8 @V6:V2.

70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.

!;V4 >15@56=> ?@87=0G0B8 078B@>

=B0F848. @8 282G5==V 2?;82C >4=>G0A=>3> 70AB>AC20==O 0=B0F84V2 =0 D0@<0:>:V=5B8:C

078B@><=5 A?>AB5@V30;>AO 74>ABC?=>ABV, E>G0 ?;07<>2V ?V:>2V :>=F5=B@0FVW 078B@>

1EV4=> ?@89<0B8 ?@8=09<=V 70 1 3>48=C 4> 01> G5@57 2 3>48=8 ?VA;O ?@89>

&5B8@878=. # 74>@>28E 4>1@>2>;LFV2 ?@8 >4=>G0A=>AC20==V 078B@>4>26 5 4=V2 V7
F5B8@878=>< 20 <3 C @V2=>206=>AB5@V30;8AL O28I0 D0@<0>:V=5B8G=>W 270T<>4VW G8
ACBBT2V 7
840=>78=. @8 >4=>G0A=>AC20==V 4>1>28E 4>7 C 1200 <3 078B@>78=>< =5 1C;> 28O2;5=> 2?;82C =0
D0@<0>:V=5B8:C 4840=>78=C ?>@V2=O=> 7 ?;0F51>.
83>:A8=. >2V4><;O;>AO, I> AC?CB=T 70AB>AC20==O <0:@>;V4=8E 0=B81V>B8:V2, 2;:NG0NG8
078B@>?@>B5W=C, B0:8E O: 483>:A8=, ?@872>48BL 4> ?V428I5==O @V2=O AC1AB@0BC -
3;V:>?@>B5W=C 2 A8@>20BFV :@>2V. B65, ?@8 AC?CB=L>AC20==V 078B@>:A8=C =5>1EV4=>
2@0E>2C20B8 <>6;82VABL ?V428I5==O :=F5=B@0FVW 483>:A8=C 2 A8@>20BFV :@>2V.
84>2C48=. 4=>@07>2V 4>78 1000 <3 B0 1200 <3 01> 600 <3 1030B>@07>2V 4>78 078B@>
=F5=B@0FVW D>AD>@8;L>20=>3> 784>2C48=C, ;:V=VG=> 0:B82=>3> <5B01>;VBC, 2
<=>=C;:50@0E C ?5@8D5@8G=>2>>1V3C. ;V=VG=0 7=0GCIVABL F8E 40=8E =5 7'OA>20=0, 0;5<>65
1CB8 :>@8A=>N 4;O ?0FVT=BV2.
>EV4=V @V6:V2. 7 >3;O4C =0 B5>@5B8G=C <>6;82VABL 28=8:=5==O 5@3>B874=>G0A=5 22545==O
078B@>EV4=8<8 @V6:V2 =5 @5:><5=4CTBLAO.
78B@> ?@5?0@0B =5 <0T D0@<0>:V=5B8G=>W ;V:0@AL:>W 270T<>4VW, I> A?>AB5@V30TBLAO 7
5@8B@>< B0 V=H8<8 <0:@>;V40<8. 78B@> V=0:B820FVN ?5GV=:>2>3> F8B>E@>E@>
C;8 ?@>2545=V D0@<0>:V=5B8G=V 4>A;V465==O 70AB>AC20==O 078B@>N 2V41C20TBLAO 7
CG0ABN F8B>E@>
B>@20AB0B8=. >4=>G0A=5 70AB>AC20==O 0B>@20AB0B8=C (10 <3 =0 4>1C) B0 078B@>
=F5=B@0FV9 0B>@20AB0B8=C C ?;072V (=0 >A=>2V 0=0;V7C V=3V1C20==O ->.@54C:B078).
0@10<075?V=. # 4>A;V465==V D0@<0>:V=5B8G=>W 270T<>4VW C 74>@>28E 4>1@>2>;LFV2
078B@>3> 2?;82C =0 ?;07<>2V @V2=V :0@10<075?V=C 01> =0 9>3> 0:B82=V <5B01>;VB8.
&8<5B848=. # D0@<0>:V=5B8G=>A;V465==V 2?;82C >4=>:@0B=>W 4>78 F8<5B848=C, ?@89=OB>W
70 2 3>48=8 4> ?@89>4=8E 7AB5@V30;>AO.
5@>@0;L=V 0=B8:>03C;O=B8 B8?C :C<0@8=C. # 4>A;V465==V D0@<0>:V=5B8G=>W 270T<>4VW
078B@>03C;O=B=89 5D5:B >4=>@07>2>W 4>78 15 <3 20@D0@8=C, ?@87=0G5=>3> 74>@>28<
4>1@>2>;LFOB@8<0=V ?>2V4><;5==O ?@> ?>B5=FN20==O 0=B8:>03C;O=B=>3> 5D5:BC ?VA;O
>4=>G0A=>3> 70AB>AC20==O 078B@>@0;L=8E 0=B8:>03C;O=V2 B8?C :C<0@8=C. %>G0
?@8G8==89 72'07>: 2AB0=>2;5=89 =5 1C2, A;V4 2@0E>2C20B8 =5>1EV4=VABL ?@>2545==O G0AB>3>
<=>VB>@8=3C ?@>B@><1V=>2>3> G0AC ?@8 ?@87=0G5==V 078B@>@0;L=V 0=B8:>03C;O=B8 B8?C
:C<0@8=C.
?>A?>@8=. 5O:V 7V A?>@V4=5=8E<0:@>;V4=8E 0=B81V>B8:V2 2?;820NBL =0 <5B01>;V7<
F8;:>A?>@8=C. A:V;L:8 =5 1C;> ?@>2545=> D0@<0>:V=5B8G=8E V ;:V=VG=8E 4>A;V465=L <>6;82>W
270T<>4VW ?@8 >4=>G0A=>A?>@8=C, A;V4 @5B5;L=> 72068B8 B5@0?52B8G=C A8BC0FVN 4>
?@87=0G5==O >4=>G0A=>3> ?@89>1V2. /:I> :<1V=>20=5 ;V:C20==O 22060TBLAO 28?@0240=8<,
=5>1EV4=> ?@>2>48B8 @5B5;L=89 <=>VB>@8=3 @V2=V2 F8;:>A?>@8=C V 2V4?>2V4=>
@53C;N20B8 4>7C20==O.
D02V@5=F. 4=>G0A=5 70AB>AC20==O >4=>@07>2>W 4>78 078B@>
\$;C:>=07>;. >4=>G0A=5 70AB>AC20==O >4=>@07>2>W 4>78 078B@>4=>G0A=>AC20==V
D;C:>=07>;C, ?@>B5 A?>AB5@V30;>AO ;:V=VG=> =57=0G=5 7=865==O <0:A8<0;L=>W
:=F5=B@0FVW 078B@>
=48=02V@. >4=>G0A=5 70AB>AC20==O >4=>@07>2>W 4>78 078B@>
5B8;?@54=V7>;>=. # 4>A;V465==V D0@<0>:V=5B8G=>W 270T<>4VW C 74>@>28E 4>1@>2>;LFV2
078B@> =5 2?;8202 =0 D0@<0>:V=5B8:C <5B8;?@54=V7>;>=C.
V407>;0<. # 74>@>28E 4>1@>2>;LFV2 >4=>G0A=5 70AB>AC20==O 078B@>;0
5;DV=02V@. >4=>G0A=5 70AB>AC20==O 078B@> 7=0GCI8E ?>1VG=8E O28I =5 A?>AB5@V30;>AO,
2V4?>2V4=>, =5<0T ?>B@518 C @53C;N20==V 4>78.
8D01CB8=. 4=>G0A=5 70AB>AC20==O 078B@> =0 :=F5=B@0FVW F8E ?@5?0@0BV2 C A8@>20BFV
:@>2V. 59B@>?5=VO A?>AB5@V30;0AL C ?0FVT=BV2, O:V ?@89<0;8 >4=>G0A=> 078B@>G0
=59B@>?5=VO 1C;0 ?>2'070=0 V7 70AB>AC20==O< @8D01CB8=C, ?@8G8==89 72'07>: 7 >4=>G0A=8<
?@89><<< 078B@>2;5=89.
!8;45=0DV;. # 728G09=8E 74>@>28E 4>1@>2>;LFV2 G>;>2VG>W AB0BV =5 1C;> >B@8<0=> 4>:07V2
2?;82C 078B@>

"5@D5=048=. # D0@<0>:V=5B8G=8E 4>A;V465==OE =5 ?>2V4<<O;>AO ?@> 270T<>4VN < V B5@D5=048=>

"5>DV;V=. V4ACB=V 40=V I>4> ;;V=VG=> ACBBT2>W D0@<0>:V=5B8G=>W 270T<>4VW ?@8 >4=>G0A=>AC20==V 078B@>DV;V=C.

"@V07>;0<. 4=>G0A=5 70AB>AC20==O 078B@> =5 2?;820;> =0 2AV D0@<0>:V=5B8G=V ?>:07=8:8 B@V07>;0@V2=O=> 7 B@V07>;0<< V ?;0F51>.

"@8<5B>?@8. >4=>G0A=5 70AB>AC20==O B@8<5B>?@8< 1200 <3 =0 7-1C =5 28O2;O;> ACBBT2>3> 2?;82C =0 <0:A8<0;L=V :=F5=B@0FVW, 7030;L=C 5:A?>78FVN 01> 5:A:@5FVN V7 A5G5N B@8 <5B>?@8 AC;LD0<5B>:A07>;C. =0G5==O :=F5=B@0FV9 078B@>20BFV :@>2V 2V4?>2V40;8 B0:8<, O:V A?>AB5@V30;8AO 2 V=H8E 4>A;V465==OE.

A>1;82>ABV 70AB>AC20==O.

;5>@3VG=V @50:FVW. !: V C 28?04:C 7 5@8B@< B0 V=H8<8 <0:@>;V4=8<8 0=B81V>B8:0<8, ?>2V4<<O;>AO ?@> @V4:VA=V A5@9>7=V 0;5@3VG=V @50:FVW, 2::NG0NG8 0=3V>=52@>B8G=89 =01@O: B0 0=0DV;0:AVN (C ?>>48=>:8E 28?04:0E □ 7 ;5B0;L=8< =0A;V4:><). 5O:V 7 F8E @50:FV9, A?@8G8=5=8E 078B@<, A?@8G8=O;8 @5F8482=V A8<8 V ?>B@51C20;8 B@820;VH>3> A?>AB5@565==O V ;V:C20==O.

>@CH5==O DC=:FVW ?5GV=:8. A:V;L:8 ?5GV=:0 T >A=>2=8< H;OE<< 282545==O 078B@>A;V4 >15@56=> ?@87=0G0B8 078B@>3> 35?0B8BC, I> A?@8G8=OT =5157?5G=5 4;O 68BBO ?>@CH5==O DC=:FV9 ?5GV=:8, ?@8 ?@89>6;82>, 45O:V ?0FVT=B8 2 0=0<=57V <0;8 70E2>@N20==O ?5GV=:8 01> 70AB>A>2C20;8 V=HV 35?0B>B>:A8G=V ;V:0@AL:V 70A>18.

5>1EV4=> ?@>2>48B8 0=0;V78/?@>18 DC=:FVW ?5GV=:8 C 28?04:C @>728B:C >7=0: V A8H284:> @>72820TBLAO V AC?@>2>46CTBLAO 6>2BO=8F5N, B5<=>N A5G5N, AE8;L=VABN 4> :@>2>B5G 01> ?5GV=:2>N 5=F5D0;>?0BVTN.

@07V 28O2;5==O ?>@CH5==O DC=:FVW ?5GV=:8 70AB>AC20==O 078B@> >EV4=V @V6:V2. # ?0FVT=BV2, O:V ?@89<0NBL ?>EV4=V @V6:V2, >4=>G0A=5 70AB>AC20==O 45O:8E <0:@>;V4=8E 0=B81V>B8:V2 A?@8OT H284:>728B:C 5@3>B874> <>6;82>ABV 270T<>4VW B5 G5@57 B5>@5B8G=C <>6;82VABL 5@3>B87 078B@>4=>G0A=> 7 ?>EV4=8<8 @V6:V2. !C?5@V=D5:FVW. !: V C 28?04:C 7 V=H8<8 0=B81V>B8:0<8, @5:><5=4CTBLAO ?@>2>48B8 A?>AB5@565==O I>4> >7=0: AC?5@V=D5:FVW, A?@8G8=5=>W =5GCB;828<8 >@30=V7<0<8, 2::NG0NG8 3@81:8.

@8 ?@89>2V4<<O;>AO ?@> *Clostridium difficile*0A>FV9>20=C 4V0@5N (CDAD), A5@9>7=VABL O:>W 20@VN20;0AO 2V4 A;01:> 28@065=>W 4V0@5W 4> :>;VBC 7 ;5B0;L=8< =0A;V4:>@<0;L=C D;>@C 2 B>2ABV9 :8HFV, I> ?@872>48BL 4> =043> @>ABC *C. difficile*

C. difficile?@>4C:CT B>:A8=8 V , O:V A?@8ONBL @>728B:CCDAD. (B0<8 *C. difficile*, I> 3V?5@?@>4C:CNBL B>:A8=8, T ?@8G8=>N ?V428I5=>3> @V2=O 70E2>@N20=>ABV V ;5B0;L=>ABV, >A:V;L:8 FV V=D5:FVW <>6CBL 1CB8 @578AB5=B=8<8 4> 0=B81=>W B5@0?VW V ?>B@51C20B8 ?@>2545==O :>;5:B>1EV4=> @>73;O=CB8 <>6;82VABL @>728B:CCDAD C 2AVE ?0FVT=BV2 7 4V0@5TN, A?@8G8=5=>N 70AB>AC20==O< 0=B81V>B8:V2. >B@V1=> @5B5;L=5 2545==O VAB>@VW E2>@>18, >A:V;L:8, O: ?>2V4<<O;>AO, CDAD <>65 <0B8 4>26 2

>@CH5==O DC=:FVW =8@>: # ?0FVT=BV2 V7 A5@9>7=>N 48ADC=:FVTN =8@>: (H284:VABL ;;C1>G:>2>W DV;LB@0FVW < 10 <;/E2) A?>AB5@V30;>AO 33 % 71V;LH5==O A8AB5<=>W 5:A?>78FVW 7 078B@>

>4>265==O A5@F52>W @5?>;O@870FVW B0 V=B5@20;C QT, O:V ?V428IC20;8 @878: @>728B:C A5@F52>W 0@8BBV==O<5@5EBV==O H:C=>G:V2 (*torsade de pointes*), A?>AB5@V30;8AO ?@8 ;V:C20==V V=H8<8 <0:@>;V4=8<8 0=B81V>B8:0<8. >4V1=89 5D5:B 078B@>15@56=VABN ?@87=0G0B8 ;V:C20==O ?0FVT=B0

7 2@>465=>N 01> 70@5TAB@>20=>N ?@>;>=30FVTN V=B5@20;C QT; O:V =0@07V ?@>E>4OBL ;V:C20==O V7 70AB>AC20==O< V=H8E 0:B82=8E @5G>28=, O:V, O: 2V4> <>, ?>4>26CNBL V=B5@20; QT, =0?@8::04, 0=B80@8B:0W=0D5BV;V4, 040@>= B0 A>B0;>;), F8A0?@84 V B5@D5=048=, =59@>;5?B8G=V 70A>18, B0:V O: ?V<>784; 0=B845?@5A0=B8, B0:V O: F8B0;>?@<0, 0 B0:>6 DB>@EV=>;>=8, B0:V O: <>:A8D;>:A0F8= B0 ;52>D;>:A0F8=;

7 ?>@CH5==O< 5;5:B@>;VB=>3> >1A>1;82> C 28?04:C 3V?>:0;VT<03=VT 7 ;;V=VG=> @5;520=B=>N 1@048:0@4VTN, A5@F52>N 0@8B BO6:>N A5@F52>N =54>AB0B=VABN. V0AB5=VO 3@02VA. >2V4<<O;>AO ?@> 703>AB@5==O A8 ?@> =>289 @>728B>: 3> A8=4@>B@8

!B@5?B>.:>:2V V=D5:FVW. □78B@>< 5D5:B82=89 C ;V:C20==V AB@5?B>.:>:2>W V=D5:FVW C
@>B>3;>BFV, AB>A>2=> ?@>DV;0:B8:8 @52<0B8G=>W 0B0:8 =5<0T 6>4=8E 40=8E, O:V 45
<=>AB@CNBL 5D5:B82=VABL 078B@>□=B81=89 ?@5?0@0B 7 0=05@>1=>N 0:B82=VABN =5>1EV4=>
?@89<0B8 2 :><1V=0FVW 7 078B@><, O:I> ?@8?CA:0TBLAO, I> 0=05@>1=V >@30=V7<8 7C
<>2;NNBL @>728B>: V=D5:FVW.
=H5.

57?5:0 B0 5D5:B82=VABL 4;O ?@>DV;0:B8:8 01> ;V:C20==OMycobacterium Avium Complex C 4VB59 =5
2AB0=>2;5=V.

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

03VB=VABL.

>A;V465==O 2?;82C =0 @5?@>4C:B82=C DC=:FVN B20@8= 1C;8 28:>=0=V ?@8 22545==V 4>7, I>
2V4?>2V40;8 ?>A;V465==OE =5 1C;> >B@8<0=> 4>:07V2 B>:A8G=>3> 2?;82C 078B@>1@5
:>=B@>;L>20=V 4>A;V465==O C 203VB=8E 6V=>.: A:V;L:8 4>A;V465==O 2?;82C =0 @5?@>4C:B82=C
DC=:FVN B20@8= =5 702648 2V4?>2V40NBL 5D5:BC C ;N48=8, 078B@>4 203VB=>ABV ;8H5 70
68BBT28<8 ?>:070==O<8.

3>4C20==O 3@C44N.

>2V4><;O;>AO, I> 078B@>=8:0T C <>.:> ;N48=8, 0;5 2V4?>2V4=8E B0 =0;56=8< G8=><
:>=B@>;L>20=8E ;V=VG=8E 4>A;V465=L, O:V 4020;8 1 <>6;82VABL >E0@0:B5@87C20B8 D0@
<0:>:V=5B8:C 5:A:@5FVW 078B@>4 3>4C20==O 3@C44N <>6;825 ;8H5 C 28?04:0E, :>;8 >GV:C20=0
:>@8ABL 4;O <0B5@V ?5@528ICT ?>B5=FV9=89 @878: 4;O 48B8=8.

\$5@B8;L=VABL.

>A;V465==O D5@B8;L=>ABV ?@>2>48;8 =0 IC@0E; ?>:07=8: 203VB=>ABV 7=8602AO ?VA;O
22545==O 078B@>A>2=> ;N48=8 =52V4><0.

40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B< 01> V=H8<8
<5E0=V7<0<8.
>:078 ?@> B5, I> 078B@>

!?!>AVI 70AB>AC20==O B0 4>78.

@5?0@0B >1>2O7:>2> =0;568BL ?@89<0B8 70 1 3>48=C 4> 01> 2 3>48=8 ?VA;O W48, B>>4=>G0A=89
?@89>< ?>@CHCT 2A<.:BC20==O 078B@>2B0B8, =5 @>76>2CNG8. @5?0@0B ?@89<0NBL 1 @07 =0
4>1C.

>@>A;V B0 4VB8 7 <0A>N BV;0 ≥ 45 :3.

@8 V=D5:FVOE ->@30=V2, 48E0;L=8E H;OEV2, H:V@8 B0 <'O:8E B:0=8=>(:@V< E@>=VG=>W W
5@8B5<8) 7030;L=0 4>70 078B@>28BL 1500 <3 (500 <3 1 @07 =0 4>1C). "@820;VABL ;V:C20==O
AB0=>28BL 3 4=V.

@8 0:=5 2C;L30@VA @5:><5=4>20=0 7030;L=0 4>70 078B@>28BL 6 3, O:C A;V4 ?@89<0B8 70 B0:>N
AE5<>N: 500 <3 1 @07 =0 4>1C ?@>BO3>< 3 4=V2, ?VA;O G>3> - 500 <3 1 @07 =0 B8645=L ?@>BO3><
9 B86=V2. >7C 4@C3>3> B86=O A;V4 ?@89<0B8 G5@57 7 4=V2 ?VA;O ?5@H>3> ?@89>7 A;V4 ?@89
<0B8 7 V=B5@20;0<8 2 7 4=V2.

@8 7030;L=0 4>70 078B@>28BL 3 3, O:C A;V4 ?@89<0B8 70 B0:>N AE5<>N: 1 3 C ?5@H89 45=L, ?VA;O
G>3> - ?> 500 <3 1 @07 =0 4>1C ?@>BO3>< 5 4=V2.

@8 V=D5:FVOE, I> ?5@540NBLAO AB0B528< H;OE><, @5:><5=4>20=0 4>70 078B@>28BL 1000 <3 (2
B01;5B:8 ?> 500 <3 01> 4 B01;5B:8 ?> 250 <3) >4=>@07>2>.

0FVT=B8 ;VB=L>3> 2V:C.

;N459 ;VB=L>3> 2V:C =5<0T =5>1EV4=>ABV 77C20==O.

A:V;L:8 ?0FVT=B8 ;VB=L>3> 2V:C <>6CBL 2E>48B8 4> 3@C? @878:C I>4> ?>@CH5=L 5;5:B@8G=>W
?@>2V4=>ABV A5@FO, @5:><5=4>20=> 4>B@815@56=>ABV ?@8 70AB>AC20==V 078B@><
@>728B:C A5@F52>W 0@8B0@8Btorsade de pointes.

0FVT=B8 7 ?>@CH5==O< DC=:FVW =8@>:.

;O ?0FVT=BV2 7 =57=0G=8<8 ?>@CH5==O<8 DC=:FV9 =8@>: (H284:VABL ;C1>G:>2>W
DV;LB@0FVW 10-80 <:/E2) <>6=0 28:>@8AB>2C20B8 B5 6 A0<5 4>7C20==O, I> 9 4;O ?0FVT=BV2 V7
=>@<0;L=>N DC=:FVTN =8@>:.. 78B@>1EV4=> 7 >15@56=VABN ?@87=0G0B8 ?0FVT=B0< 7 B06:8<
?>@CH5==O< DC=:FVW =8@>: (H284:VABL ;C1>G:>2>W DV;LB@0FVW <5=H5 10 <:/E2).

0FVT=B8 7 ?>@CH5==O< DC=:FVW ?5GV=:8.

A:V;L:8 078B@>2>48;>AO.

VB8.

8B@>:A A;V4 70AB>A>2C20B8 4VBO< 7 <0A>N BV;0 ≥ 45 :3.

5@54>7C20==O.

>A2V4 ;:V=VG=>3> 70AB>AC20==O 078B@> B5, I> ?>1VG=V ?@>O28, O:V @>72820NBLAO ?@8
?@89><5=4>20=>, 4>7 ?@5?0@0BC, ?>4V1=V 4> B0:8E, I> A?>AB5@V30NBLAO ?@8 70AB>AC20==V
728G09=8E B5@0?52B8G=8E 4>7, 0 A0<5: 2>=8 <>6CBL 2;:NG0B8 4V0@5N, =C4>BC, 1;N20==O,
>1>@>B=C 2B@0BC A;CEC. # @07V ?5@54>7C20==O ?@8 =5>1EV4=>ABV @5:×5=4CTBLAO ?@89>
< 0:B82>20=>3> 2C3V;;O B0 ?@>2545==O 7030;L=8E A8<0B8G=8E V ?V4B@84V2.

>1VG=V @50:FVW.

=D5:FVW B0 V=207VW: :0=484>7, >@0;L=89 :0=484>7, ?VE2>2V V=D5:FVW, ?=52<>=VO, 3@81:>20
V=D5:FVO, 10:B5@V0;L=0 V=D5:FVO, D0@8=3VB, 30AB@>5=B5@8B, ?>@CH5==O DC=:FVW
48E0==O, @8=VB, ?A524><5<1@0=>7=89 :>;VB.

I>:C A8AB5<8 :@>2V: ;59:>?5=VO, =59B@>?5=VO, 5>78=>DV;VO, ;59:>?5=VO, =59B@>?5=VO,
5>78=>DV;VO, B@><1>F8B>?5=VO, 35<>;VB8G=0 0=5

I>:C VW A8AB5<8: 0=3V>=52@>B8G=89 =01@0.; @50:FVW ?V428I5=>W GCB;82>ABV,
0=0DV;0:B8G=0 @50:FVO.

I>:C >128=: 0=>@5:AVO.

I>:C ?A8EV:8: =5@2>7=VABL, 157A>==O, 068B0FVO, 03@5A82=VABL, =5A?>:V9, 45;V@V9,
30;NF8=0FVW.

I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L, 70?0<>@>G5==O, A>=:82VABL, ?0@5AB57VO, 48A3527VO,
=5?@8B><=VABL, AC4×8, ?A8E×>B>@=0 ?V428I5=0 0:B82=VABL, 0=>AA 3V?5AB57VO.

I>:C >@30=V2 7>@C: 7>@>2V @>7;048.

I>:C >@30=V2 A;CEC: ?>@CH5==O A;CEC; 25@B83>; ?>3V@H5==O A;CEC, 2;:NG0NG8 3;CE>BC B0
/01> 472V= C 2CE0E.

I>:C A5@F52>-AC48==>W A8AB5<8: ?0;L?VB0FVO, B@V?>BV==O-<5@5EBV==O H;C=>G:V2 (*torsade de pointes*),
0@8B 2;:NG0NG8 H;C=>G:>2C B0EV:0@4VN, ?>4>265==O QT-V=B5@20;C =0, ?@8?;828, 0@B5@V0;L=0 3V?>B5=7VO.

I>:C 48E0;L=>W A8AB5<8: 48A?=>5, =>A>20 :@>2>B5G0.

I>:C B@02=>3> B@0:BC: 4V0@50, 1;N20==O, 1V;L C 682>BV, =C4>B0,30AB@8B, 70?>@, <5B5>@87
<, 48A?5?AVO, 48AD03VO, ACEVABL C @>BV, 2V4@86:0, 28@07:8 C @>B>2V9 ?>@>6=8=V,
3V?5@A5:@5FVO A;8=8, ?0=:@50B8B, 7;L>@C O78:0.

I>:C 35?0B>1V;V0@=>W A8AB5<8: ?>@CH5==O DC=:FVW ?5GV=:8, E>;5AB0B8G=0 6>2BO=8FO,
?5GV=:>20 =54>AB0B=VABL, (O:0@V4:> ?@872>48;0 4> ;5B0;L=>3> =0A;V4:C), DC;LB8G=89 35?0B8B.

I>:C H:V@8: 28A8?0==O, A25@1V6, :@>?82'O=:0, 45@<0B8B, ACEVABL H:V@8, 3V?5@3V4@>7,
D>B>GCB;82VABL, A8=4@× !BV25=A0-6>=A>=0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7, ?>;V
<>@D=0 5@8B5<0.

I>:C :VAB:>2>-<O7>2>W A8AB5<8: >AB5>0@B@8B,

I>:C A5G>284V;L=>W A8AB5<8: 487C@VO, 1V;L C =8@:0E, 3>AB@0 =8@:>20 =54>AB0B=VABL,
V=B5@AB8FV0;L=89 =5D@8B.

I>:C @5?@>4C:B82=>W A8AB5<8: <0B:>20 :@>2>B5G0, B5AB8:C;O@=V ?>@CH5==O.

030;L=V ?>@CH5==O: 1V;L C 3@C4OE, =01@0.; =574C60==O, 0AB5=VO, ?V428I5=0 2B>
<;N20=VABL, =01@0: >1;8GG0, 3V?5@B5@

01>@0B>@=V ?>:07=8:8: 7=865=0 :V;L:VABL ;59:>F8BV2, ?V428I5=0 :V;L:VABL 5>78=>DV;V2,

7=865=89 @V25=L 1V:0@1>=0BC :@>2V, ?V428I5==O @V2=O 107>DV;V2, ?V428I5==O @V2=O
<=>F8BV2, ?V428I5==O @V2=O =59B@>DV;V2, ?V428I5=89 @V25=L 0A?0@B0B0B@0=AD5@078,
?V428I5=89 @V25=L 0;0=V=0B@0=AD5@078, ?V428I5=89 @V25=L 1V;V@C1V=C 2 :@>2V, ?V428I5=89
@V25=L A5G>28=8 2 :@>2V, ?V428I5=89 @V25=L :@50B8=V=C 2 :@>2V, 7?>:07=8:V2 :0;VN C :@>2V,

?V428I5==O @V2=O ;C6=>W D>AD0B078, ?V428I5==O @V2=O E;>@84C, ?V428I5==O @V2=O 3;N:>78,
?V428I5==O @V2=O B@><1>F8BV2, 7=865==O @V2=O 35<0B>:@8BC, ?V428I5==O @V2=O
1V:0@1>=0BC, 2V4E8;5==O @V2=O =0B@VN.
#@065==O B0 >B@CT==O: CA;:04=5==O ?VA;O ?@>F54C@8.

=D>@<0FVO ?@> =51060=V @50:FVW, O:V,<>6;82>, ?>2'O70=V 7 ?@>DV;0:B8:>N B0 ;V:C20==O<
Mycobacterium Avium Complex, 107CTBLAO =0 40=8E ;:V=VG=8E 4>A;V465=L B0 A?>AB5@565=L C
?>AB<0@:5B8=3>289 ?5@V>4. &V =51060=V @50:FVW 2V4@V7=ONBLAO 70 B8?< 2V4 B8E, ?@>
O:V ?>2V4><;O;>AO ?@8 70AB>AC20==V H284:>4VNG8E ;V:0@AL:8E D>@< B0 ;V:0@AL:8E D>@<
B@820;>W 4VW.

I>:C >128=: 0=>@5:AVO.

I>:C ?A8EV:8: 70?0<>@>G5==O, 3>;>2=89 1V;L, ?0@5AB57VO, 48A3527VO, 3V?5AB57VO.

I>:C >@30=V2 7>@C: ?>3V@H5==O 7>@C.

I>:C >@30=V2 A;CEC: 3;CE>B0, ?>3V@H5==O A;CEC, 472V= C 2CE0E.

I>:C A5@F52>-AC48==>W A8AB5<8: ?0;L?VB0FVO.

I>:C B@02=>3> B@0:BC: 4V0@5O, 1V;L C 682>BV, =C4>B0,<5B5>@87<, H;C=:>2>:-8H:>289 48A:>
@B, G0ABV @V4:V 28?>@>6=5==O.

I>:C 35?0B>1V;V0@=>W A8AB5<8: 35?0B8B.

I>:C H:V@8: 28A8?0==O, A25@1V6, A8=4@< !BV25=A0-6>=A>=0, D>B>GCB;82VABL.

I>:C :VAB:>2>-< O7>2>W A8AB5<8: 0@B@0;3VO.

030;L=V ?>@CH5==O: ?V428I5=0 2B><;N20=VABL, 0AB5=VO, =574C60==O.

"5@ABV.2 @>:8.

#<>28 715@V30==O.

15@V30B8 ?@8 B5 2 >@83V=0;L=V9 C?0:>2FV.

15@V30B8 2 =54>ABC?=>

#?0:>2:0.

"01;5B:8 ?> 250 <3: ?> 6 B01;5B>: C AB@8?V; :>65= AB@8? C :0@B>==V9 C?0:>2FV;

"01;5B:8 ?> 500 <3: ?> 3 B01;5B:8 C AB@8?V; :>65= AB@8? C :0@B>==V9 C?0:>2FV.

0B53>@VO 2V4?CA:C. 0 @5F5?B>

8@>1=8:.

! \$!, "!" "

VAF57=0E>465==O 28@>1=8:0 B0 04@5A0 20465==O 9>3> 4VO;L=>ABV.

V;546 "E540, □>4EV 09@0, "5EAV;0;030@E, □VAB. !>;0= %V<0G0; @045H, 174 101 (;>: 1), =4VO.