Phụ lục 5: Khả năng áp dụng và các khuyến cáo về giám sát nồng độ thuốc trong máu đối với các thuốc kháng sinh, kháng nấm, kháng virus ở bệnh nhân nặng

Kháng sinh	Biến thiên về PK	Có mối tương quan giữa phơi nhiễm và đáp ứng lâm sàng		Phương pháp định lượng	Khuyến cáo TDM bởi chuyên gia	Số mẫu và đích TDM khuyến cáo ở bệnh nhân nặng (nếu có định lượng)
		Về hiệu quả	Về độc tính			
Aminoglycosid	Có [1-8]	Có	Có	▪ Xét nghiệm miễn dịch [9] ▪ LC-MS/MS [10]	Có [11-14]	<u>Giám sát dựa trên AUC</u> ▪ **Đích**: 70 – 120 mg.h/L ▪ **Lấy mẫu** - 2 mẫu - Lấy 1 mẫu vào 30 phút và 1 mẫu vào 6 – 22 h sau khi kết thúc truyền
						<u>Giám sát C_{max}/MIC</u> ▪ **Đích:** ≥8 – 10 ▪ **Lấy mẫu** - 1 mẫu - 30 phút sau khi kết thúc truyền
						<u>Giám sát C_{min}</u> ▪ **Đích** - Amikacin <2.5 mg/L - Gentamicin và tobramycin <0.5 mg/L ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước liều kế tiếp
Beta-lactam	Có [15-23]	Có	Có	▪ HPLC-UV [24-26] ▪ LC-MS/MS [24, 27, 28]	Có [29-35]	<u>Giám sát C_{min}</u> ▪ **Đích**: 100% $fT_{>MIC}$ ▪ **Lấy mẫu** - Một mẫu - 30 phút hoặc ngay trước liều tiếp theo - Nên định lượng sau 24 – 48 h từ khi bắt đầu điều trị
Co-trimoxazol	Có [36,37]	Không	Không	▪ LC-MS/MS [38]	Không	Chưa đủ dữ liệu/kinh nghiệm về TDM
Daptomycin	Có [39-48]	Có	Có	▪ HPLC-UV [49-52] ▪ LC-MS/MS [53-55]	Không khuyến cáo cũng như không phản đối [41, 56-58]	<u>Giám sát dựa trên AUC/MIC</u> ▪ **Đích**: >666 ▪ **Lấy mẫu**: - 2 mẫu - 1 mẫu lấy sau truyền từ 1.5 – 3 h và 1 mẫu lấy trong vòng 1 h trước khi truyền liều tiếp theo

Kháng sinh	**Biến thiên về PK**	**Có mối tương quan giữa phơi nhiễm và đáp ứng lâm sàng**		**Phương pháp định lượng**	**Khuyến cáo TDM bởi chuyên gia**	**Số mẫu và đích TDM khuyến cáo ở bệnh nhân nặng (nếu có định lượng)**
		Về hiệu quả	**Về độc tính**			
						Giám sát Cmin ▪ **Đích**: <24 mg/L ▪ **Lấy mẫu**: - Một mẫu - Trong vòng 1 h trước khi truyền liều tiếp theo - Nên lấy vào thời điểm sau 72 h kể từ khi dùng thuốc
Fluoroquinolon	Có [59-69]	Có	Không	▪ HPLC-UV [70, 71] ▪ LC-MS/MS [72, 73]	Không khuyến cáo cũng như không phản đối [65, 74-76]	Giám sát dựa trên AUC/MIC ▪ **Đích**: ≥125 ▪ **Lấy mẫu**: - 2 mẫu (1 mẫu với AFC) - 1 mẫu lấy 2 h sau khi truyền và 1 mẫu lấy 6 h sau khi truyền
						Giám sát dựa trên C_{max}/MIC ▪ **Đích**: 8 - 12 ▪ **Lấy mẫu**: - Một mẫu - 30 phút sau khi kết thúc truyền
Glycopeptid						
Teicoplanin	Có [77, 78]	Không	Không	▪ Xét nghiệm miễn dịch [79] ▪ HPLC-UV [80, 81] ▪ LC-MS/MS [82, 83]	Có [80, 81, 84]	Giám sát Cmin ▪ **Đích**: - ≥15 – 30 mg/L ▪ **Lấy mẫu** - 1 mẫu - Lấy trong vòng 30 phút hoặc ngay trước khi truyền liều tiếp theo - Nên lấy sau khoảng 96 h kể từ khi dùng thuốc
Vancomycin	Có [18, 85-87]	Có	Có	▪ Xét nghiệm miễn dịch	Có [88]	Giám sát dựa trên AUC/MIC ▪ **Đích**: ≥400 ▪ **Lấy mẫu** - 2 mẫu (1 mẫu với AFC) - 1 mẫu lấy lúc 1 h sau khi kết thúc truyền và 1 mẫu lấy trong vòng 1 – 2 h trước khi truyền liều tiếp theo

Kháng sinh	**Biến thiên về PK**	**Có mối tương quan giữa phơi nhiễm và đáp ứng lâm sàng**		**Phương pháp định lượng**	**Khuyến cáo TDM bởi chuyên gia**	**Số mẫu và đích TDM khuyến cáo ở bệnh nhân nặng (nếu có định lượng)**
		Về hiệu quả	**Về độc tính**			
						Giám sát C_{min} trong truyền gián đoạn ▪ **Đích:** - >10 mg/L - ≥15 – 20 mg/L đối với nhiễm khuẩn nặng ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước liều tiếp theo
						Giám sát Css đối với truyền liên tục ▪ **Đích**: - 20 – 25 mg/L ▪ **Lấy mẫu** - 1 mẫu - Vào bất kì thời điểm nào trong quá trình truyền thuốc
Linezolid	Có [89-99]	Có	Có	▪ Xét nghiệm miễn dịch [100] ▪ HPLC-UV [101, 102] ▪ LC-MS/MS [103, 104]	Có [96, 105]	Giám sát C_{min} ▪ **Đích**: 2 – 7 mg/L ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước liều tiếp theo - Nên lấy sau 48 h kể từ khi dùng thuốc
Colistin	Có [106-111]	Không	Có	▪ HPLC-FL [112] ▪ LC-MS/MS [113-115]	Không khuyến cáo cũng như không phản đối	Giám sát C_{min} ▪ **Đích**: 2 mg/L ▪ **Lấy mẫu** - 1 mẫu - Ngay trước khi truyền liều tiếp theo - Nên lấy sau 48 – 72 h sau khi bắt đầu dùng thuốc
Polymycin B	Có [116-118]	Không	Có	▪ LC-MS/MS [119, 120]	Không khuyến cáo cũng như không phản đối [121, 122]	Giám sát dựa trên AUC ▪ **Đích**: AUC_{0-24}: 50 – 100 mg.h/L ▪ **Lấy mẫu** - Ít nhất một mẫu - Nên lấy sau 12 – 24 h kể từ khi dùng thuốc

Kháng nấm	**Biến thiên PK**	**Có mối tương quan giữa phơi nhiễm và đáp ứng lâm sàng**		**Phương pháp định lượng**	**Khuyến cáo TDM bởi chuyên gia**	**Số mẫu và đích TDM khuyến cáo ở bệnh nhân nặng**
		Về hiệu quả	**Về độc tính**			
Echinocandin	Chưa rõ ràng [123-133]	Chưa rõ ràng	Không	▪ LC-MS/MS [134, 135]	Không khuyến cáo cũng như không phản đối [136]	Chưa đủ dữ liệu/kinh nghiệm về TDM
Fluconazol	Có [130, 137-139]	Có	Không	▪ HPLC-UV [140, 141] ▪ LC-MS/MS [142, 143]	Không khuyến cáo cũng như không phản đối	Thường không cần TDM thường quy nếu tuân thủ các khuyến cáo về liều hiện hành
Flucytosin	Có [144-146]	Không	Có	▪ HPLC-UV ▪ LC-MS/MS [147, 148]	Không khuyến cáo cũng như không phản đối	Giám sát C_{max} ▪ **Đích**: <100 mg/L ▪ **Lấy mẫu** - 1 mẫu - 2 h sau khi truyền thuốc - Nên lấy trong vòng 72 h kể từ khi dùng thuốc
						Giám sát C_{min} ▪ **Đích**: ≥25 mg/L ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước khi truyền liều tiếp theo - Nên lấy trong vòng 72 h kể từ khi dùng thuốc
Isavuconazol	Rất ít [149, 150]	Chưa rõ	Không	▪ HPLC-UV [151, 152] ▪ LC-MS/MS [143, 153]	Không khuyến cáo cũng như không phản đối [149, 150, 154]	Chưa đủ dữ liệu/kinh nghiệm về TDM

Kháng nấm	Biến thiên PK	Có mối tương quan giữa phơi nhiễm và đáp ứng lâm sàng		Phương pháp định lượng	Khuyến cáo TDM bởi chuyên gia	Số mẫu và đích TDM khuyến cáo ở bệnh nhân nặng
		Về hiệu quả	Về độc tính			
Itraconazol	Có [155-159]	Có	Có	▪ HPLC-UV [152] ▪ LC-MS/MS [142, 143, 160, 161]	Không khuyến cáo cũng như không phản đối	Giám sát Cmin ▪ **Đích**: >0.5 – 1 mg/L (dự phòng hoặc điều trị nhiễm nấm xâm lấn) ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước khi truyền liều tiếp theo - Nên lấy trong vòng 5 – 7 ngày kể từ khi dùng thuốc
Posaconazol	Có [162-166]	Có	Không	▪ HPLC-UV [152] ▪ LC-MS/MS [143, 153]	Không khuyến cáo cũng như không phản đối [162-167]	Giám sát Cmin ▪ **Đích** - Dự phòng: >0.5 – 0.7 mg/L - Điều trị: >1 mg/L ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước liều tiếp theo - Nên lấy sau 7 ngày kể từ khi dùng thuốc
Voriconazol	Có [168-171]	Có	Có	▪ HPLC-UV [152] ▪ LC-MS/MS [143, 153]	Có [172]	Giám sát Cmin ▪ **Đích**: 2 – 6 mg/L (dự phòng hoặc điều trị nhiễm nấm xâm lấn) ▪ **Lấy mẫu** - 1 mẫu - 30 phút hoặc ngay trước khi truyền liều tiếp theo - Nên lấy sau 2 – 5 ngày kể từ khi dùng thuốc

Kháng virus	Biến thiên PK	Có mối tương quan giữa phơi nhiễm và đáp ứng lâm sàng		Phương pháp định lượng	Chỉ định TDM	Khuyến cáo về lấy mẫu và đích TDM ở bệnh nhân nặng
		Về hiệu quả	Về độc tính			
Acyclovir/valacyclovir	Chưa rõ [173-175]	Chưa rõ	Chưa rõ	▪ HPLC-UV [176-178] ▪ LC-MS/MS [179, 180]	Không khuyến cáo cũng như không phản đối	Chưa đủ dữ liệu/kinh nghiệm về TDM
Foscarnet	Có [181-187]	Chưa rõ	Chưa rõ	▪ HPLC-UV [188, 189]	Không khuyến cáo cũng như không phản đối	Chưa đủ dữ liệu/kinh nghiệm về TDM
Ganciclovir/valganciclovir	Rất ít [190-194]	Chưa rõ	Chưa rõ	▪ HPLC-UV [178, 195] ▪ LC-MS/MS [196, 197]	Không khuyến cáo cũng như không phản đối	Chưa đủ dữ liệu/kinh nghiệm về TDM
Oseltamivir/oseltamivir carboxylat	Rất ít [198-204]	Chưa rõ	Chưa rõ	▪ HPLC-UV [205] ▪ LC-MS/MS [20t6-208]	Không khuyến cáo cũng như không phản đối	Chưa đủ dữ liệu/kinh nghiệm về TDM
Ribavirin	Có [209-214]	Chưa rõ	Chưa rõ	▪ HPLC-UV [215] ▪ LC-MS/MS [216, 217]	Không khuyến cáo cũng như không phản đối	Chưa đủ dữ liệu/ kinh nghiệm về TDM

AFC = kiểm soát phản hồi thích nghi; HPLC-UV = sắc kí lỏng hiệu năng cao với detector UV; LC-MS/MS = sắc kí lỏng kết hợp khối phổ; PK = dược động học; TDM = giám sát nồng độ thuốc điều trị

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