Table 1. By type of infection, microorganisms to be suspected in relation to the presence or not of risk factors for multidrug resistance and suggested empirical treatments [VAP: ventilador-associated pneumonia; MDR: multidrug resistance; ESBL: extended-spectrum β-lactamase; ESCPM group (*Enterobacter cloacae*, *Enterobacter aerogenes*, *Serratia marcescens*, *Citrobacter freundii*, *Providencia rettgeri* and *Morganella morganii*); MRSA: methicillin-resistant *S. aureus*; HACEK (*Haemophilus* spp., *Aggregatibacter* -formerly *Actinobacillus-actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* spp)]

INFECTION TYPE	SUSPECTED PATHOGENS	EMPIRICAL TREATMENT	COMMENTS
Pneumonia or Tracheobronchitis	**No risk factors for MDR bacteria** *S. pneumoniae* *H. influenzae* *S. aureus* (methicillin-susceptible) *Enterobacteriaceae* *Legionella*	Cefotaxime or ertapenem ± Azithromycin or levofloxacin	IV antibiotic treatment should not exceed >7 days Addition of macrolides/azalides improves the prognosis of pneumococcal pneumonia
	Presence of risk factors for first-level of resistance[a] Above microorganisms plus: ESBL-producing enterobacteria Penicillin-resistant *S. pneumoniae* *P. aeruginosa* MRSA	Piperacillin/tazobactam or cefepime or meropenem or doripenem PLUS Levofloxacin or amikacin ± Linezolid	ESBL-producing isolates are involved in ≈10% pneumonia caused by enterobacteria. When confirmed, monotherapy with carbapenems (meropenem, imipenem, ertapenem) is indicated Suspiction of infection by *P. aeruginosa*: It is recommended the association of two antipseudomonal compounds In bacteremic infections by MRSA, consider the association of linezolid + daptomycin
	Presence of risk factors for second-level of resistance[b] Above microorganisms plus: N…	Antipseudomonal betalactam different from those previously used, with preference for carbapenems PLUS L…	Treatment election should consider previous antibiotic treatments and susceptibility of isolates in surveillance cultures of colonizing flora C…

Bloodstream infections: primary bacteremia/ catheter-associated bacteremia	Coagulase-negative staphylococci *S. aureus* (including MRSA) *Enterococcus* spp. *E. coli* *Klebsiella* spp. ESCPM group *P. aeruginosa* *Acinetobacter* spp.	Daptomycin or vancomycin PLUS Cefepime or piperacillin/tazobactam or meropenem or doripenem ± Amikacin	Gram-negative bacteria should always be suspected in the critically ill patient regardless site of central venous catheter If methicillin-susceptibility in staphylococci is confirmed, change to cloxacillin In persistent (>5-7 days) or recurrent (without endovascular foci) bacteremia by *S. aureus*, a second anti-staphylococcal drug (with or without rifampicin) should be added. If the patient is under cloxacillin treatment, add daptomycin with or without rifampicin. If the patient is under daptomycin treatment, add linezolid or fosfomycin or cloxacillin, with or without rifampicin. If the patient is under vancomycin treatment, change to daptomycin + cloxacillin, with or without rifampicin
	Candida spp.	Echinocandin or fluconazol	An antifungal drug with activity against *Candida* spp. should be considered in critically ill patients with central venous catheter in the femoral vein and/or parenteral nutrition, severe sepsis or recent abdominal surgery
Urinary tract infections	**With criteria for severe sepsis or presence of risk factors for first-level of resistance**[a] ESBL-producing enterobacteria	Meropenem or doripenem ± Amikacin	Due to its high frequency, ESBL-producing enterobacteria should be covered in patients with severe sepsis or septic shock
	Presence of risk factors for second-level of resistance[b] Above microorganisms plus: ESCPM group Multidrug-resistant *P.aeruginosa,* *Enterococcus* spp. *Acinetobacter* spp. *Candida* spp.	Meropenem or Doripenem + Amikacin ± Fluconazol	Treatment election should consider previous antibiotic treatments and susceptibility of isolates in surveillance cultures of colonizing flora Use of colimycin or tigecyclin may be necessary. Although tigecycline concentrations in urine are not high, it may be useful in case of pyelonephritis

[a]Risk factors for first-level of resistance: Significant comorbidities and/or antibiotic treatment for >3-5 days
[b]Risk factors for second-level of resistance: Hospital admission and/or prolonged antibiotic treatment (>7 days)

Intraabdominal infections	**No risk factors for MDR bacteria** *E. coli* *K. pneumoniae* *B. fragilis*	Ertapenem or Cefotaxime + metronidazole	In case of lack of control of the infectious foci, follow treatment recommendations in the presence of risk factors for first-level resistance
	Presence of risk factors for first-level of resistance[a] Above microorganisms plus: ESBL-producing enterobacteria *P. aeruginosa* *Enterococcus* spp. MRSA	Meropenem or imipenem or ertapenem ± Daptomycin or linezolid or vancomycin **OR** Tigecycline ± Piperacillin/tazobactam or cefepime or amikacin	In case of lack of control of the infectious foci, follow treatment recommendations in the presence of risk factors for second-level resistance
	Presence of risk factors for second-level of resistance[b] All the above microorganisms plus: Non-fermenter gramnegative bacilli AmpC and/or carbapenemase-producing enterobacteria Multidrug-resistant *P.aeruginosa* *Candida* spp.	Meropenem or doripenem + daptomycin or linezolid or vancomycin **OR** Tigecycline + piperacillin/tazobactam or cefepime ± Amikacin ± Echinocandin	Treatment election should consider previous antibiotic treatments and susceptibility of isolates in surveillance cultures of colonizing flora In critically ill patients, echinocandins are the elective treatment for *Candida* antifungal therapy

[a]Risk factors for first-level of resistance: Significant comorbidities and/or antibiotic treatment for >3-5 days
[b]Risk factors for second-level of resistance: Hospital admission and/or prolonged antibiotic treatment (>7 days)

<u>Endocarditis</u> Native valve Prosthetic valve >12 months post-surgery	*S. aureus* Coagulase-negative staphylococci Viridans group streptococci *Enterococcus* spp. *Streptococcus bovis* HACEK group	Ampicillin + cloxacillin ± Gentamicin (3-5 days)	If glomerular filtrate is <40 ml/min or concomitant treatment with potentially neurotoxic drugs, change gentamicin by daptomycin
	Risk for MRSA (including intravenous drug users and healthcare facilities)	Ampicillin + daptomycin + fosfomycin ± Gentamicin (3-5 days) **OR** Ampicillin + vancomycin	If vancomycin MIC ≥1 mg/l, severe sepsis or bacteremia for >5 days, consider heteroresistance or tolerance and change to daptomycin Addition of gentamin should be avoided if glomerular filtrate is <40 ml/min. Consider change to cotrimoxazole. Addition of fosfomycin should be avoided if MIC ≥32 mg/l. Consider change to cotrimoxazole
Prosthetic valve <12 months post-surgery	MRSA Coagulase-negative staphylococci *Viridans* group streptococci *Enterococcus spp.* *Streptococcus bovis* HACEK group *E. coli* *K. pneumoniae* *Salmonella enteritidis* *P. aeruginosa*	Daptomycin ± fosfomycin ± gentamicin or amikacin PLUS Meropenem	Initiate rifampicin from the 3rd-5th day on. Vancomycin could be considered when MIC≤1 mg/l for the MRSA and normal renal function Addition of gentamin should be avoided if glomerular filtrate is <40 ml/min. Consider change to cotrimoxazole. Addition of fosfomycin should be avoided if MIC ≥32 mg/l. Consider change to cotrimoxazole Considerar gentamicin if *Enterococcus* spp. is isolated
<u>Skin and Soft tissue infections</u> **Necrotizing fasciitis** (Fournier's gangrene, early surgical wound infection 24-48 h post-surgery)	Group A streptococci ***Clostridium perfringes*** ***Clostridium septicum*** ***Staphylococcus aureus*** **Mixed polymicrobial infection:** *Enterococcus* spp. *Bacillus cereus* *E. coli* *P. aeruginosa* *Klebsiella* spp. *Proteus* spp. *Peptostreptococcus* spp. *Bacteroides* spp.	Piperacillin/tazobactam or meropenem PLUS Daptomycin or linezolid or clindamycin **OR** Tigecycline	In infections by *S. aureus* producing panton valentine leukocidin or superantigens, the antibiotic regimen should include linezolid or clindamicin Consider high doses of tigecycline in moderately severe polymicrobial infections involving MRSA and in patients with allergy to β-lactams

Table 2. Doses of common antibiotics for the treatment of infections in the critically ill patient

Drug	**Dose (iv)**	**Comments**
Amikacin	20-30 mg /kg / 24 h	
Ampicillin	2 g / 6 h	1-2 g as initial dose followed by 8g in 24h continuous infusion
Azitromycin	500 mg / 24 h	
Cefepime	2 g / 8 h	1-2 g as initial dose followed by 6g in 24h continuous infusion
Ceftazidime	2 g / 8 h	1-2 g as initial dose followed by 6g in 24h continuous infusion
Cefotaxima	2 g / 6-8 h	1-2 g as initial dose followed by 6g in 24h continuous infusion
Ciprofloxacin	400 mg / 8 h	
Cloxacillin	2 g / 4 h	1-2 g as initial dose followed by 12g in 24h continuous infusion
Cotrimoxazole	5 mg / kg of trimetropin / 8 h	
Colimycin	9×10^6 U followed by 4.5×10^6 U / 12 h	
Daptomycin	10 mg /kg/day	May be administered as bolus
Doripenem	1 g / 8 h	Administered as intermittent slow infusion (4 h)
Ertapenem	1 g / 12 h	
Fosfomycin	4-8 g / 8 h	Administered as intermittent slow infusion (4 h) or continuous infusion

Gentamicin	7-9 mg /kg/d (1 dose)	referred to adjusted body weigth; body weight = ideal body weight + 0.4 × (total weight – ideal weight)
Imipenem	1 g / 8 h	Intermittent slow infusion (2 h)
Levofloxacin	500 mg / 12 h	
Linezolid	600 mg / 8-12 h	1200 mg in 24 h continuous infusion
Meropenem	2 g / 8 h	Intermittent slow infusion (3 h)
Metronidazole	500 mg / 8 h	
Piperacillin-tazobactam	4-0.5 g / 6 h	2 g as initial dose followed by 16g in 24h continuous infusion
Rifampicin	600 mg / 12-24 h h	
Tigecycline	100- 200 mg followed by 50- 100 mg / 12 h	
Vancomycin	15-20 mg / kg / 8 h (in 1-2 h) 35 mg / kg followed by 35 mg / kg / day in continuous infusion	Kg referred to total body weight