Intravenous Push Administration of Antibiotics: Literature and Considerations

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Abstract

Intravenous (IV) push administration can provide clinical and practical advantages over longer IV infusions in multiple clinical scenarios, including in the emergency department, in fluid-restricted patients, and when supplies of diluents are limited. In these settings, conversion to IV push administration may provide a solution. This review compiles available data on IV push administration of antibiotics in adults, including preparation, stability, and administration instructions. Prescribing information, multiple tertiary drug resources, and primary literature were consulted to compile relevant data. Several antibiotics are Food and Drug Administration–approved for IV push administration, including many beta-lactams. In addition, cefepime, ceftriaxone, ertapenem, gentamicin, and tobramycin have primary literature data to support IV push administration. While amikacin, ciprofloxacin, imipenem/cilastatin, and metronidazole have limited primary literature data on IV push administration, available data do not support that route. In addition, a discussion on practical considerations, such as IV push best practices and pharmacodynamic considerations, is provided.

Keywords

anti-infectives, drug stability, intravenous therapy

Introduction

Antibiotics are commonly administered intravenous (IV) medications. Many of these drugs can be administered via IV push, intermittent IV infusion, and/or continuous IV infusion, depending on the medication. IV push allows for administration of an antibiotic in a minimal fluid volume. Small fluid volumes can be particularly useful in patients who are fluid-restricted, such as patients with acute volume overload or acute renal failure.¹ In addition, the faster administration time may provide advantages in the emergency department (ED), so that time-to-first-dose can be shortened.^{2,3} There may also be interest in IV push administration in the setting of drug or fluid shortages, such as the current shortage of small volume parenteral (SVP) solutions (ie, 50 or 100 mL bags for intermittent IV infusion).⁴ In response, the American Society of Health-Systems Pharmacists recommends switching medication administration to IV push when possible to help conserve SVP supplies in the context of a shortage. Therefore, the purpose of this article is to summarize the available data that support IV push administration of antibiotics in adults.

Methods

A list of commercially available injectable antibiotics was generated from *The Sanford Guide* and the Food and Drug

Administration (FDA) Orange Book.^{5,6} The prescribing information (PI) was used as the primary resource for FDA-approved routes of administration and stability data.^{7–9} The PIs for vials for reconstitution were selected if available because vial formulations are most readily prepared for IV push administration. Additional tertiary drug resources were used to confirm the information found in the PI and provide additional data, if available.^{60–66} Primary literature citations from tertiary sources were reviewed in their full-text form. A primary literature search was also performed of the MEDLINE and International Pharmaceutical Abstracts (IPA) databases. Each drug name was paired with the following terms to capture published data on IV push administration: intravenous, inject*, parenteral*, “administration and dosage” [MeSH Subheading], push, bolus, rapid, fast. All sources were consulted for each drug to ascertain consensus recommendations; in cases when information could only be located in one source, a note is included in the comment column of Table 1 or in the text summaries for the antibiotics.

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Table I . Summary of Available IV Push or Slow Injection Data.^{a,7-29}

Antibiotic		FDA-approved administration	Preparation	Stability ^b	Administration	Notes
Aminoglycosides	Gentamicin	<ul style="list-style-type: none"> Intermittent IV infusion IM <p>Not approved for IV push administration</p>	Off-label preparation Loewenthal 2010 ⁶⁷ : Dilute doses <800 mg to 20 mL with NS; larger doses administered as 40 mg/mL solution supplied in manufacturer's vials	Polypropylene syringe, 40 mg/mL ^{63,71} ; 30 d at 4°C or 25°C	Off-label administration Loewenthal 2010 ⁶⁷ : Inject over 3 to 5 min	<p>Loewenthal 2010⁶⁷: Described IV push administration of gentamicin and tobramycin in OPAT setting; report of 5593 doses</p> <p>Mendelson 1976⁶⁸: Compared IV push with 2 h infusion in 63 patients with various infections</p> <p>Meunier 1987⁶⁹: PK study in 10 healthy volunteers that compared IV push with slow IV injection (same dose diluted in 100 mL given over 15 min); authors endorsed slow IV injection administration based on PK parameters (IV push resulted in high peak serum concentrations)</p> <p>Scott 1989⁷⁰: PK study in 19 patients and 2 healthy volunteers that compared IV push with IM administration</p> <p>Refer to text for additional data with IV push</p>
			Mendelson 1976 ⁶⁸ : Dilute dose in 50-mL D5W or NS (most patients received 120-mg doses) Meunier 1987 ⁶⁹ : 80 mg prediluted in 2-mL NS (40 mg/mL) Scott 1989 ⁷⁰ : Dilute doses to 20 mL with NS (doses were 6 mg/kg/d in divided doses or 2 mg/kg/dose)	Plastic syringe, 40 mg/mL ^{63,72} ; average loss of 16% after 30 d and brown precipitate formed at both 4°C and 25°C Glass syringe, 40 mg/mL ^{63,72} ; average loss of 7% after 30 d, brown precipitate formed at 60 d at both 4°C and 25°C Possible instability with storage in plastic packaging due to potential oxygen exposure ^{63,73}	Mendelson 1976 ⁶⁸ : Inject over 3 to 5 min using Soluset system Meunier 1987 ⁶⁹ : Inject over <1 min Scott 1989 ⁷⁰ : Inject over 5 min	
Tobramycin		<ul style="list-style-type: none"> Intermittent IV infusion IM <p>Not approved for IV push administration</p>	Off-label preparation Loewenthal 2010 ⁶⁷ : Dilute doses <800 mg to 20 mL with NS; larger doses administered as 40 mg/mL solution supplied in manufacturer's vials Aoyama 1987 ⁷⁴ : 2 mg/kg dose diluted in 10-mL D5W	Plastic syringe, 40 mg/mL solution from reconstituted 1.2-g vial ^{63,72} ; after 2 mo, no significant change in concentration detected at 4°C and 25°C	Off-label administration Loewenthal 2010 ⁶⁷ : Inject over 3 to 5 min Aoyama 1987 ⁷⁴ : IV push, administration time not reported; injected within 2 to 3 min of preparation	<p>Loewenthal 2010⁶⁷: Described IV push administration of gentamicin and tobramycin in OPAT setting; report of 5593 doses</p> <p>Aoyama 1987⁷⁴: Evaluated different routes of tobramycin administration in 21 burn patients, included IV push (5 patients)</p> <p>Refer to text for additional data with IV push</p>
			Off-label preparation Wiskirchen 2013 ⁷⁶ : Dilute 1 g dose in NS to a total volume of 10 mL (100 mg/mL)	Wiskirchen 2013 ⁷⁶ : Prepared doses used within 6 h of reconstitution; stored under refrigeration until administered Polypropylene syringes, 100 mg/mL in NS ^{63,77} ; 30 min at RT, 24 h under refrigeration followed by 4 h at RT, 14 d frozen followed by 5 h at RT, or 28 d frozen followed by 3 h at RT Reconstituted vial: 3 h at 25°C and 13 h at 5°C Plastic luer-tip syringes with tubing attached and capped, 50 mg/mL in SWFI ⁶⁴ ; 8 h at RT and 44 h under refrigeration	Wiskirchen 2013 ⁷⁶ : Inject over 5 min, at a rate of 2 mL/min through peripheral IV catheter	
Meropenem		<ul style="list-style-type: none"> IV push Intermittent IV infusion 	Vials of 500 mg or 1 g; reconstitute with 10-mL and 20-mL SWFI, respectively, to a resulting concentration of 50 mg/mL No further dilution required		Inject over 3 to 5 min (adults and children ≥3 months) Children <3 months should receive IV infusion over 30 min	<p>Wiskirchen 2013⁷⁶: Evaluated IV push administration in a PK study of 12 healthy volunteers; did not specifically evaluate stability</p>
			Vials of 500 mg or 1 g; reconstitute with 2- and 2.5-mL SWFI to resulting concentrations of 225 and 330 mg/mL, respectively Further dilute reconstituted solution with approximately 5 mL of SWFI for IV push administration Off-label preparation McLaughlin 2017, Poole 1999, Garrelts 1988 ^{78,79} : 1 or 2 g diluted with 10-mL SWFI	Reconstituted vial: 24 h at RT and 10 d under refrigeration Extended stability data ⁷⁸ : 500 mg diluted in 2 mL of SWFI ⁸⁰ ; 4 d at 25°C Plastic syringes, 100 and 200 mg/mL in SWFI ⁸¹ ; 13 d at 24°C, 28 d at 4°C, 3 mo when frozen at -15°C (time to 10% loss) Polypropylene syringes, 100 and 200 mg/mL in SWFI ⁸² ; 30 d at 5°C with light protection, followed by 72 h at 21 to 25°C with light exposure	Inject over 3 to 5 min, directly into vein or through the tubing of a running compatible IV infusion Off-label administration McLaughlin 2017 ⁷⁸ : Inject over 2 min Poole 1999 ⁷⁹ : Inject over 3 to 5 min Garrelts 1988 ⁷⁸ : Inject over 1 to 2 min/g	
Cephalosporins	Cefazolin	<ul style="list-style-type: none"> IV push Intermittent IV infusion IM 				<p>McLaughlin 2017⁷⁸: Evaluated use of IV push for first dose only in ED</p> <p>Poole 1999⁷⁹: Evaluated IV push for patient-administered doses at home (OPAT)</p> <p>Garrelts 1988⁷⁸: Evaluated rates of postinfusion phlebitis with IV push compared with IV infusion in a tertiary hospital</p>

(continued)

Table 1. (continued)

Antibiotic	FDA-approved administration	IV push/IV slow injection			Notes
		Preparation	Stability ^a	Administration	
Cefepime	• Intermittent IV infusion	Off-label preparation Tran 2017 ⁷ : 1- and 2-g doses diluted in NS to a total volume of 10 mL	Reconstituted solutions in compatible solutions: 24 h at 20 to 25°C and 7 d at 2 to 8°C (see PI for further details)	Off-label administration Tran 2017 ⁷ : Inject over 2 to 5 min	Tran 2017 and McLaughlin 2017 ^{2,3} : Evaluated use of IV push for first dose only in ED An additional study ⁶⁵ evaluated 2 g over 3, 5, 10, and 15 min in healthy volunteers; however, concentration was 40 mg/mL (total volume, 50 mL)
	• IM Not approved for IV push administration	McLaughlin 2017 ² : 1- and 2-g doses diluted in 10 and 20 mL of SWFI, respectively	Polypropylene syringes, 100 and 200 mg/mL in DSW, NS, or SWFI ^{63,63,64} ; 14 d at 4°C, 1 d at RT, and up to 90 d at -20°C	McLaughlin 2017 ² : Inject over 5 min	
Cefotaxime	• IV push	Vials of 500 mg, 1 g, and 2 g; reconstitute with 10-mL SWFI to resulting concentrations of 50, 95, and 180 mg/mL, respectively	Reconstituted vial: 24 h at RT, 7 d under refrigeration, and 13 wk frozen for 500-mg and 1-g vials; 12 h at RT, 7 d under refrigeration, and 13 wk frozen for 2-g vial	Inject over 3 to 5 min	Do not administer over <3 min; injection over <1 min through a central venous catheter has resulted in life-threatening arrhythmias Maximum IV push concentration only reported in <i>Pediatric Injectable Drugs text</i>
	• Intermittent IV infusion	No further dilution required	Plastic syringe, reconstituted solutions for IV push: 5 d under refrigeration and 13 wk frozen	Can be given directly into vein or through the tubing of a running compatible IV infusion ^{66,65}	
	• IM	Maximum dilution required for IV push is 200 mg/mL in SWFI ⁶⁵			
Cefotetan	• IV push	Vials of 1 and 2 g; reconstitute with 10-mL and 10- to 20-mL SWFI to resulting concentrations of 95 mg/mL and 95 or 182 mg/mL, respectively	Reconstituted vial: 24 h at 25°C, 96 h at 5°C, and 1 wk at -20°C	Inject over 3 to 5 min	
	• Intermittent IV infusion	No further dilution required	Plastic or glass syringes, reconstituted solutions for IV push: 24 h at 25°C and 96 h at 5°C		
Cefoxitin	• IV push	Vials of 1 and 2 g; reconstitute with 10-mL SWFI to resulting concentrations of 95 mg/mL and 180 mg/mL, respectively	Reconstituted vials with 1 g/10 mL concentration: 6 h at RT and 1 wk under refrigeration, for all compatible diluents	Inject over 3 to 5 min, directly into vein or through the tubing of a running compatible IV infusion	McLaughlin 2017 ² : evaluated use of IV push for first dose only in ED; both 1 and 2 g doses were diluted in 10 mL SWFI
	• Intermittent IV infusion	No further dilution required	Plastic syringes, 1 and 2 g diluted in 10 mL of SWFI ^{63,64} ; 2 d at 24°C, 23 d at 4°C, 3 mo frozen at -15°C (time to 10% loss)	Off-label administration McLaughlin 2017 ² : Inject 1 g dose over 2 min and 2 g dose over 5 min	
Ceftazidime	• IV push	Fortaz vials of 500 mg, 1 g or 2 g; reconstitute with 5.3-, 10-, and 10-mL SWFI to resulting concentrations of 100, 100, and 170 mg/mL, respectively	Reconstituted vials for Fortaz (all sizes): 12 h at RT or 3 d under refrigeration; reconstituted solution in original container may be frozen for 3 mo at -20°C	Garrelts 1988 ⁷⁸ : Inject over 1 to 2 min/g	McLaughlin 2017 ² : Evaluated use of IV push for first dose only in ED Garrelts 1988 ⁷⁸ : Evaluated rates of postinfusion phlebitis with IV push compared with IV infusion in a tertiary hospital; 1 g diluted in 10 mL SWFI and 2 not reported
	• Intermittent IV infusion	Tazicef vials of 1 or 2 g; reconstitute with 10-mL SWFI to concentrations of 95 and 180 mg/mL, respectively	Reconstituted vials for Tazicef (all sizes): 24 h at RT or 7 d under refrigeration; reconstituted solution in original container may be frozen for 3 mo at -20°C	Inject over 3 to 5 min, directly into vein or through the tubing of a running compatible IV infusion	
Cefazidime	• IV push	No further dilution required		Off-label administration McLaughlin 2017 ² : Inject over 5 min	Specific formulation of ceftazidime in Studies 1 and 2 not reported
	• Intermittent IV infusion	Off-label preparation McLaughlin 2017 ² : 1 or 2 g diluted with 10 or 20 mL SWFI, respectively	Polypropylene syringes, 100 and 200 mg/mL in SWFI (Fortaz) ^{63,66} ; 8 h at 22°C, 96 h at 4°C, and 91 d at -20°C	Garrelts 1988 ⁷⁸ : Inject over 1 to 2 min/g	

(continued)

Table 1. (continued)

Antibiotic	FDA-approved administration	IV push/IV slow injection			Notes
		Preparation	Stability ^b	Administration	
Ceftriaxone	<ul style="list-style-type: none"> Intermittent IV infusion IM 	<p>PI reconstitution</p> <p>Vials of 250 mg, 500 mg, 1 g, and 2 g: reconstitute with 2.4-, 4.8-, 9.6-, and 19.2-mL SWFI; NS, or D5W, respectively, to a resulting concentration of 100 mg/mL (PI recommends further dilution for administration via IV infusion)</p> <p>Off-label preparation</p> <p>McLaughlin 2017⁷: 1 and 2 g diluted in 10 mL SWFI</p> <p>Poole 1999⁷⁹: 1 g diluted in 10 mL SWFI</p> <p>Garrelts 1988⁷⁸: 1 g diluted in 10 mL SWFI</p>	<p>Reconstituted vials (100 mg/mL): 2 d at 25°C and 10 d at 4°C</p> <p>Polypropylene syringes, 100 mg/mL in SWFI^{43,81}: 72 h at 20°C; 40 d at 4°C, and 180 d frozen at -20°C</p>	<p>Off-label administration</p> <p>McLaughlin 2017⁷: Inject over 2 min (adults only)</p> <p>Poole 1999⁷⁹: Inject over 2 to 4 min in those aged >11 years</p> <p>Garrelts 1988⁷⁸: Inject over 1 to 2 min/g (adults only)</p>	<p>McLaughlin 2017⁷: Evaluated use of IV push for first dose only in ED</p> <p>Poole 1999⁷⁹: Evaluated IV push for patient-administered doses at home (OPAT)</p> <p>Garrelts 1988⁷⁸: Evaluated rates of postinfusion phlebitis with IV push compared with IV infusion in a tertiary hospital</p>
Cefuroxime	<ul style="list-style-type: none"> IV push Intermittent IV infusion Continuous IV infusion IM 	<p>Vials 750 mg and 1.5 g: reconstitute with 8.3- and 16-mL SWFI, respectively, to a resulting concentration of 90 mg/mL</p> <p>No further dilution required</p> <p>Off-label preparation</p> <p>Poole 1999 and Garrelts 1988^{78,79}: 750 mg diluted with 10 mL SWFI</p>	<p>Reconstituted vials: 24 h at RT and 48 h under refrigeration</p>	<p>Inject over 3 to 5 min, directly into vein or through the tubing of a running compatible IV infusion</p> <p>Off-label administration</p> <p>Garrelts 1988⁷⁸: Inject over 1 to 2 min/g</p>	<p>Poole 1999⁷⁹: Evaluated IV push for patient-administered doses at home (OPAT); over 3 to 5 min</p> <p>Garrelts 1988⁷⁸: Evaluated rates of postinfusion phlebitis with IV push compared with IV infusion in a tertiary hospital</p> <p>No relevant syringe stability was located</p>
Glycopeptides/lipoglycopeptides/lipopeptides					
Daptomycin	<ul style="list-style-type: none"> IV push (adults only) Intermittent IV infusion (adults and pediatric patients aged 1 to 17 years) 	<p>Cubicin</p> <p>Cubicin vials: reconstitute with 10 mL of NS to concentration of 50 mg/mL</p> <p>No further dilution required</p> <p>Cubicin RF</p> <p>Cubicin RF vials: reconstitute with 10 mL of SWFI or BWFI to concentration of 50 mg/mL</p> <p>No further dilution required</p>	<p>Cubicin</p> <p>Reconstituted Cubicin vials: 12 h at RT and 48 h under refrigeration</p> <p>Cubicin RF</p> <p>Reconstituted Cubicin RF vials: 24 and 48 h at RT in SWFI and BWFI, respectively; 3 d under refrigeration in both SWFI and BWFI</p> <p>Polypropylene syringes (with elastomeric rubber stopper), 50 mg/mL (Cubicin RF): 24 h and 3 d at RT and under refrigeration, respectively, when diluted with SWFI; 48 h and 5 d at RT and under refrigeration, respectively, when diluted with BWFI</p>	<p>Cubicin and Cubicin RF</p> <p>Do not administer by IV push in pediatric and adolescent patients aged ≤17 years.</p> <p>2 formulations are available (Cubicin and Cubicin RF), which have differences in reconstitution and storage</p> <p>Cubicin</p> <p>No relevant syringe stability for Cubicin formulation was located</p> <p>Cubicin RF</p> <p>Do not use saline-based diluents to reconstitute Cubicin RF; this results in hyperosmotic solution that may cause infusion-site reactions when given as IV push</p>	
Monobactam					
Aztreonam	<ul style="list-style-type: none"> IV push Intermittent IV infusion IM 	<p>Vials of 1 and 2 g: reconstitute with 6- to 10-mL SWFI</p> <p>No further dilution required</p>	<p>Reconstituted solutions >20 mg/mL in SWFI; 48 h at RT and 7 d under refrigeration</p>	<p>Inject over 3 to 5 min, directly into vein or through the tubing of a running compatible IV infusion</p>	<p>No relevant syringe stability was located</p>
Others					
Chloramphenicol	<ul style="list-style-type: none"> IV push 	<p>Vials of 1 g: reconstitute with 10 mL of SWFI or D5W to resulting concentration of 100 mg/mL</p> <p>No further dilution required</p>	<p>Reconstituted via^{42,43}: 30 d at RT</p>	<p>Inject over at least 1 min</p>	<p>No relevant syringe stability was located</p>

(continued)

Table 1. (continued)

Antibiotic	FDA-approved administration	IV push/IV slow injection			Notes
		Preparation	Stability ^b	Administration	
Penicillins					
Ampicillin	<ul style="list-style-type: none">• IV push• Slow IV injection• IM	Vials of 125, 250, and 500 mg; reconstitute with 5-mL SWFI or BWFI Vials of 1 and 2 g; reconstitute with 7.4 or 14.8 mL, respectively, SWFI or BWFI No further dilution required	IM and IV push injections should be administered within 1 h after reconstitution as potency may decrease Additional stability information in text summary	Inject over 3 to 5 min for 125-, 250-, and 500-mg doses Inject over 10 to 15 min for 1- and 2-g doses	Administration of ampicillin more rapidly than recommended may result in convulsive seizures ^c No relevant syringe stability was located
Ampicillin/subactam	<ul style="list-style-type: none">• Slow IV injection• Intermittent IV infusion• IM	Vials of 1.5 and 3.0 g; Reconstitute with 3.2 or 6.4 mL of SWFI, respectively, to a concentration of 250 mg ampicillin/mL Further dilute with suitable diluent to a final concentration of 30 mg ampicillin/mL (maximum concentration for IV administration)	Reconstituted solution (30 mg ampicillin/mL), in SWFI or NS; 8 h at 25°C and 48 h at 4°C	Inject over at least 10 to 15 min	See PI for detailed information on stability for various diluents and storage conditions No relevant syringe stability was located
Nafcillin	<ul style="list-style-type: none">• Slow IV injection• Intermittent IV infusion• IM	Vials of 1 or 2 g; reconstitute, respectively, with 3.4 or 6.6 mL SWFI, NS, or BWFI (with benzyl alcohol or parabens) to final concentration of 250 mg/mL Further dilute reconstituted solution with at least 15 to 30 mL SWFI, NS, or ½ NS Off-label preparation Poole 1999 ⁷⁹ : 1 g diluted with 25 mL NS (for central line administration only)	Initial reconstituted solution (250 mg/mL): 3 d at RT, 7 d under refrigeration, and 90 d frozen Stability of further diluted solutions: 10 to 200 mg/mL; 24 h at RT and 7 d under refrigeration, in SWFI and NS	Inject over 5 to 10 min, recommended to be given through the tubing of a running compatible IV infusion	Poole 1999 ⁷⁹ : Evaluated IV push for patient-administered dose at home (OPAT); given over 5 to 10 min No relevant syringe stability was located
Oxacillin	<ul style="list-style-type: none">• Slow IV injection• Intermittent IV infusion• IM	Vials of 1 and 2 g; Reconstitute with 10 or 20 mL, respectively, of SWFI, ½ NS, or NS to 100 mg/mL No further dilution required	Reconstituted solution (10-100 mg/mL): 4 d at RT and 7 d under refrigeration, in SWFI and NS Reconstituted solution (100 mg/mL): 30 d frozen in SWFI and NS (for SWFI, includes 50-100 mg/mL) Plastic luer-tip syringes with tubing attached and capped, 100 mg/mL in NS ⁶⁴ ; 92 h at RT and 2 wk under refrigeration	Inject over 10 min	
Polymyxins					
Colistimethate sodium	<ul style="list-style-type: none">• IV push• IV continuous infusion• IM injection	150 mg vial: reconstitute with 2 mL SWFI to resulting concentration of 75 mg/mL No further dilution required	Reconstituted vial: 7 d at refrigerated (2°-8°C) or RT (20°-25°C)	Inject over 3 to 5 min	See text summary for additional stability information No relevant syringe stability was located

Note. FDA = Food and Drug Administration; ½ NS = half-normal saline (0.45% sodium chloride); D5W = dextrose 5% in water; OPAT = outpatient parenteral antibiotic therapy; ED = emergency department; IM = intramuscular; IV = intravenous; NS = normal saline (0.9% sodium chloride); PI = prescribing information; PK = pharmacokinetic; RT = room temperature; SWFI = sterile water for injection; BWFI = bacteriostatic water for injection; USP = United States Pharmacopeia.

^aInformation sourced from PI unless otherwise noted.

^bFor assigning beyond use dates, in addition to stability data, USP <797> recommendations for sterility still apply. The shorter of the times should be used.

^cClinical Pharmacology reported 100 mg/min as maximum rate; however, this information could not be confirmed in additional resources. In addition, this rate is slower than what would be administered if following PI-recommended dilution and administration.

Aminoglycosides:	Penicillins:
Amikacin ^a	Penicillin G
Streptomycin	Piperacillin/tazobactam
Carbapenems:	Tetracyclines:
Doripenem	Doxycycline
Imipenem/cilastatin ^a	Minocycline
Meropenem/vaborbactam	Tigecycline
Cephalosporins:	Others:
Ceftaroline	Azithromycin
Ceftolozane/tazobactam	Clindamycin
Ceftazidime/avibactam	Erythromycin
Fluoroquinolones:	Lincomycin
Ciprofloxacin ^a	Linezolid
Levofloxacin	Metronidazole ^a
Moxifloxacin	Polymixin B
Glycopeptides/lipoglycopeptides/lipopeptides:	Quinupristin/dalfopristin
Dalbavancin	Rifampin
Oritavancin	Tedizolid
Telavancin	Trimethoprim-sulfamethoxazole
Vancomycin	

Figure 1. Antibiotics with limited or no data for IV push administration. See the text summaries for each drug class for further information.

^aLimited data available, not recommended for IV push administration.

Table 1 provides a summary of antibiotics that can be administered IV push. Stability data are limited to solutions (eg, concentrations, diluents) that can be used for IV push administration. Because there is no exact definition of IV push and a wide range of administration durations were considered IV push in the original sources, Table 1 separates administration recommendations into 2 categories. Administration over 5 minutes or less are listed as IV push, while administration over longer durations of time (eg, over 5-10 minutes) are listed as slow IV injection; however, specific administration times are provided. Figure 1 lists antibiotics that had no data or limited data suggesting IV push as a viable administration method; therefore, these antibiotics are excluded from Table 1.

Aminoglycosides

None of the aminoglycosides are indicated for IV push administration.^{7-9,46} Aminoglycosides are generally not recommended for IV push administration due to the concern that elevated peak levels after rapid administration may cause toxicity, such as ototoxicity.^{9,65,88} Specifically, the PI for tobramycin notes that peak serum levels may exceed 12 µg/mL when administered over periods <20 minutes.⁹

However, IV push administration of gentamicin and tobramycin has been reported frequently in primary literature.⁸⁹⁻¹⁰⁰ Table 1 includes a summary of studies with sufficient detail to replicate administration, including a descriptive report demonstrating that gentamicin and tobramycin can be safely administered IV push based on experience

with 5593 doses in the setting of outpatient parenteral antibiotic therapy (OPAT).⁶⁷ In addition to the studies cited in Table 1, gentamicin has reportedly been administered over time periods ranging from <10 seconds to 5 minutes,^{89-91,93-96} while tobramycin has been administered over time periods ranging from 15 seconds to 5 minutes.^{89,90,96-101} Most administration times for gentamicin and tobramycin ranged from approximately 3 to 5 minutes. These studies were of varying quality and instructions for preparation were not described. There are limited reports of IV push administration with amikacin; one healthy volunteer study (n = 5) evaluated administration of 7.5 mg/kg directly from the manufacturer vial (250 mg/mL) over 2 minutes, but this resulted in potentially toxic peak serum concentrations (68-122 µg/mL).¹⁰² Amikacin has been administered over 3 minutes and 5 minutes, respectively, in 2 additional pharmacokinetic studies; however, dilution and preparation instructions were not reported.^{103,104} Reports of streptomycin administered via IV push were not identified.

Carbapenems

Of the carbapenems, only meropenem is FDA-approved to be administered IV push.¹¹ Doripenem and meropenem/vaborbactam should only be given via intermittent IV infusion; no data are available to support IV push administration.^{35,37} One pharmacokinetic study was identified describing administration of imipenem/cilastatin 500 mg over 10 minutes in 6 patients undergoing continuous ambulatory peritoneal dialysis; the volume/concentration of the

administered solution was not provided.¹⁰⁵ However, IV push administration of imipenem/cilastatin is not recommended due to adverse events associated with rapid administration, such as nausea and vomiting.^{61,66} Administration of ertapenem 1 gram IV push over 5 minutes was bioequivalent to the 30-minute infusion for maximum serum concentration (C_{max}) and area under the curve (AUC) in a study in 12 healthy volunteers, and no serious adverse events, such as vomiting or seizures, occurred (Table 1).⁷⁶

Cephalosporins

Cefazolin, cefotaxime, cefotetan, cefoxitin, ceftazidime, and cefuroxime are FDA-approved for IV push administration.^{12,14-18,20} Studies comparing IV push and short-term infusion administration of cephalosporins have generally found similar rates of phlebitis and other complications.^{78,79,106} Although not FDA-approved, cefepime and ceftriaxone may also be administered IV push.^{2,3,78,79,85} Data for cefepime are limited to use as the first-dose in the ED, with limited outcome and adverse event data provided in reports.^{2,3} One additional study evaluated cefepime administered IV push, but the required volume for preparation was 50 mL, losing volume minimization advantages of IV push.⁸⁵ Ceftriaxone IV push administration has been evaluated in several settings, including in the ED, with OPAT, and in hospitalized patients, with no noted concerns.^{2,78,79} Additional data on ceftriaxone IV push administration exist, but the majority of studies did not robustly report both preparation and administration details or focused solely on pediatric populations.¹⁰⁷⁻¹⁰⁹ Only 3 cephalosporins lack information for IV push administration: ceftazidime/avibactam, ceftolozane/tazobactam, and ceftaroline.

Specific adverse events related to IV push administration of cefotaxime and ceftriaxone are noted in the literature. A potentially life-threatening arrhythmia occurred in 6 patients who received rapid (<1 minute) administration of cefotaxime through a central venous catheter.¹⁴ Rapid ceftriaxone administration (2 grams over 5 minutes) was associated with a case of palpitation, tachycardia, restlessness, shivering, and diaphoresis in an adult.¹¹⁰ Ceftriaxone has also been reported to be associated with increased biliary pseudolithiasis in children given ceftriaxone over 3 to 5 minutes, and with the formation of calcium-ceftriaxone precipitate in neonates receiving concurrent calcium-containing solutions who received ceftriaxone over 2 to 4 minutes, which led to adverse cardiopulmonary events.^{111,112}

Glycopeptides/Lipoglycopeptides/Lipopeptides

Daptomycin (both Cubicin and Cubicin RF) may be administered IV push in adults when reconstituted to a concentration of 50 mg/mL.^{21,22} While this practice has been reported to be safe in adults,¹¹³⁻¹¹⁵ a case report exists documenting an IV

push-related reaction to daptomycin (Cubicin) administered over 2 minutes involving redness and a warm sensation on the face, neck, and upper chest that resolved with diphenhydramine and did not recur with rechallenge of a 30- to 40-minute infusion.¹¹⁶ The newer agents of these classes are not amenable to IV push administration; dalbavancin, oritavancin, and telavancin are administered via extended infusions ranging from 1 to 3 hours, and no recent literature reports their administration over shorter periods.³⁸⁻⁴⁰ Vancomycin, because of the risk for infusion reaction (ie, “red-man syndrome”), should be administered no more rapidly than 10 mg/minute or over a period of ≥60 minutes, whichever is longer.^{60,61,65,66} Infusion reactions can be mediated by both the concentration and rate of administration of vancomycin. For patients in need of fluid restriction, vancomycin may be administered at concentrations up to 10 mg/mL, though this may increase the risk for infusion reaction.

Fluoroquinolones

Fluoroquinolones (ciprofloxacin, levofloxacin, and moxifloxacin) are not recommended for IV push administration due to adverse events associated with rapid administration.^{57-59,61,66} These adverse events include venous irritation with ciprofloxacin, hypotension with levofloxacin, and an increase in the incidence and magnitude of QT prolongation with moxifloxacin. In addition, moxifloxacin is only available in premix formulations intended for intermittent IV infusion.^{6,58} In order to reduce venous irritation, slow IV infusion of ciprofloxacin into a large vein is recommended.⁵⁹ Although reports of ciprofloxacin administration over a period ranging from 3 to 15 minutes were identified, these studies did not specifically aim to evaluate the safety and efficacy of the IV push administration.¹¹⁷⁻¹¹⁹ In 2 pharmacokinetic studies in healthy volunteers, ciprofloxacin was administered via rapid injection over 3 or 5 minutes, but the volume and concentration of the administered solutions were not specified.^{117,118} In one of these studies, observed adverse events with administration of ciprofloxacin 250 mg over 5 minutes in 8 healthy volunteers included localized numbness (n = 1), local thrombophlebitis (n = 1), and nausea (n = 1).¹¹⁷ In another study in 12 healthy volunteers, ciprofloxacin 50 mg and 100 mg was prepared in 50 mL normal saline and administered over 15 minutes with a constant pump, with no observed adverse events.¹¹⁹ However, these doses are lower than those commonly used in clinical practice.⁶⁰

Penicillins and Monobactam

Among the penicillins, ampicillin may be administered IV push or as a slow IV injection after reconstitution, depending on the dose.²⁶ Administration faster than recommended by the PI may increase the risk of seizures.^{26,60,65} In addition, ampicillin has limited stability, which decreases with increasing concentrations.⁶³ Nafcillin and oxacillin require

administration via slow IV injection (eg, over 5-10 minutes).^{28,29} Phlebitis may occur if these agents are injected too rapidly.⁶⁰ Of note, profound hypotension has been reported among patients receiving IV push administration of nafcillin during coronary artery bypass graft surgery, presumed to be due to histamine-mediated vasodilation.¹²⁰ Penicillin G and piperacillin/tazobactam are not recommended for IV push administration. Ampicillin/sulbactam is recommended to be diluted in volumes that may preclude practical administration via slow IV injection (eg, 1.5 g vials in 50 mL to obtain maximum 30 mg/mL concentration).²⁷ Although a study in 16 patients undergoing colorectal surgery reported IV push administration of 2 g/1 g ampicillin/sulbactam over 3 minutes, the concentration of the solution was not reported.¹²¹ Similarly to ampicillin, seizures may occur with rapid administration of ampicillin/sulbactam.⁶⁶ Finally, the monobactam aztreonam is indicated for IV push administration after reconstitution of vials.²³

Polymyxins

Colistimethate sodium can be administered IV push.²⁵ After reconstitution, the manufacturer recommends use within 7 days. However, colistimethate sodium can hydrolyze to colistin in aqueous solution. Although this conversion was minimally observed in one stability study (<1% after storage of reconstituted solution at 4° or 25°C for 7 d in the dark), the authors cautioned that reconstitution should still be done as close to administration as possible, and if it is necessary to store the solution, they recommend storage at 4°C to minimize bacterial contamination.¹²² With regard to the safety of IV push administration, 1 patient out of 12 in a trial assessing the safety and tolerability of IV push colistimethate reported dizziness/lack of coordination after receiving 160 mg in 10 mL over 5 minutes.¹²³ This resolved when the patient was switched to an intermittent IV infusion over 30 minutes. Polymyxin B is FDA-approved to be given as an IV infusion, intramuscularly, or intrathecally.⁴⁵ Administration of polymyxin B over a period <30 minutes is not recommended, and rapid IV injections should be avoided due to the potential for nephro- or neurotoxicity.^{62,124}

Tetracyclines

Doxycycline, minocycline, and tigecycline are recommended to be administered as an intermittent IV infusion and are not suitable for IV push administration.⁴²⁻⁴⁴ The PIs for doxycycline and minocycline specifically state that rapid administration is not recommended, and oral administration is preferred over parenteral administration.^{42,43} Phlebitis and burning have been observed with more concentrated solutions of doxycycline.^{65,125}

Others

Of the antibiotics that are not included in the classes already discussed, only chloramphenicol can be administered IV push.²⁴ All of the other agents have specific statements against IV push administration in at least one tertiary resource.^{60-63,65,66} Of note, Seifert and colleagues documented a report of severe nausea, cramping, and hypotension after administration of erythromycin 1 g in 100 mL of normal saline over 10 minutes.¹²⁶ In addition, Aucoin and colleagues reported a case of complete heart block following administration of clindamycin 600 mg over several minutes; the same patient tolerated subsequent clindamycin infusions over 30 minutes without incident.¹²⁷ Rapid lincomycin administration has also been associated with severe cardiac events including cardiopulmonary arrest.¹²⁸

Linezolid and metronidazole are not available in a vial formulation so these drugs are not practical to administer IV push.^{6,51,52} One observational pharmacokinetic study documented rapid IV push of metronidazole 500 mg over 5 minutes, but the volume/concentration of the administered solution was not specified so these data are not readily applicable to current clinical practice.¹²⁹

Practical Considerations for IV Push Antibiotics

Several organizations have issued guidance or recommendations for safe IV administration practices.¹³⁰ The Institute for Safe Medication Practices (ISMP) provides guidance on adult IV push medication safety.¹³¹ Briefly, this guidance supports preparation of IV push medications in the pharmacy so that a ready-to-administer form can be provided to patient care areas. In cases where immediate administration is required for medication stability, preparation and dilution of the medication can occur in patient care areas. In those instances, dilution should take place in a clean, uncluttered area with clear instructions on the type and volume of diluent that is needed. Syringes should be promptly labeled; supplying blank, ready-to-apply labels may help with adherence to that step. Considerations for safe administration of IV push medications can be found in the ISMP guidance document. The 2016 Infusion Nurses Society (INS) Infusion Therapy Standards of Practice largely mirror the ISMP recommendations for safe preparation of medications for IV push administration.¹³²

Osmolality is a concern when administering concentrated solutions. The 2016 INS Infusion Therapy Standards of Practice state that solutions with osmolality >900 mOsm/kg should be administered through a central line and solutions with osmolalities below this limit can be administered via peripheral or midline catheters.¹³² The Standards of Practice do not have any statements that connect osmolality and administration rate; therefore, there does not seem to be any

added concern with IV push administration of solutions with higher osmolalities compared with slower administration rates. Osmolality data is not readily available in product labeling or other tertiary resources and most published osmolality values are based on historical literature that is not readily applicable to current practice.^{1,78,133-135} With the limitation that not all agents have relevant data, our review of all available published and unpublished (manufacturer-supplied) osmolality information for the antibiotics that can be administered IV push suggests that the recommended solutions for IV push administration all have osmolalities well below 900 mOsm/kg.

Additional steps that help ensure safe use of IV push medications include providing a specific administration duration on the label or in the electronic medication administration record (eg, “administer over 10 minutes” rather than “slow IV injection”).¹³¹ Nurse education on proper dilution of IV push medications may also facilitate proper preparation. A 2014 ISMP survey found that 83% of nurse respondents further dilute certain IV push medications prior to administration.¹³⁶ Unnecessary dilution of medications can lead to contamination of sterile products, dosing errors, or administration errors. Multidose vials should not be kept in patient care areas per the Centers for Disease Control and Prevention *One & Only Campaign*, which prevents both inadvertent use in multiple patients and errors related to IV push administration of these solutions.¹³⁷

Pharmacodynamic Considerations for IV Push Antibiotics

The pharmacodynamic effect of antibiotics can be generalized into either concentration-dependent or time-dependent bactericidal activity.¹³⁸ For agents that are concentration-dependent, maximizing the AUC per unit of time in relation to the bacterial minimum inhibitory concentration (MIC) generally increases the rapidity of bacterial killing and thus increases the likelihood of a good clinical outcome. For example, daptomycin has concentration-dependent bactericidal activity and a change in the rate of infusion (eg, a 30-minute infusion versus a 5-minute injection) does not significantly affect the resulting AUC. For beta-lactams, increasing the infusion duration can substantially increase the duration of time that the drug concentration remains above the MIC ($T > \text{MIC}$); therefore, changing from an infusion to IV push administration may negatively affect the pharmacodynamics of these agents. One Monte Carlo simulation study and one healthy volunteer pharmacokinetic study have investigated the impact of IV push administration.^{76,139} Based on these results, 3- to 5-minute IV push injections and 30-minute infusions of aztreonam, cefepime, ertapenem, and meropenem are expected to achieve similar $T > \text{MIC}$ profiles.

In contrast, the difference in $T > \text{MIC}$ between a 3- to 5-minute IV push injection (or 30-minute infusion) and an

extended (eg, over 3 or 4 hours) or continuous infusion can be clinically significant.¹⁴⁰ Several studies have found that extended and continuous infusion strategies are associated with improved clinical cure and survival, particularly in severely ill patients, compared with shorter infusion durations.¹⁴¹⁻¹⁴³ Therefore, current data do not support the substitution of IV push administration for extended or continuous infusion schemes in patients who are critically ill, immunocompromised, or infected with organisms with MICs at or above the clinical breakpoint for susceptibility (eg, *Pseudomonas* with a piperacillin/tazobactam MIC of 16 µg/mL).

Conclusion

Several antibiotics, particularly in the cephalosporin class, are FDA-approved for IV push or slow IV injection administration. In addition, there are primary literature data that support IV push administration of cefepime, ceftriaxone, ertapenem, gentamicin, and tobramycin. Syringe stability data are not available for all antibiotics, which may preclude IV push administration if preparation in patient care areas for immediate use is not possible. Precautions should be taken to ensure safe IV push administration, including clear labeling and staff education. Pharmacodynamic changes due to IV push administration should be considered, including effects on time above MIC when administering antibiotics via IV push that are normally administered as extended or continuous infusions.

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