

Appendix 1: Cost Analysis**1. Pretomanid**

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Pretomanid [49502-0476-26]	200 mg daily orally for 26 weeks, <i>in combination with</i> : <ul style="list-style-type: none"> Linezolid 1,200 mg daily orally for up to 26 weeks Bedaquiline 400 mg orally once daily for 2 weeks followed by 200 mg 3 times per week for 24 weeks for a total of 26 weeks 	<ul style="list-style-type: none"> Pretomanid 19.78/200 mg tablet (Package Size: 26 tablets) Linezolid 2.43/600 mg tablet (Package Size: 20 tablets) Bedaquiline: 159.57/100 mg tablet (Package Size: 188 tablets) 	<ul style="list-style-type: none"> Pretomanid: 3,599.96 Linezolid: 884.52 Bedaquiline: 31,914.00 <p>36,398.48</p>
Comparator	Isoniazid (INH) [10135-0584-01] Rifampin (RIF) [00904-5282-61] Pyrazinamide (PZA) [61748-0012-05] & Ethambutol (EMB) [68850-0012-02]	<u>Intensive Phase</u> : 300 mg INH, 600 mg RIF, 1500 mg PZA, and 1200 EMB once daily for 8 weeks <u>Continuation Phase</u> : 300 mg INH and 600 mg RIF once daily for 18 weeks	<ul style="list-style-type: none"> INH 0.16040/300 mg tablet (Package Size: 100 tablets) RIF 1.10550/300 mg tablet (Package Size: 100 tablets) PZA: 4.86616/500 mg tablet (Package Size: 500 tablets) EMB 0.78000/400 mg tablet (Package Size: 100 tablets) 	Intensive <ul style="list-style-type: none"> INH: 8.98 RIF: 123.82 PZA: 817.51 EMB: 131.04 Continuation <ul style="list-style-type: none"> INH: 20.21 RIF: 278.59 <p>1,380.15</p>
Cost Factor	26.37			
Notes	<ul style="list-style-type: none"> Total costs are calculated based on unit cost rather than package cost. Additional Reference NDCs <ul style="list-style-type: none"> Linezolid: 72606-0001-07 			

	<ul style="list-style-type: none">○ Bedaquiline: 59676-0701-01○ Isoniazid: 10135-0584-01○ Rifampin: 00904-5282-61○ Pyrazinamide: 61748-0012-05○ Ethambutol: 68850-0012-02▪ Costs as of Date<ul style="list-style-type: none">○ Pretomanid: 11.07.2019○ Linezolid: 10.08.2019○ Bedaquiline: 04.19.2013○ Isoniazid: 05.01.2015○ Rifampin: 09.12.2016○ Pyrazinamide: 02.28.2017○ Ethambutol: 11.01.2016
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2. Imipenem-Cilastatin-Relebactam

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Imipenem-Cilastatin-Relebactam [00006-3856-02]	[All Indications] 1.25 g by IV infusion over 30 minutes, every 6 hours, for 4-14 days	267.50/1.25 g vial (Package Size: 25 vials)	4,280 - 14,980
Comparator	Imipenem-Cilastatin (IMI) [63323-0349-93] (Study PN003, PN004)	500 mg IV infusion every 6 hours, for 4 – 14 days	[Imipenem-Cilastatin] 6.50000/unit of 250-250 mg powder for solution (Package Size: 25 units of 250-250 mg)	104.00 – 364.00
	Colistimethate Sodium (CMS) [25021-0159-10] & Imipenem-Cilastatin (IMI) [63323-0349-93] (Study PN013)	Loading dose of colistimethate sodium (300 mg), followed by 300 mg CMS every 12 hours and 500 mg IMI IV infusion every 6 hours, for 4 – 14 days	[Colistimethate Sodium] 24.00000/unit of 150 mg powder for solution (Package Size: 1 unit) [Imipenem-Cilastatin] 6.50000/unit of 250-250 mg powder for solution (Package Size: 25 units of 250-250 mg)	536.00 – 1,756.00
Cost Factor		IMI 41.15 IMI+CMS 7.99, 8.53		
Notes	<ul style="list-style-type: none"> ▪ Imipenem-Cilastatin-Relebactam is available in a combination of 500 mg imipenem, 500 mg cilastatin, and 250 mg relebactam. ▪ Cost ranges, and cost factor ranges, reflect cost for the shortest and longest course of treatment indicated. ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Imipenem-cilastatin (250-250 mg): 63323-0349-93 ○ Colistimethate sodium: 25021-0159-10 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Imipenem-Cilastatin-Relebactam: 01.06.2020 ○ Imipenem-cilastatin (250-250 mg): 06.16.2016 ○ Colistimethate sodium: 12.15.2014 			

3. Lefamulin

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Lefamulin [72000-0110-30, 72000-0120-06]	150 mg every 12 hours by IV infusion over 60 minutes for 5 – 7 days OR 600 mg tablets every 12 hours for 5 days	6.83/mL (Package Size: 6 vials, 15 mL each, at 10 mg/mL) 137.50/600 mg tablet (Package Size: 30 tablets)	IV: 1,024.50 - 1,434.50 Oral: 1,375.00
Comparator	Moxifloxacin [67457-0323-25, 65862- 0603-30]	[For CABP] 400 mg moxifloxacin orally OR by IV infusion once daily for 7 – 14 days	0.18/mL (Package Size: 12 units of 250 mL at 400 mg/250 mL) 2.94/400 mg tablet (Package Size: 30 tablets)	IV: 315.00 – 630.00 Oral: 20.58 – 41.16
Cost Factor	IV: 3.25, 2.28 Oral: 66.81, 33.41			
Notes	<ul style="list-style-type: none"> ▪ Costs as of Date <ul style="list-style-type: none"> ○ Lefamulin (IV 72000-0110-30, tablet 72000-0120-06): 09.01.2019 ○ Moxifloxacin (IV, 67457-0323-25): 10.03.2017 ○ Moxifloxacin (tablet, 65862-0603-30): 05.15.2018 			

4. Rifamycin

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Rifamycin [71068-0001-10]	388 mg twice a day for 3 days	14.67/194 mg tablet (Package Size: 12 tablets)	176.04
Comparator	Ciprofloxacin [55111-0127-01]	[For Traveler's Diarrhea] 500 mg orally twice daily for 5 – 7 days	0.19/500 mg tablet (Package Size: 100 tablets)	1.9 – 2.66
Cost Factor	92.65, 66.18			
Notes	<ul style="list-style-type: none"> ▪ Note that in rifamycin's two pivotal trials, the comparator was placebo in one and ciprofloxacin in the other. The course of treatment with ciprofloxacin in the pivotal was 3 days, but here we have used more conservative guidelines of 5 to 7 days for cost calculation here. ▪ Costs as of Date <ul style="list-style-type: none"> ○ Rifamycin: 01.01.2021 ○ Ciprofloxacin: 07.05.2017 			

5. Omadacycline

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Omadacycline [71715-0001-01, 71715-0002-21]	[ABSSSI] Loading - 200 mg by IV infusion over 60 min OR 100 mg by IV infusion over 30 minutes twice on Day 1. Maintenance - 100 mg IV infusion over 30 minutes once daily OR 300 mg tablets once daily. Alternative - 450 mg tablet once on Day 1 and 2, and 300 mg tablet once daily thereafter. Total course of treatment 7 – 14 days. [CABP] Loading - 200 mg by IV infusion over 60 min OR 100 mg by IV infusion over 30 minutes twice on Day 1. Maintenance - 100 mg IV infusion over 30 minutes once daily OR 300 mg tablets once daily. Total course of treatment 7 – 14 days.	345.00/100 mg package (Package Size: 100 mg solution) 216.71/150 mg tablet (Package Size: 6 tablets)	[All Indications, IV Infusion] 2,760 - 5,175
Comparator	ABSSSI: Linezolid [25021-0169-87, 72606-0001-08] CABP: Moxifloxacin [67457-0323-25, 65862-0603-30]	[ABSSSI, Linezolid] 600 mg IV infusion OR tablets twice daily for 10 – 14 days [CABP, Moxifloxacin] 400 mg moxifloxacin orally OR by IV infusion once daily for 7 – 14 days	[ABSSSI, Linezolid] 0.12/mL (Package Size: 10 units of 300 mL at 600 mg/300 mL) 3.43/600 mg tablet (Package Size: 30 tablets) --- [CABP, Moxifloxacin] 0.18/mL (Package Size: 12 units of 250 mL at 400 mg/250 mL) 2.94/400 mg tablet (Package Size: 30 tablets)	IV: 720.00 – 1,440.00 Oral: 68.60 – 137.20 [ABSSSI, Linezolid] IV: 315.00 – 630.00 Oral: 20.58 – 41.16 [CABP, Moxifloxacin]
Cost Factor	<p style="text-align: center;">ABSSSI</p> <p style="text-align: center;">IV Omadacycline: IV Linezolid = 3.83 – 3.59 IV Omadacycline: Oral Linezolid = 40.23 – 37.72</p> <p style="text-align: center;">CABP</p> <p style="text-align: center;">IV Omadacycline: IV Moxifloxacin = 8.76 – 8.21 IV Omadacycline: Oral Moxifloxacin = 134.11 – 125.73</p>			

<p>Notes</p>	<ul style="list-style-type: none">▪ The alternative dosage and administration for the ABSSSI indication was not used in total cost calculation. Only the IV administration in maintenance was used in total cost calculation. That is, the oral route was disregarded to simplify cost calculation.▪ Note that each study drug may have more than one NDC, not all of which are noted in these tables. The NDC chosen to calculate total cost of a course of treatment is based on the NDC(s) with the lowest unit cost at the time of writing OR NDCs for which cost information was available in the IBM Micromedex Red Book.▪ Costs as of Date<ul style="list-style-type: none">○ Omadacycline (IV, 71715-0001-01): 12.10.2018○ Omadacycline (tablet, 71715-0002-21): 01.01.2021○ Linezolid (IV, 25021-0169-87): 08.01.2019○ Linezolid (tablet, 72606-0001-08): 06.05.2020○ Moxifloxacin (IV, 67457-0323-25): 10.03.2017○ Moxifloxacin (tablet, 65862-0603-30): 05.15.2018
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6. Eravacycline

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Eravacycline [71773-0050-05]	1 mg/kg IV infusion over 60 minutes every 12 hours for total of 4 – 14 days	49.00/50 mg powder for solution (Package Size: 50 mg)	[75 kg patient] 588.00 – 2,058.00
Comparator	Ertapenem [55150-0282-09] (Study TP-434-008)	1.0 g IV infusion once daily for 4 to 14 days	100.0000/1 g powder (Package Size: 10 units at 1 g each)	400.00 – 1,400.00
	Meropenem [72572-0415-10] (Study TP-434-025)	1.0 g IV infusion three times daily for 4 to 14 days	7.11000/1 g powder (Package Size: 10 units at 1 g each)	85.32 – 149.31
Cost Factor	Ertapenem: 1.47 Meropenem: 6.89, 13.78			
Notes	<ul style="list-style-type: none"> ▪ Note that each study drug may have more than one NDC, not all of which are noted in these tables. The NDC chosen to calculate total cost of a course of treatment is based on the NDC(s) with the lowest unit cost at the time of writing OR NDCs for which cost information was available in the IBM Micromedex Red Book. ▪ Costs were calculated based for a 75 kg male patient. ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Ertapenem: 55150-0282-09 ○ Meropenem: 72572-0415-10 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Eravacycline: 05.30.2019 ○ Ertapenem: 05.03.2019 ○ Meropenem: 08.27.2020 			

7. Plazomicin

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Plazomicin [71045-0010-02]	15 mg/kg IV infusion over 30 minutes once daily for 4 -7 days	31.5000/10 ml vial (Package Size: 10 vials of 10 mL at 50 mg/ml)	[75 kg patient] 283.50 - 496.13
Comparator	Meropenem [72572-0415-10]	1 g IV infusion three times daily for 4 - 7 days	7.11000/1 g powder (Package Size: 10 units at 1 g each)	85.32 – 149.31
Cost Factor	3.32			
Notes	<ul style="list-style-type: none"> ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Meropenem: 72572-0415-10 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Plazomicin: 07.17.2018 ○ Meropenem: 08.27.2020 			

8. Delafloxacin

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Delafloxacin [70842-0102-03, 70842-0101-01]	300 mg IV infusion over 60 minutes every 12 hours for 5 – 14 days OR 450 mg tablet twice daily for 5 – 14 days	132.5000/300 mg powder (Package Size: 10 300 mg units) 74.42/450 mg tablet (Package Size: 20 tablets)	IV: 1,325 - 3,710 Oral: 744.19 - 2,083.76
Comparator	Vancomycin [70594-0042-03] & Aztreonam [63323-0401-26]	15 mg/kg IV vancomycin & 2 g IV aztreonam, twice daily for 5 – 14 days	[Vancomycin] 0.15/1 mL solution (Package Size: 12 units of 200 mL solution at 1 g/200 mL) [Aztreonam] 27.31000/1 g powder (Package Size: 10 units of 1 g powder each)	[75 kg patient] Vancomycin: 337.50 – 945.00 Aztreonam: 546.20 – 1,529.36 883.70 – 2,474.36
Cost Factor	IV Delafloxacin: 1.50, 1.10 Oral Delafloxacin: 0.84			
Notes	<ul style="list-style-type: none"> ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Vancomycin: 70594-0042-03 ○ Aztreonam: 63323-0401-26 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Delafloxacin IV: 10.20.2017 ○ Delafloxacin tablets: 04.01.2019 ○ Vancomycin: 04.01.2019 ○ Aztreonam: 09.04.2015 			

9. Secnidazole

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Secnidazole [27437-0051-01]	2 grams of granules once orally	282.25/2 g granules (Package Size: 2 g granules)	282.25
Comparator	Metronidazole [62332-0016-31]	[Bacterial vaginosis] 750 mg orally once daily for 7 days	0.28/250 mg tablet (Package Size: 100 tablets)	5.88
Cost Factor	48.00			
Notes	<ul style="list-style-type: none"> ▪ Costs as of Date <ul style="list-style-type: none"> ○ Secnidazole: 12.01.2019 ○ Metronidazole: 12.02.2016 			

10. Meropenem-vaborbactam

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Meropenem-vaborbactam [70842-0120-06]	2 g/2 g IV infusion over 3 hours, every 8 hours, for up to 14 days	178.200/1 g powder for solution (Package Size: 6 1 g units)	29,937.60
Comparator	Piperacillin-tazobactam [00206-8862-02]	4 g/0.5 g IV infusion, every 8 hours, for up to 10 days	0.25125/mL premix solution (Package Size: 12 units of 100 mL solution at 4 g/0.5 g)	753.75
Cost Factor	39.72			
Notes	<ul style="list-style-type: none"> ▪ Note that the length of treatment in the pivotal trials with meropenem-vaborbactam was up to 10 days. The FDA label indicates a course of treatment up to 14 days, which we have opted to use to calculate cost of treatment here. ▪ Optional stepdowns to oral treatment (typically levofloxacin) not included in cost calculation. ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Piperacillin-tazobactam: 00206-8862-02 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Meropenem-vaborbactam: 04.01.2019 ○ Piperacillin-tazobactam: 01.01.2021 			

11. Ozenoxacin

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Ozenoxacin [70363-0011-30]	Apply thin layer to affected area twice daily for up to 5 days (Dosage unspecified.)	9.90/g 1% cream (Package Size: 30 g tube)	297.00 [One 30 g tube ozenoxacin]
Comparator	Retapamulin [16110-0518-30]	Apply thin layer to the affected area twice a day for 5 days (Dosage unspecified.)	20.76033/g 1% cream (Package Size: 30 g tube)	622.81 [One 30 g tube retapamulin]
Cost Factor	0.48			
Notes	<ul style="list-style-type: none"> ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Retapamulin: 16110-0518-30 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Ozenoxacin: 10.26.2018 ○ Retapamulin: 01.02.2021 			

12. Bezlotoxumab

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Bezlotoxumab [00006-3025-00]	One-time IV infusion of 10 mg/kg over 60 minutes	95.00/mL (Package Size: 40 mL at 25 mg/mL)	2,850.00 [75 kg patient]
Comparator	None available.	-	-	-
Cost Factor	No calculation possible.			
Notes	<ul style="list-style-type: none"> ▪ Costs as of Date <ul style="list-style-type: none"> ○ Bezlotoxumab: 12.08.2016 			

13. Amikacin liposome inhalation suspension

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Amikacin liposome inhalation suspension [71558-0590-28]	Once daily oral inhalation of one 590 mg/8.4 mL vial, for 8 – 16 months	52.64/mL (Package Size: 28 vials of 8.4 mL at 590 mg/8.4 ml)	12,380.93 [28-day supply] 161,394.24 – 215,191.78 [8 – 16 months]
Comparator	Rifampin [00904-5282-61] Ethambutol [62991-3060-01] & Azithromycin [00069-3070-30]	Azithromycin (500 mg), rifampin (600 mg), and ethambutol (25 mg/kg) three times a week, for 8 – 16 months.	[Rifampin] 1.10550/300 mg capsule (Package Size: 100 capsules) [Ethambutol] 2.16750/g powder (Package Size: 25,000 grams) [Azithromycin] 2.94800/500 mg tablet (Package Size: 30 tablets)	[For a 75 kg patient] Rifampin: 2.21/dose Ethambutol: 4.06/dose Azithromycin: 2.95/dose 110.64 [28-day supply] 1,438.32 – 1,917.76 [8 – 16 months]
Cost Factor	[28-day supply] 111.90 [8 -16 months] 112.21 (across the range)			
Notes	<ul style="list-style-type: none"> ▪ Pivotal trials for amikacin sulfate used a background regimen of at least two ATS/IDSA recommended drugs as the comparator. More than half of the comparison group in the pivotal trial were on a rifamycin, ethambutol, and a macrolide. Here we've used azithromycin as the representative macrolide based on IDS guidelines, and rifampin as the representative rifamycin. ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Rifampin: 00904-5282-61 ○ Ethambutol: 62991-3060-01 ○ Azithromycin: 00069-3070-30 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Amikacin sulfate: 01.01.2021 ○ Rifampin: 01.01.2021 ○ Ethambutol: 01.01.2013 			

	○ Azithromycin: 01.01.2021
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14. Cefiderocol

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Cefiderocol [59630-0266-10]	2 g IV infusion over 3 hours, every 8 hours, for 7 to 14 days	183.33/g powder for solution (Package Size: 10 units of 1 g each)	7,699.86 – 15,399.72
Comparator	Imipenem/Cilastatin [00409-3507-10]	Imipenem/cilastatin (1 g: 1 g) IV infusion every 8 hours for 7 – 14 days	9.45/500 mg-500 mg powder for solution (Package Size: 25 units)	396.90 – 793.80
Cost Factor	19.6, 19.4			
Notes	<ul style="list-style-type: none"> ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Imipenem/Cilastatin: 00409-3507-10 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Cefiderocol: 02.24.2020 ○ Imipenem/Cilastatin: 07.01.2013 			

15. Omeprazole magnesium-amoxicillin-rifabutin

	Drug [NDC]	Dosage & Administration	Unit Cost (WAC, \$)	Total Cost (WAC, \$)
Study Antibiotic	Omeprazole magnesium-amoxicillin-rifabutin [57841-1150-02]	4 capsules every 8 hours for 14 days	3.98/capsule (Package Size: 168 capsules)	668.64
Comparator	Amoxicillin [65862-0016-05] & Omeprazole [62175-0114-37]	1000 mg amoxicillin & 10 mg omeprazole every 8 hours for 14 days	[Amoxicillin] 0.047/250 mg tablet (Package Size: 500 capsules) [Omeprazole] 0.018/10 mg capsule (Package Size: 100 capsules)	Amoxicillin: 7.90 Omeprazole: 0.76 8.66
Cost Factor	77.21			
Notes	<ul style="list-style-type: none"> ▪ Talicia is available in a combination of 250 mg amoxicillin, 10 mg omeprazole magnesium, and 12.5 mg rifabutin capsules. ▪ Additional Reference NDCs <ul style="list-style-type: none"> ○ Amoxicillin: 65862-0016-05 ○ Omeprazole: 62175-0114-37 ▪ Costs as of Date <ul style="list-style-type: none"> ○ Omeprazole magnesium-amoxicillin-rifabutin: 01.01.2021 ○ Amoxicillin: 09.12.2006 ○ Omeprazole: 10.18.2019 			