Appendix 4: Post-Market Commitments and Requirements

See https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm. All PMCs are copied verbatim from the FDA source.

Drug	Commitments and Requirements	Reportable Under*	Current Status (as of Q 1 2021)
Pretomanid	1. Conduct a study to evaluate the effect of Pretomanid Tablets on human semen.	FDAAA Section 505 (o)(3)	Pending
	2. Conduct a global surveillance study for a five-year period after the introduction of Pretomanid Tablets to the market to monitor changes in M. tuberculosis susceptibility to pretomanid.	FDAAA Section 505 (o)(3)	Pending
	3. Conduct a study to evaluate pharmacokinetics and safety of Pretomanid Tablets in subjects with renal impairment.	FDAAA Section 505 (o)(3)	Pending
	4. Conduct a study to evaluate pharmacokinetics and safety of Pretomanid Tablets in subjects with mild, moderate, and severe hepatic impairment.	FDAAA Section 505 (o)(3)	Pending
	5. Conduct a two-year rat carcinogenicity study with pretomanid.	FDAAA Section 505 (o)(3)	Pending
	6. Conduct the ZeNix trial to evaluate various doses and treatment durations of linezolid plus bedaquiline and Pretomanid Tablets for treatment of extensively drug-resistant pulmonary tuberculosis.	FDAAA Section 505 (o)(3)	Pending
	7. Conduct the SimpliciTB trial to evaluate Pretomanid Tablets, bedaquiline, moxifloxacin, and pyrazinamide for treatment of drugresistant pulmonary tuberculosis.	FDAAA Section 505 (o)(3)	Pending
Imipenem-cilastatim-relebactam	1. Conduct an open label, single-dose study to evaluate the pharmacokinetics, safety and tolerability of imipenem, cilastatin and relebactam in children from birth to less than 18 years of age with proven or suspected Gram-negative infections.	Pediatric Research Equity Act	Pending
	2. Conduct a randomized, open-label, active controlled trial to evaluate the safety and tolerability of imipenem, cilastatin and relebactam in children from birth to less than 18 years of age with complicated urinary tract infections and complicated intra-abdominal infections.	Pediatric Research Equity Act	Released [As of 06/04/2020]
	3. Conduct a United States surveillance study for 5 years from the date of marketing to determine if resistance to imipenem, cilastatin, and relebactam had developed in those organisms specific to the indication in the label.	FDAAA Section 505(o)(3)	Pending
Lefamulin	1. Conduct a single-dose study to evaluate the pharmacokinetics and safety of intravenous XENLETA (lefamulin) in children from birth to less than 18 years of age with suspected or confirmed bacterial infections receiving standard of care.	Pediatric Research Equity Act	Pending

	2. Conduct a single-dose study to evaluate the pharmacokinetics and safety of oral XENLETA (lefamulin) in children from birth to less than 18 years of age with suspected or confirmed bacterial infections receiving standard of care.	Pediatric Research Equity Act	Pending
	3. Conduct a randomized active-controlled study to assess the safety and pharmacokinetics of XENLETA (lefamulin) in children from 2 months to less than 18 years of age with CABP.	Pediatric Research Equity Act	Pending
	4. Conduct a United States surveillance study for 5 years from the date of marketing to determine if resistance to XENLETA (lefamulin) has developed in those organisms specific to the CABP indication in the label.	FDAAA Section 505 (o)(3)	Pending
	5. Conduct a pregnancy surveillance program to collect and analyze information for a minimum of 10 years on pregnancy complications and birth outcomes in women exposed to XENLETA (lefamulin) during pregnancy.	FDAAA Section 505 (o)(3)	Pending
	6. Conduct an in vitro Mouse Lymphoma Assay (MLA) that evaluates higher doses of lefamulin reaching 10-20% Relative Total Growth (RTG) and in accordance with the Organisation for Economic Co-operation and Development (OECD) Guidelines for the Testing of Chemicals #476.	FDAAA Section 505 (o)(3)	Pending
	7. Conduct an in vitro Mouse Lymphoma Assay (MLA) that evaluates higher doses of the lefamulin metabolite BC-8041 reaching 10-20% Relative Total Growth (RTG) and in accordance with the OECD Guideline for the Testing of Chemicals #476.	FDAAA Section 505 (o)(3)	Pending
Rifamycin	1. Conduct a randomized, placebo-controlled study to evaluate the safety, tolerability, and efficacy of AEMCOLO (rifamycin) for the treatment of travelers' diarrhea in children from 6 to 11 years of age.	Pediatric Research Equity Act	Delayed [Final protocol due 12/2019; submitted 01/2020.]
	2. Conduct a randomized, placebo-controlled study to evaluate the safety, tolerability, and efficacy of AEMCOLO (rifamycin) for the treatment of travelers' diarrhea in children from 12 to 17 years of age.	Pediatric Research Equity Act	Pending
	3. Conduct human factors validation study for AEMCOLO (rifamycin) packaging.	Section 506B	Fulfilled
Omadacycline	1. Conduct a single dose pharmacokinetic and safety study in children ages 8 to 17 years who are receiving antibacterial drug therapy for an infectious disease.	Pediatric Research Equity Act	Delayed [Final protocol submitted 02/2020, after original milestone]
	2. Conduct an active-controlled safety study in children 8-17 years who have acute bacterial skin and skin structure infections.	Pediatric Research Equity Act	Pending
	3. Conduct an active-controlled safety study in children 8-17 years who have community-acquired bacterial pneumonia.	Pediatric Research Equity Act	Pending

	4. Conduct an active-controlled safety and efficacy study in adults with community-acquired bacterial pneumonia.	FDAAA Section 505 (o)(3)	Pending
	5. Conduct a United States surveillance study for 5 years from the date of marketing to determine if resistance to NUZYRA (omadacycline) has developed in those organisms specific to the indications in the label.	FDAAA Section 505 (o)(3)	Pending
Eravacycline	1. Conduct a study to evaluate the pharmacokinetics, safety, and tolerability of a single dose of intravenous XERAVA (eravacycline) in pediatric patients from 8 years to less than 18 years of age with suspected or confirmed bacterial infection.	Pediatric Research Equity Act	Released [As of 01/02/2020]
	2. Conduct a randomized, multicenter, active-controlled trial to evaluate the safety and tolerability of intravenous XERAVA (eravacycline) in pediatric patients from 8 years to less than 18 years of age with complicated intra-abdominal infections. The dose for this study will be determined upon review of the data from the single-dose, non-comparative study assessing the pharmacokinetics of XERAVA (eravacycline) in pediatric patients from 8 years to less than 18 years of age.	Pediatric Research Equity Act	Released [As of 01/02/2020]
	3. A United States surveillance study for 5 years from the date of marketing to determine if resistance to XERAVA (eravacycline) has developed in those organisms specific to the indication in the label.	FDAAA Section 505(o)(3);	Ongoing
Plazomicin	1. Conduct an open-label multiple dose pharmacokinetic and safety study of plazomicin in hospitalized children ages birth to 18 years with infections and receiving standard-of-care antibacterial drugs.	Pediatric Research Equity Act	Released [As of 03/13/2020]
	2. Conduct a randomized active-controlled pharmacokinetic and safety trial of plazomicin in children ages birth to 18 years with cUTI including acute pyelonephritis.	Pediatric Research Equity Act	Released [As of 03/13/2020]
	3. Conduct US surveillance studies for five years from the date of marketing plazomicin to determine if resistance to plazomicin has developed in those organisms specific to the indication in the label.	FDAAA Section 505(o)(3)	Pending
	4. Conduct a clinical study in subjects with end stage renal disease (ESRD) receiving hemodialysis to evaluate the pharmacokinetics of plazomicin.	Section 506B	Pending

	5. Establish an FDA cleared or approved in vitro diagnostic device for therapeutic drug monitoring of plazomicin that is recommended for patients with baseline creatinine clearance <90 mL/min in patients with complicated urinary tract infections (cUTI).	Section 506B	No longer listed
Delafloxacin	1. Conduct US surveillance studies for five years from the date of marketing Baxdela to determine if resistance to delafloxacin has developed in those organisms specific to the ABSSSI indication in the label.	FDAAA Section 505(o)(3)	Released
	2. Conduct a tissue distribution study in pregnant rats treated during the period of organogenesis with the oral formulation and with the intravenous formulation of Baxdela with the excipient sulfobutylether beta-cyclodextrin (SBECD) to assess the distribution of the drug substance to the reproductive tract and developing fetus.	FDAAA Section 505(o)(3)	No longer listed
	3. If the results of the tissue distribution studies from PMR 3220-2 demonstrate greater exposure of the fetus / maternal reproductive tract to delafloxacin with the intravenous formulation, conduct an embryo-fetal developmental toxicology study in pregnant rats treated during the period of organogenesis with the intravenous formulation of Baxdela to identify possible effects of delafloxacin with the excipient sulfobutylether betacyclodextrin (SBECD) on fetal development during the period of organogenesis.	FDAAA Section 505(o)(3)	No longer listed
Secnidazole	1. Conduct an open label, multicenter, safety study of Solosec (secnidazole) oral granules in healthy postmenarchal adolescent females ages 12 years to less than 18 years of age with bacterial vaginosis.	Pediatric Research Equity Act	Ongoing
Meropenem-vaborbactam	1. Conduct an open-label, sequential study to assess the pharmacokinetics (PK), safety, and tolerability of VABOMERE and the PK of meropenem and vaborbactam in children from birth to < 18 years of age with selected serious bacterial infections.	Pediatric Research Equity Act	Ongoing
	2. Conduct a randomized, single-blind, active comparator study to evaluate the safety, tolerability, and PK of VABOMERE versus piperacillin-tazobactam for the treatment of pediatric subjects from 3 months to <18 years of age with complicated Urinary Tract Infections (cUTI) including acute pyelonephritis.	Pediatric Research Equity Act	Pending

	3. Conduct an open-label, active comparator study to evaluate the PK, safety, and tolerability of multiple doses of VABOMERE vs. comparator in neonates (less than or equal to 90 days of age) with late onset sepsis.	Pediatric Research Equity Act	Pending
	4. Conduct a US surveillance study for five years from the date of marketing to determine if resistance to VABOMERE has developed in those organisms specific to the indications in the label.	FDAAA Section 505(o)(3)	Ongoing
	5. Conduct a "Thorough QT/QTc Study" to evaluate whether VABOMERE has a threshold pharmacologic effect on cardiac repolarization.	FDAAA Section 505(o)(3)	Fulfilled
Ozenoxacin	**None listed**		
Bezlotoxumab	1. Conduct a randomized, double-blind, placebo-controlled trial of safety, efficacy, and pharmacokinetics of Zinplava (bezlotoxumab) in pediatric patients from 1 to less than 18 years of age receiving antibacterial therapy for C. difficile infection.	Pediatric Research Equity Act	Ongoing
Amikacin liposome inhalation suspension (Arikayce)	1. Conduct a randomized, double-blind, placebo-controlled clinical trial to assess and describe the clinical benefit of ARIKAYCE in patients with nontuberculous mycobacterial (NTM) lung disease caused by MAC. The trial will evaluate the effect of ARIKAYCE on a clinically meaningful endpoint, as compared to an appropriate control in the intended patient population of patients with MAC infection.	Accelerated Approval	Delayed
	2. Provide and implement an email, standard mail, and facsimile communication plan to include a Dear Healthcare Provider letter as well as targeted educational materials to clinicians and professional societies.	Section 506B	Submitted
	3. Provide results of a drug utilization assessment including ICD-10 code or other information on the indication and patient demographic/clinical characteristics of users of ARIKAYCE through pharmacies that will be distributing ARIKAYCE, and the results of chart reviews of a random subset of patients who are prescribed ARIKAYCE.	Section 506B	Ongoing
Cefiderocol	1. Conduct an open-label, randomized, multicenter, active-controlled trial to evaluate the pharmacokinetics, safety and tolerability of FETROJA (cefiderocol) in children from 3 months to less than 18 years of age with cUTI. The dose for this study for children 3 months to less than 12 years of age will	Pediatric Research Equity Act	Released [As of 09/25/2020]

	be determined by the data from a single-dose, non-comparative study assessing the pharmacokinetics of FETROJA (cefiderocol) in pediatric patients from 3 months to less than 12 years of age with suspected or confirmed Gram-negative infections.		
	2. Conduct an open-label, single arm non-comparative study to evaluate the pharmacokinetics, safety and tolerability of multiple doses of FETROJA (cefiderocol) in children from birth to less than 3 months of age with suspected or confirmed cUTI. The dose for this study will be determined by the data from a single-dose, noncomparative study assessing the pharmacokinetics of FETROJA (cefiderocol) in pediatric patients from birth to less than 3 months of age with suspected or confirmed Gram-negative infections.	Pediatric Research Equity Act	Released [As of 09/25/2020]
	3. Conduct US surveillance studies for five years from the date of marketing FETROJA to determine if resistance to cefiderocol has developed in those organisms specific to the cUTI indication in the label.	FDAAA Section 505 (o)(3)	Pending
	4. Conduct a study to define the mechanism(s) of resistance to FETROJA (cefiderocol) for isolates identified as being resistant to cefiderocol in the surveillance study (five years from the date of marketing).	FDAAA Section 505 (o)(3)	Pending
	5. Submit the final study report for the completed CREDIBLE-CR trial (1424R2131), "A Multicenter, Randomized, Open-label Clinical Study of S-649266 or Best Available Therapy for the Treatment of Severe Infections Caused by Carbapenem-resistant Gram-negative Pathogens".	FDAAA Section 505 (o)(3)	Fulfilled
	6. Submit the final study report for the completed APEKS-NP trial, "Clinical Study of S-649266 for the Treatment of Nosocomial Pneumonia Caused by Gram-negative Pathogens".	FDAAA Section 505 (o)(3)	Fulfilled
Omeprazole magnesium-amoxicillin-rifabutin (Talicia)	**None listed**		

* PMRs reportable under: FDAAA Section 505(o)(3); Pediatric Research Equity Act; Accelerated Approval
PMCs reportable under: Section 506B
Only PMRs and PMCs that are reportable and included in original approval letter have been included, unless otherwise noted.

** This PMR was not originally listed in the approval letter, but according to the FDA, it replaces PMR 1 and PMR 2. As such, it has been included here.