

Table II: Summary of Published Tissue-Penetration Data For UW Medicine Formulary Fluoroquinolone Antibiotics

FDA Approval	Drug	N	Patients	Dose	Time to Peak or Mean Sample Time	Tissue Type	Mean Tissue Concentration	Plasma Level	Ratio	
Abscesses										
No human data are available for levofloxacin. Ciprofloxacin and moxifloxacin levels cannot be extrapolated to all abscesses.										
N	Ciprofloxacin ¹⁸	5	w/ thoracic empyema undergoing surgical drainage	200mg x 1 iv	Peak: 4h	Empyema	1.214 ± 0.886µg/mL	0.598 ± 0.185µg/mL	2.03*	
Y	Moxifloxacin ¹⁹	10	w/ peritonitis undergoing surgery for drainage	400mg x 1 iv	Peak: 2h	Exudate	3.64 (1.62-8.65) µg/mL	3.61 (2.27-5.6) µg/mL	1*	
Bone										
FQs penetrate cancellous bone > cortical bone. Penetration for bone w/ osteomyelitis (OM) > bone without infection. Penetration requirements for acute vs. chronic OM, OM from trauma, & diabetic OM can differ. Penetration for patients w/ instrumentation or in salvage therapy remains to be studied.										
Y	Ciprofloxacin ²⁰	28	undergoing hip or knee replacements, osteotomy (prophylaxis) or osteomyelitis debridement (treatment)	Prophylaxis group	500mg x 1 po	Mean: 1.5 - 4.75h	Cortical bone	0.4 ± 0.3µg/g	1.4 ± 0.6µg/mL	0.29*
					750mg x 1 po			0.7 ± 0.4µg/g	2.6 ± 1.1µg/mL	0.27*
				Treatment group	500mg x 1 po	Mean: 2 - 4.5h		0.7 ± 0.4µg/g	2 ± 0.9µg/mL	0.35*
					750mg x 1 po			1.4 ± 1µg/g	2.9 ± 2.2µg/mL	0.48*
N	Levofloxacin ²¹	21	undergoing corrective orthopedic surgeries or surgical debridement	500mg x 1 iv	Mean: 1.5h	Cancellous bone Cortical bone	6.6 ± 3.6µg/g 2.8 ± 1.1µg/g	8.6 ± 2.3µg/mL	0.77* 0.33*	
N	Moxifloxacin ²²	30	undergoing total knee arthroplasty	400mg x 1 po	Peaks Cancellous bone: 2h Cortical bone: 4h	Cancellous bone Cortical bone	1.89 ± 1.45µg/mL 1.56 ± 0.81µg/mL	3.45 ± 1.24µg/mL 3.73 ± 0.88µg/mL	0.52 ± 0.29 0.42 ± 0.2	
				400mg Q 12h x 2 po		Cancellous bone Cortical bone	2.97 ± 0.83µg/mL 2.54 ± 1.43µg/mL	6.26 ± 0.86µg/mL	0.48 ± 0.11 0.4 ± 0.21	
CNS										
No human CNS tissue level data is available for moxifloxacin.										
N	Ciprofloxacin ¹⁴	23	w/ bacterial meningitis or ventriculitis; ciprofloxacin added to empiric antibiotic regimen	200mg Q 12h x 3 iv	Peak: 2h	CSF (inflamed sampled on day 2 - 4) CSF (uninflamed sampled on day 10 - 20)	0.56 ± 0.39µg/mL 0.27 ± 0.09µg/mL	1.44 ± 0.68µg/mL 1.12 ± 0.29µg/mL	0.37 ± 0.12 0.22 ± 0.04	
N	Levofloxacin ²³	5	w/ bacterial meningitis on β-lactam regimen	500mg BID x 2 (n = 4) or x 1 (n = 1) iv	Mean: 2h	CSF	1.99 ± 0.67µg/mL	5.93 ± 1.11µg/mL	0.34 ± 0.09	
Eye										
Levels in anterior/posterior chambers are difficult to sustain in patients w/ healthy drainage structures. Data is lacking for patients with poor ocular vascularization (i.e., diabetes) & prosthetic lenses. Consider systemic antibiotic therapy for intraocular infections, penetrating ocular injuries, and posterior chamber infections.										
Y	Ofloxacin ^{24,25}	23	w/ intact corneal surfaces undergoing penetrating keratoplasty	2gtt (0.3%) separated by 15 minutes	Mean: 10 minutes	Cornea Aqueous humor	10.77 ± 5.9µg/g 0.13 ± 0.11µg/g	None obtained	-	
		26	undergoing pars plana vitrectomy for various ocular pathologies	2gtt (0.3%) Q 0.5h x 6, then Q 1h x 3	Mean: 1h	Aqueous humor Vitreous humor	1.44 ± 0.24µg/mL 0.37 ± 0.05µg/mL			
Y	Gatifloxacin ^{26,27}	24	undergoing phacoemulsification or intraocular lens implantation	1gtt (0.3%) QID x 4 + 1h prior to surgery	Mean: 1h	Aqueous humor	0.94 ± 0.72µg/mL			
		6	undergoing elective pars plana vitrectomy; subjects had uninflamed corneal surfaces	1gtt (0.3%) Q 0.25h x 3	Mean: 0.25h	Vitreous humor	0.001µg/mL			
N	Ciprofloxacin ²⁸	16	undergoing pars plana vitrectomy with uninflamed corneal surfaces and crystalline lenses	1000mg x 1 po	Mean: 6h	Aqueous humor Vitreous humor	0.59 ± 0.06µg/mL 0.64 ± 0.06µg/mL			
N	Levofloxacin ²⁹	45	undergoing various ophthalmic procedures; subjects had uninflamed corneal surfaces	500mg x 1 po	Mean: 2h	Aqueous humor Vitreous humor	0.59 ± 0.48µg/mL 0.32 ± 0.34µg/mL			4.34 ± 3.59µg/mL
				500mg Q 12h x 2 po		Aqueous humor Vitreous humor	1.9 ± 0.97µg/mL 2.39 ± 0.7µg/mL	8.02 ± 3.14µg/mL	0.24* 0.3*	
N	Moxifloxacin ³⁰	15	undergoing various ophthalmic procedures; subjects had uninflamed corneal surfaces	400mg Q 24h x 2 po	Mean: 3.71 ± 0.89h	Aqueous humor	1.58 ± 0.8µg/mL	3.56 ± 1.31µg/mL	0.44*	
					Mean: 3.77 ± 0.92h	Vitreous humor	1.34 ± 0.66µg/mL		0.38*	
Gynecologic Tissues										
No English language human gynecologic tissue data are available for levofloxacin or moxifloxacin. CDC does NOT recommend FQs for treatment of <i>N. gonorrhoeae</i> infections due to increasing resistance rates.										
N	Ciprofloxacin ^{31,32}	36	undergoing uterus extirpation	500mg x 1 po	Peak: 2h	Vagina Uterus Endometrium Fallopian tube	1.26 ± 0.66µg/g 1.58 ± 0.97µg/g 1.4 ± 0.7µg/g 1.36 ± 0.91µg/g	1.42 ± 0.87µg/mL	1.01 ± 0.27 1.28 ± 0.51 1.22 ± 0.5 1.07 ± 0.37	
				100mg x 1 iv	Peak: 0.5h	Vagina Uterus Endometrium Fallopian tube	1.13 ± 0.21µg/g 1.07 ± 0.15µg/g 1.56 ± 0.34µg/g 0.95 ± 0.17µg/g	0.61 ± 0.12µg/mL	1.85 ± 0.43 1.82 ± 0.49 2.86 ± 0.92 1.6 ± 0.36	
		25	undergoing vaginal or total hysterectomy for non-malignant diseases	500mg x 1 po	Peaks Myometrium: 4h Other tissues: 7 - 9h	Myometrium Cervix Endometrium Fallopian tube	0.91 ± 0.37µg/g 0.82 ± 0.97µg/g 0.99 ± 0.98µg/g 1.4 ± 1.4µg/g	0.64 ± 0.44µg/mL	1.42* 1.44* 1.74* 2.46*	
Heart										
No human heart tissue level data are available for levofloxacin or moxifloxacin. The majority of evidence showing cure with FQs as monotherapy are in animal studies, with scattered case reports of cure in humans for certain types of endocarditis pathogens. Beware that FQs may prolong QT interval.										
N	Ciprofloxacin ³³	36	without endocarditis undergoing mitral/aortic valve replacement	400mg x 1 iv	Peaks Myocardium 0 - 1h; Valve 1 - 3h; Sternal bone 0 - 1h; Mediastinal fat 3 - 5h	Myocardium Valve Sternal bone Mediastinal fat	31.6 ± 25µg/g 8.6 ± 5.5µg/g 7.8 ± 7.6µg/g 3.1 ± 3.8µg/g	2.26 ± 0.43µg/mL 1.64 ± 0.39µg/mL 2.26 ± 0.43µg/mL 0.79 ± 0.27µg/mL	14* 5.24* 3.45* 3.92*	
				750mg po Q 12h x 3, then 400mg iv	Peaks Myocardium 0 - 1h; Valve 1 - 3h; Sternal bone 1 - 3h; Mediastinal fat 1 - 3h	Myocardium Valve Sternal bone Mediastinal fat	21.8 ± 13µg/g 12 ± 11µg/g 8.8 ± 6.8µg/g 2 ± 1.8µg/g	2.26 ± 0.43µg/mL	9.65* 7.32* 5.37* 1.22*	

* ratio calculated by author

An Imperfect Science: Antibiotic Tissue Penetration - Will This Fluoroquinolone Reach The Site of Infection? (continued)

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FDA Approval	Drug	N	Patients	Dose	Time to Peak or Mean Sample Time	Tissue Type	Mean Tissue Concentration	Plasma Level	Ratio
Hepatic									
No human hepatic tissue level data are available for levofloxacin or moxifloxacin; hepatic ascites are usually NOT polymicrobial; FQ tissue penetration may be altered depending on severity of alcoholic hepatitis or hepatic cirrhosis. ⁵⁹									
N	Ciprofloxacin ^{34,35}	8	w/ sterile hepatic ascites secondary to abdominal malignancy or heart failure	750mg x 1 po	Peak: 4.8 ± 1.7h	Ascitic fluid	2.6 ± 0.6µg/mL	4 ± 0.7µg/mL	0.65*
		6	w/ uncompensated cirrhosis	300mg q 12h x 3 iv	Peak: 1h	Ascitic fluid	0.45 ± 0.13µg/mL	0.86 ± 0.35µg/mL	0.52*
Peritoneal									
No human peritoneal tissue level data are available for levofloxacin or moxifloxacin. Peritoneal infections are usually POLYmicrobial. It is unclear whether peritoneal antibiotic tissue or fluid concentrations are more predictive of treatment success.									
N	Ciprofloxacin ^{36,37}	10	undergoing elective laparotomy; uninfamed peritoneal tissue collected	750mg x 1 po	Mean: 5.6 ± 1.3h	Peritoneal tissue	0.29 ± 0.27µg/g	1.3 ± 0.6µg/mL	0.22 ± 0.15*
		30	undergoing various abdominal surgeries	100mg x 1 iv	Mean: 0.5h	Peritoneal fluid	1.1 ± 0.04µg/mL	2 ± 0.5µg/mL	0.55*
Prostate									
No human data are available for moxifloxacin prostatic & seminal fluid concentrations. Determination of drug concentration in the prostate is problematic because of urinary contamination. It is still uncertain whether prostatic antibiotic tissue or fluid concentrations are more predictive of treatment success.									
Y	Ciprofloxacin ^{38,39}	10	males undergoing transurethral resection of prostate (TURP) for cancer or hyperplasia	500mg q 12h x 3 po	Mean: 1.25 - 2h	Prostate tissue	3.03 ± 0.38µg/g	Not reported	3
Y	Levofloxacin ³⁸	8	healthy males	250mg x 1 po	Mean: 3h	Prostatic fluid	0.16µg/mL	1.37µg/mL	0.3
							0.89µg/mL	3.1µg/mL	0.52
N	Moxifloxacin ⁴⁰	39	males with benign hyperplasia undergoing TURP	400mg x 1 iv	Mean: at end of infusion	Prostate tissue	9.54 ± 3.36µg/g	5.28 ± 2.16µg/g	1.81
Pulmonary⁴¹									
Drugs are not evenly distributed throughout the lungs. Extracellular & intracellular measurements reflect free + bound drug (blood contamination); interpret cautiously. Levels in pulmonary edema or CF may differ from healthy lungs. Sputum levels - Limited utility as levels reflect pooling over prolonged periods of time prior to production; blood/saliva contamination may also skew results. Lung tissue - Constitutes whole lung. Epithelial Lining Fluid (ELF) - Drugs must cross capillary membranes, interstitial fluid, and alveolar epithelium to reach ELF; most relevant pulmonary sample site for treatment of pneumonia. Alveolar Macrophage (AM) - Pulmonary ample site most relevant for intracellular pathogens. Bronchial Mucosa (BM) - Pulmonary sample site most relevant for infective bronchitis pathogens.									
Y	Ciprofloxacin ^{42,43}	20	undergoing elective lung surgery for various pulmonary pathologies	200mg x 1 iv	Peak: 3 - 4h	Lung tissue (sample inadequate to assess BM)	4.7 ± 3.1µg/g	0.6 ± 0.5µg/mL	7.8*
		36	healthy nonsmoking subjects undergoing venipuncture, bronchoscopy, and bronchoalveolar lavage	500mg q 12h x 9 po	Peak: 4h	Epithelial lining fluid	1.87 ± 0.91µg/mL	2.11 ± 0.35µg/mL	0.89*
750mg q 24h x 5 po	Alveolar macrophage			34.9 ± 23.2µg/mL		16.54*			
Y	Levofloxacin ⁴³⁻⁴⁵	35	undergoing elective bronchoscopy	500mg x 1 po	Peaks BM: 1h; AM: 2h	Epithelial lining fluid	22.12 ± 14.92µg/mL	11.98 ± 2.99µg/mL	1.85*
						Alveolar macrophage	105.1 ± 65.5µg/mL		8.77*
Y	Moxifloxacin ^{46,47}	18	undergoing lung surgery for various pathologies	500mg x 1 po	Peak: 4.6 - 6.33h	Bronchial mucosa	8.3µg/g	6.6µg/mL	1.2
						Alveolar macrophage	41.9µg/g		7.3
Y	Moxifloxacin ^{46,47}	19	healthy subjects underwent bronchoalveolar lavage and bronchial mucosa biopsies	400mg x 1 po	Peak: 2.2h	Epithelial lining fluid	20.7 ± 1.92µg/mL	3.22 ± 1.25µg/mL	6.78 ± 2.29
						Alveolar macrophage	56.7 ± 1.61µg/mL		18.59 ± 1.87
		49	undergoing lung surgery for various pathologies	400mg q 24h x 5 po	Peak: 2.4 ± 0.3h	Bronchial mucosa	5.36 ± 1.29µg/mL	2.5 ± 0.5µg/mL	1.67 ± 1.18
				400mg q 24h x 5 iv		Lung tissue	16.2 ± 4.9µg/g		6.34 ± 0.86
Lung tissue	12.4 ± 5.9µg/g	2.5 ± 1µg/mL	4.73 ± 0.59						
Sinus Mucosa									
Ciprofloxacin has FDA approval for sinusitis but no published human sinus mucosa tissue level data are available.									
Y	Levofloxacin ⁴⁸	15	w/ chronic rhinosinusitis undergoing functional endoscopic sinus surgery	500mg x1 po	Peak: 3h	Mucosa	5.84 (2.09 - 9.34) µg/mL	1.88µg/mL (0.65 - 5.14)	2.56
Y	Moxifloxacin ⁴⁹	42	w/ chronic sinusitis undergoing elective sinus surgery	400mg q 24h x 5 po	Peak: 3h	Maxillary sinus mucosa	7.48 (5.61 - 9.79) µg/g	3.58µg/mL (2.82 - 5.49)	2.09*
						Anterior ethmoid mucosa	8.19 (4.98 - 13.4) µg/g		2.28*
						Nasal polyps	9.09 (5.72 - 16.2) µg/g		2.53*
Skin and Soft Tissues									
Peak skin antibiotic levels persisted for ~4 h.									
Y	Ciprofloxacin ⁵⁰	23	undergoing skin-punch biopsies	100mg x 1 iv	Peak: 1 - 2h	Skin	0.23 ± 0.07µg/g	0.46 ± 0.06µg/mL	0.5*
						Subcutaneous tissue	0.27 ± 0.07µg/g		0.59*
Y	Levofloxacin ^{51,52}	10	healthy subjects undergoing skin-punch biopsies	750mg q 24h x 3 po	Peak: 1 - 4h	Skin	11.87 ± 2.58µg/g	4.71 ± 0.84µg/mL	2.58 ± 0.52
		7	w/ soft-tissue infections	500mg x 1 iv	Peak: 1.06 ± 0.14h	Inflamed skin	5.45 ± 3.74µg/mL	8.37 ± 1.93µg/mL	0.65*
Y	Moxifloxacin ⁵³	6	details not included in reference (product labeling)	400mg x 1 po	Peak: 1.39 ± 1.29h	Uninflamed skin	4.42 ± 2.09µg/mL		0.53*
Y	Moxifloxacin ⁵³	6	details not included in reference (product labeling)	400mg x 1 po	Mean: 3h	Subcutaneous tissue	2.3 ± 0.4µg/g	0.9 ± 0.3µg/mL	0.4 ± 0.6
Synovial Fluid & Tissue									
Penetration characteristics for patients with instrumentation or in salvage therapy remains to be studied. CDC does NOT recommend FQs for treatment of septic arthritis where <i>N. gonorrhoeae</i> is the causal pathogen due to increasing resistance rates.									
N	Ciprofloxacin ⁵⁴	12	w/ infection of knee or hip joint	750mg q 12h x 2 po	Mean: 2h	Synovial fluid	2.93 ± 1.99µg/mL	3.24 ± 2.32µg/mL	0.9 ± 0.17
N	Levofloxacin ⁵⁵	12	undergoing hip replacement involving femoral bone resection; synovial fluid taken from non-infected tissues	500mg x 1 iv	Mean: 1.2h	Synovial tissue	8.9 ± 2.1µg/g	7.5 ± 1.3µg/mL	1.2 ± 0.4
N	Moxifloxacin ⁵⁶	20	undergoing knee arthroscopy	400mg q 24h x 3 po	Peak: 6h	Synovial fluid	3.42 ± 0.51µg/mL	3.46 ± 0.78µg/mL	0.99*
Urine									
Peaks are difficult to interpret due to pooling in bladder.									
Y	Ciprofloxacin ⁵⁷	14	healthy subjects; cross-over study of ciprofloxacin vs. levofloxacin, with 7-day washout period	500mg x 1 po	Peak: 0 - 6h	Urine	268 (130 - 967) µg/mL	0.47 ± 0.1µg/mL	570.2*
Y	Levofloxacin ⁵⁷						406 (202 - 1002) µg/mL		
N	Moxifloxacin ⁵⁸	6	healthy subjects	400mg x 1 po	Peak: 2h		83 ± 58µg/mL	Not reported	-

* ratio calculated by author