TEXAS Health and Human Services

Medicaid Drug Use Criteria

Oral Fluoroquinolones

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Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.

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1 Dosage

1.1 Adults

Maximum recommended adult daily doses for fluoroquinolones are summarized in Table 1. Prescribed dosages exceeding these recommendations will be reviewed.

Table 1. Adult Oral Fluoroquinolone Maximum Dosage Recommendations

Drug Name	Dosage Form / Strength	Treatment Indication	Maximum Recommended Dosage
ciprofloxacin (Cipro®, generics)	immediate-release (IR)#: 100 mg, 250 mg, 500 mg, 750 mg tablets; 250 mg/5 mL, 500 mg/5 mL suspension	acute sinusitis	1000 mg/day
ciprofloxacin IR		bone and joint infections	1500 mg/day
ciprofloxacin IR		chronic bacterial prostatitis	1000 mg/day
ciprofloxacin IR		complicated intra-abdominal infections (in combination with metronidazole)	1000 mg/day
ciprofloxacin IR		complicated, uncomplicated skin/skin structure infections	1500 mg/day
ciprofloxacin IR		infectious diarrhea	1000 mg/day
ciprofloxacin IR		inhalational anthrax (post-exposure)	1000 mg/day
ciprofloxacin IR		lower respiratory tract infections	1500 mg/day
ciprofloxacin IR		moderate, complicated urinary tract infection (UTI)	1000 mg/day
ciprofloxacin IR		typhoid fever	1000 mg/day
ciprofloxacin IR		uncomplicated cervical, urethral gonococcal infections*	250 mg as single dose
ciprofloxacin IR		uncomplicated UTI	500 mg/day
ciprofloxacin (Cipro® XR, generics)	extended-release (ER)#: 500 mg, 1000 mg tablets	acute uncomplicated pyelonephritis	1000 mg/day
ciprofloxacin ER		complicated UTI	1000 mg/day
ciprofloxacin ER		uncomplicated UTI	500 mg/day
delafloxacin (Baxdela®	450 mg tablets	acute bacterial skin/skin structure infections	900 mg/day in divided doses

Drug Name	Dosage Form / Strength	Treatment Indication	Maximum Recommended Dosage
delafloxacin		community acquired pneumonia (CAP)	900 mg/day in divided doses
gemifloxacin (Factiv®)	320 mg tablets	chronic bronchitis (acute exacerbation)	320 mg daily
gemifloxacin		CAP	320 mg daily
levofloxacin (Levaquin®, generics)	250 mg, 500 mg, 750 mg tablets, 25 mg/mL solution	acute maxillary sinusitis	750 mg once daily
levofloxacin		acute pyelonephritis	750mg once daily
levofloxacin		chronic bacterial prostatitis	500 mg once daily
levofloxacin		chronic bronchitis (acute exacerbation)	500 mg once daily
levofloxacin		CAP	750 mg once daily
levofloxacin		complicated skin/skin structure infections	750 mg once daily
levofloxacin		inhalational anthrax	500 mg once daily
levofloxacin		mild/moderate complicated UTI	750 mg once daily
levofloxacin		nosocomial pneumonia	750 mg/day
levofloxacin		plague or plague prophylaxis	500 mg once daily^
levofloxacin		uncomplicated skin/skin structure infections	500 mg once daily
levofloxacin		uncomplicated UTI	250 mg once daily
moxifloxacin (Avelox®, generics)	400 mg tablets	acute bacterial sinusitis	400 mg once/day
moxifloxacin		chronic bronchitis (acute exacerbation)	400 mg once/day
moxifloxacin		CAP	400 mg once/day
moxifloxacin		complicated intra-abdomina infections	400 mg once/day
moxifloxacin		complicated skin/skin structure infections	400 mg once/day
moxifloxacin		plague or plague prophylaxis	400 mg once/day

Drug Name	Dosage Form / Strength	Treatment Indication	Maximum Recommended Dosage
moxifloxacin		uncomplicated skin/skin structure infections	400 mg once/day
ofloxacin (generics)	200 mg, 300 mg, 400 mg tablets	acute pelvic inflammatory disease (PID) ^	800 mg/day in divided doses
ofloxacin		acute, uncomplicated urethral, cervical gonorrhea*	400 mg as single dose
ofloxacin		chronic bronchitis (acute exacerbation)	800 mg/day in divided doses
ofloxacin		CAP	800 mg/day in divided doses
ofloxacin		complicated UTI	400 mg/day in divided doses
ofloxacin		mixed infection of urethra, cervix due to C. trachomati and N. gonorrhoeae*	600 mg/day in divided doses
ofloxacin		nongonococcal cervicitis/urethritis due to Chlamydia trachomatis	600 mg/day in divided doses
ofloxacin		prostatitis due to E. coli	600 mg/day in divided doses
ofloxacin		uncomplicated cystitis due to E. coli or K. pneumoniae	400 mg/day in divided doses
ofloxacin		uncomplicated cystitis due to other organisms	400 mg/day in divided doses
ofloxacin		uncomplicated skin and ski structure infections	800 mg/day in divided doses

- # ciprofloxacin immediate-release and extended-release tablets are not interchangeable
- * CDC no longer recommends fluoroquinolones for treatment of infections due to N. gonorrhoeae
- ^ CDC no longer recommends fluoroquinolones for treating PID; may be considered in combination with metronidazole if parenteral therapy not feasible

1.2 Pediatrics

Fluoroquinolones are not drugs of choice in pediatric patients due to an increased incidence of musculoskeletal adverse reactions, including arthralgias and events related to surrounding joints and tissues. However, ciprofloxacin and levofloxacin

have been evaluated for use in pediatric patients and are FDA-approved for use in select circumstances. Recommended dosage guidelines for fluoroquinolones in pediatric patients are summarized in Table 2.

Table 2. Fluoroquinolone Recommended Dosage Guidelines in Pediatric Patients

Treatment Indication	Drug Name	Maximum Recommended Dosage
complicated urinary tract infection (UTI) or pyelonephritis	ciprofloxacin	10-20 mg/kg orally every 12 hours (not to exceed 750 mg/dose)
inhalational anthrax (postexposure prophylaxis)	ciprofloxacin	15 mg/kg orally every 12 hours (not to exceed 500 mg/dose)
inhalational anthrax (postexposure prophylaxis)	levofloxacin	Greater than or equal to 6 months of age and less than 50 kg: 8 mg/kg orally every 12 hours (not to exceed 250 mg/dose) Greater than or equal to 6 months of age and greater than 50 kg: 500 mg orally once daily
plague	levofloxacin	Greater than or equal to 6 months of age and less than 50 kg: 8 mg/kg orally every 12 hours (not to exceed 250 mg/dose) Greater than or equal to 6 months of age and greater than 50 kg: 500 mg orally once daily

2 Duration of Therapy

Therapy duration for antibiotics like fluoroquinolones is based on the type and severity of infection. Recommendations for usual or documented therapy durations for adults are summarized in Table 3. However, severe or complicated infections may require prolonged therapy.

Table 3. Adult Oral Fluoroquinolone Maximum Recommended Therapy Duration

Drug Name	Treatment Indication	Maximum Therapy Duration
ciprofloxacin, IR	acute sinusitis	10 days
ciprofloxacin, IR	bone and joint infections	4 to 6 weeks
ciprofloxacin, IR	chronic bacterial prostatitis	28 days

Drug Name	Treatment Indication	Maximum Therapy Duration
ciprofloxacin, IR	complicated intra-abdominal infections (in combination with metronidazole)	7 to 14 days
ciprofloxacin, IR	complicated, uncomplicated skin/skir structure infections	7 to 14 days
ciprofloxacin, IR	infectious diarrhea	5 to 7 days
ciprofloxacin, IR	inhalational anthrax (post-exposure)	60 days
ciprofloxacin, IR	lower respiratory tract infections	7 to 14 days
ciprofloxacin, IR or ER	moderate, complicated UTI	7 to 14 days
ciprofloxacin. IR	typhoid fever	10 days
ciprofloxacin, IR	uncomplicated cervical, urethral gonococcal infections*	single dose
ciprofloxacin, IR or ER	uncomplicated UTI	3 days
delafloxacin	acute bacterial skin/skin structure infections	5-14 days
delafloxacin	community acquired pneumonia (CAP)	5-10 days
gemifloxacin	chronic bronchitis (acute exacerbation)	5 days
gemifloxacin	CAP	5 to 7 days
levofloxacin	acute maxillary sinusitis	10 to 14 days (500 mg dose); 5 days (750 mg dose)
levofloxacin	acute pyelonephritis	10 days (250 mg dose); 5 days (750 mg dose)
levofloxacin	chronic bacterial prostatitis	28 days
levofloxacin	chronic bronchitis (acute exacerbation)	7 days
levofloxacin	CAP	7 to 14 days (500 mg dose); 5 days (750 mg dose)
levofloxacin	complicated skin/skin structure infections	7 to 14 days (750 mg dose)
levofloxacin	inhalational anthrax	60 days
levofloxacin	mild/moderate complicated UTI	10 days (250 mg dose); 5 days (750 mg dose)
levofloxacin	hospital acquired pneumonia	7 to 14 days
levofloxacin	plague or plague prophylaxis	10 to 14 days (500 mg dose; 750 mg dose considered if clinically warranted)

Drug Name	Treatment Indication	Maximum Therapy Duration
levofloxacin	uncomplicated skin/skin structure infections	7 to 10 days (500 mg dose)
levofloxacin	uncomplicated UTI	3 days (250 mg dose)
moxifloxacin	acute bacterial sinusitis	10 days (5 to 7 days IDSA guidelines)
moxifloxacin	chronic bronchitis (acute exacerbation)	5 days
moxifloxacin	CAP	7 to 14 days
moxifloxacin	complicated intra-abdominal infections	5 to 14 days
moxifloxacin	complicated skin/skin structure infections	7 to 21 days
moxifloxacin	plague or plague prophylaxis	10 to 14 days
moxifloxacin	uncomplicated skin/skin structure infections	7 days
ofloxacin	acute pelvic inflammatory disease (PID)	10 to 14 days^
ofloxacin	acute, uncomplicated urethral, cervical gonorrhea*	(400 mg dose) 1 day
ofloxacin	chronic bronchitis (acute exacerbation)	10 days
ofloxacin	CAP	10 days
ofloxacin	complicated UTI	10 days
ofloxacin	mixed infection of urethra, cervix due to C. trachomatis and N. gonorrhoeae*	7 days
ofloxacin	nongonococcal cervicitis/urethritis due to Chlamydia trachomatis	7 days
ofloxacin	prostatitis due to E. coli	6 weeks
ofloxacin	uncomplicated cystitis due to E. coli or K. pneumoniae	3 days
ofloxacin	uncomplicated cystitis due to other organisms	7 days
ofloxacin	uncomplicated skin and skin structure infections	10 days

- + Levofloxacin safety greater than 28 days in adults and greater than 14 days in pediatric patients to manage anthrax has not been studied; use for

greater than 28 days in adults and greater than 14 days in pediatrics when benefits outweigh risks

- * CDC no longer recommends fluoroquinolones for treatment of infections due to N. gonorrhoeae
- ^ CDC no longer recommends fluoroquinolones for treating PID; may be considered in combination with metronidazole if parenteral therapy not feasible

Fluoroquinolone therapy duration in pediatric patients is summarized in Table 4.

Table 4. Pediatric Oral Fluoroquinolone Maximum Recommended Therapy Duration

Treatment Indication	Drug Name	Maximum Therapy Duration
UTI, pyelonephritis	ciprofloxacin	10 to 21 days
inhalational anthrax (postexposure prophylaxis)	ciprofloxacin	60 days
inhalational anthrax (postexposure prophylaxis)	levofloxacin	60 days+
plague	levofloxacin	10 to 14 days

- UTI = urinary tract infection
- + Levofloxacin safety when used for longer than 14 days in pediatric patients has not been studied; use for greater than 14 days when benefit outweighs risk

3 Duplicative Therapy

The adjunctive use of two or more fluoroquinolones is not recommended. Additional therapeutic benefit is not realized when fluoroquinolones are administered in combination. Patient profiles containing concurrent prescriptions for multiple fluoroquinolones will be reviewed.

4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for oral fluoroquinolones are summarized in Table 5. Only those

drug-drug interactions classified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed.

Table 5. Oral Fluoroquinolone Drug-Drug Interactions

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level[#]
ciprofloxacin	drugs metabolized by CYP1A2 (e.g., alosetron, caffeine, clozapine, duloxetine, mexiletine, ropinirole, tizanidine)	concurrent administration ciprofloxacin, a known CYP1A2 inhibitor, with drugs metabolized by CYP1A2 may result in increased serum levels of drugs metabolized by CYP1A2 and potentially increased pharmacologic/adverse effects	if combination necessary, monitor for increased adverse effects; alternative FQ that does not affect CYP1A2 enzymes may be considered	contraindicated, major, moderate (DrugReax) 2-major, 3-moderate (CP)
ciprofloxacin	methotrexate	co-administration may result in reduced methotrexate renal tubular transport and potential for increased methotrexate levels and increased pharmacologic/adverse effects	measure methotrexate concentrations and observe patients for increased adverse effects	moderate (DrugReax) 3-moderate (CP)
ciprofloxacin	mycophenolate	concurrent administration may decrease mycophenolic acid concentrations	monitor response to therapy when ciprofloxacin is started or stopped	moderate (DrugReax) 3-moderate (CP)
ciprofloxacin	phenytoin	concurrent use may result in increased or decreased phenytoin concentrations ; mechanism unknown	measure phenytoin concentrations and observe patients for increased or decreased pharmacologic effects	moderate (DrugReax) 3-moderate (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level[#]
ciprofloxacin	phosphodiesterase type 5 (PDE5) inhibitors	concurrent administration may increase PDE5 inhibitor plasma levels and risk of adverse reactions	during coadministration, consider lower dose of PDE5 inhibitor or withholding PDE5 inhibitor in patients at high risk of developing PDE5 inhibitor adverse reactions	moderate (DrugReax)
ciprofloxacin	probenecid	co-administration may result in increased serum ciprofloxacin levels due to probenecid inhibition of renal tubular secretion	monitor patients for increased ciprofloxacin adverse effects	moderate (DrugReax) 4-minor (CP)
ciprofloxacin	theophyllines	adjuvant administration may result in decreased theophylline clearance and potential for increased serum theophylline levels and enhanced pharmacologic/toxic effects as ciprofloxacin interferes with theophylline clearance	if adjunctive therapy necessary, closely monitor theophylline levels and observe for increased adverse effects; may consider alternative FQ that does not interfere with theophylline clearance	major (DrugReax) 3-moderate (CP)
ciprofloxacin	tizanidine (Ziaflex®)	combined administration may result in enhanced tizanidine pharmacologic effects and/or adverse effects (e.g., sedation, hypotension) due to ciprofloxacin inhibition of CYP1A2-mediated tizanidine metabolism	avoid concurrent administration; use alternative spasticity medication	contraindicated (DrugReax) 1-severe (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level[#]
fluoroquinolones (FQ)	antacids	simultaneous administration may result in reduced absorption/bioavailability and clinical effectiveness of the FQ due to chelation of the antacid cations with the quinolone molecule	avoid concurrent administration; give FQ 2 hours before or 6 hours after giving antacids; may consider H2 receptor antagonist as alternative to antacids (e.g., ranitidine) in some clinical situations	moderate (DrugReax) 2-major (CP)
FQ	antidiabetic agents	adjunctive administration may result in altered blood glucose levels and increased risk for hypo- or hyperglycemia	monitor serum glucose levels closely with concurrent administration	major (DrugReax) 3-moderate (CP)
FQ	corticosteroids	concurrent therapy may increase risk for tendon rupture, especially in patients over 60 years of age	discontinue FQ therapy with any signs of tendon inflammation or pain	moderate (DrugReax) 3-moderate (CP)
FQ	didanosine (Videx®) oral solution	didanosine buffers consist of magnesium-aluminum cations; concomitant administration with FQ may result in reduced FQ absorption/ bioavailability and clinical effectiveness due to chelation of the antacid cations with the quinolone molecule	avoid concurrent administration; give FQ 2 hours before or 6 hours after giving didanosine	moderate (DrugReax) 2-major (CP)
FQ	iron salts (including iron in multivitamins)	iron salts may bind FQ in GI tract forming insoluble, unabsorbable complexes with resultant reduced FQ serum concentrations/pharmacologic effects	avoid concurrent administration; give FQ 2 hours before or 6 hours after giving drugs containing iron	moderate (DrugReax) 2-major (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level[#]
FQ	nonsteroidal anti-inflammatory drugs (NSAIDs)	concurrent administration may increase risk of central nervous system (CNS) stimulation and convulsive seizures	administer cautiously together and monitor patients closely for increased CNS adverse effects	moderate (DrugReax) 3-moderate (CP)
FQ	QTc interval-prolonging medications (e.g., class IA, III anti-arrhythmics, tricyclic antidepressants, clozapine, cyclobenzaprine, macrolide antibiotics, cisapride, ziprasidone)	concurrent administration may increase risk of significant cardiotoxicity (e.g., life-threatening arrhythmias, cardiac arrest) as FQ may cause QTc interval prolongation and, rarely, torsades de pointes	adjunctive administration should be avoided	contraindicated, major (DrugReax) 1-severe, 2-major (CP)
FQ	sevelamer (Renagel®)	concurrent administration may cause decreased FQ bioavailability and potential for reduced pharmacologic effects	avoid concurrent administration; administer FQ 1 hour before or 3 hours after sevelamer	moderate (DrugReax) 2-major (CP)
FQ	sucralfate	concurrent administration may result in decreased FQ efficacy due to FQ chelation by sucralfate in GI tract	avoid concurrent administration; give FQ 2 hours before or 6 hours after giving sucralfate	moderate (DrugReax) 2-major (CP)
FQ	warfarin	concomitant administration may result in enhanced hypoprothrombinemic effects and increased bleeding risk; mechanism of this interaction not identified; changes in PT/INR may occur 2-16 days after addition of FQ to warfarin therapy	if combination cannot be avoided, monitor PT/INR closely and observe for increased adverse effects	major (DrugReax) 2-major (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level[#]
FQ	zinc salts, calcium	zinc salts or calcium may bind FQ in GI tract forming insoluble, unabsorbable complexes with resultant reduced FQ serum concentrations/ pharmacologic effects	avoid concurrent administration; give FQ 2 hours before or 6 hours after giving drugs containing zinc	moderate (DrugReax)
select FQ (ciprofloxacin, levofloxacin)	cyclosporine	adjunctive administration has resulted in transiently increased serum creatinine levels and/or increased cyclosporine levels	monitor serum creatinine and cyclosporine levels; observe patients for cyclosporine adverse effects	moderate (DrugReax)

5 References

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