

Fluoroquinolone Adverse Effects Need for ICD-10 Code

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Fluoroquinolone Overview

- Rationale for an ICD-10 Code
- Fluoroquinolone background
- Occurrence of adverse events
- Adverse effects statistics 2022
- Fluoroquinolone FDA warnings
- FDA – significant safety concerns
- Ineffective patient-doctor experience
- Selection of antibiotics that have ICD-10 codes and Black Box warnings
- Conclusion

Rationale for an ICD-10 Code

- Current ICD-10 code list is comprised of 7 antibiotic classes: penicillins, cephalosporins, chloramphenicols, macrolides, tetracyclines, aminoglycosides, rifampicin (rifamycin), discovered, developed or introduced in the 1940s/50s
- Fluoroquinolones (first synthetic antibiotic) are the youngest group of antibiotics introduced in the 1980s and are now among the most prescribed antibiotics
- This current ICD-10 exclusion for fluoroquinolones is likely due to historical rather than substantive reasons
- The drug rifampicin and the class of chloramphenicols have ICD-10 codes, despite their significantly lower prescription rate over fluoroquinolones
- The problematic group of fluoroquinolones is not specifically represented; to correct this systematic omission, we request the introduction of an ICD-code for fluoroquinolone adverse effects

Fluoroquinolone Background

- Fluoroquinolones were introduced in the 1980s
- Fluoroquinolones are the first fully synthetic antibiotic group ever, comprised of: ciprofloxacin, ofloxacin, norfloxacin, levofloxacin, gemifloxacin and moxifloxacin
- Fluoroquinolones are the most common and effective group of antibiotics, however, have a distinct spectrum of adverse effects
- Adverse reactions, while rare in percentage terms, are frequent in absolute numbers due to the vast quantities of prescriptions
- Certain adverse effects flagged by the FDA, can manifest collectively as severe conditions, usually resembling a syndrome in its clinical presentation
- Vast number of prescriptions will reflect in the higher occurrence of adverse effects, severity, and potential for causing disability
- As noted by the FDA, fluoroquinolone AEs are underreported¹
- In 2022, there were 44 prescriptions of fluoroquinolones per 1,000 population² (USA)
- There were 14.8 million total fluoroquinolone prescriptions dispensed in 2022² (USA)
- Statistics do not include dispensary in hospitals, nursing homes, urgent care, or surgical centers

Occurrence of Adverse Events

Adverse Events - Open FDA Reporting 2004-2023:

- Fluoroquinolones top the list at 107,659 adverse events²¹
- Fluoroquinolone adverse events occur 4 times more than Corticosteroids, the second highest drug class at 26,911 adverse events²¹
- 87% (94,656 records) of fluoroquinolone severe adverse events resulted in a life-threatening condition, hospitalization, disability, congenital anomaly, other serious conditions, or death²¹

Adverse Events Statistics 2022

Data Base		The ADRs range of scale								
Type of Adverse Drug Reaction	Quantity Rx 2022	Average	References	Low	References	High	References	Average	Low	High
Fluoroquinolone prescription	14,800,000		[2]							
Estimated to trigger serious AEs by FQ	14,800,000	0.0062	[3]	0.0031	[3]	0.033	[3]	91,760	45,880	448,400
Mortality	14,800,000	0.0021	[3]					31,080		
Stevens-Johnson Syndrome	14,800,000	0.00001	[3] [4]	0.0000001	[3] [5]	0.00008	[3] [6]	148	1.48	1,184
Clostridium Difficile	14,800,000	0.0055	[3] [7] [8]	0.0028	[3] [7] [9]	0.0074	[3] [7] [10]	81,140	41,400	109,520
Tendon rupture	14,800,000	0.00029	[3] [11]	0.00004	[3] [12]	0.021	[3] [13]	4,292	595	310,800
Aortic rupture	14,800,000	0.00018	[3] [14]	0.000018	[3] [14]	0.00357	[3] [15]	2,664	266.4	52,836
Liver injury	14,800,000	0.00023	[3] [15]	0.000106	[3] [15]	0.0011	[3] [16]	3,404	1,568.8	16,280

Calculation based on number of fluoroquinolone prescriptions amount and percentage of AEs [3]
 Transferring the results of statistics into numbers of prescription only, rate data for United States general population 2022 [2]

Fluoroquinolone FDA Warnings

Date	FDA Warning
July 2008	First warning, increased risk of tendinitis and tendon rupture ¹⁷
February 2011	Risk of worsening symptoms for those with Myasthenia Gravis ¹⁷
August 2013	Potential for irreversible peripheral neuropathy ¹⁷
May and July 2016	Disabling and potentially irreversible side effects that can occur together - of the tendons, muscles, joints, nerves, and central nervous system ¹⁸
June and December 2018	Disabling and potentially permanent blood glucose disturbances and psychiatric effects ¹⁷ Aorta tears and dissections ¹⁹

FDA – Significant Safety Concerns

- Adverse events from this antibiotic class range from acute to chronic, as noted in numerous FDA Black Box Warnings²⁰
- Should be reserved for use in patients who have no alternative treatment options¹⁸
- These side effects can occur hours to weeks after exposure to fluoroquinolones and may potentially be permanent²⁰
- Side effects continue for an average of 14 months to as long as 9 years or continued²⁰
- In 2015, the FDA reported statistics showing that the top 5 disabling antibiotics were all fluoroquinolones, ranging from 9.9% - 31.1% of the total disabled percentage¹
- FDA data is limited due to FAERS (FDA Adverse Event Reporting System):²¹
 - Duplicate and incomplete reports
 - Report does not establish causation
 - Information and reports have not been verified
 - Rate of occurrence cannot be established

Ineffective Patient-Doctor Experience

Current Situation

- Doctors can be unaware of the possible severity of diverse issues
 - Deterioration to the level of requiring palliative or hospice care
 - Heightened risks of depression and suicidal tendencies
 - Worsening of symptoms and further complications
- Link of adverse effects to the fluoroquinolone prescription is not made
- Lack of guidelines results in self-treatment perils
- Patients can experience gaslighting and dismissal of complaints

Selection of Antibiotics that have ICD-10 Code and Black Box Warnings

Antibiotic Class/Group	Black Box Warning within Family of Drugs	ICD-10 Code
Aminoglycosides	Yes- gentamicin, tobramycin, amikacin, neomycin, plazomicin, streptomycin	Yes
Cephalosporins	Yes - cephalexin, ceftriaxone	Yes
Fluoroquinolones	Yes - ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin, delafloxacin, cinoxacin, sparfloxacin, gemifloxacin and many others were removed from market	No
Macrolides	Yes – azithromycin, erythromycin	Yes
Penicillins	Yes - penicillin G benzathine	Yes
Rifamycin (Rifampicin)	No	Yes
Tetracyclines	Yes - Tygacil	Yes

Conclusion

Why ICD-10 Code is needed for fluoroquinolone AEs

- ✓ Although one of the most clinically important antibiotic groups, fluoroquinolones are unrepresented in the ICD system
- ✓ Fluoroquinolone adverse events occur **4 times more** than Corticosteroids (the second highest drug class at 26,911 adverse events 2004-2023)
- ✓ Fluoroquinolones can cause disabling and irreversible systemic damage; such severity of AEs requires the most substantiated coding
- ✓ The large number and clinical significance of side effects require the prerogative of documentation
- ✓ ICD-10 codes are needed to help individuals seek a diagnosis and treatment
- ✓ ICD-10 codes are needed to obtain the needed statistics and scientific data
- ✓ All patients deserve diagnosis and same standard of care

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