MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

ORAL MEDICATIONS THAT SHOULD NOT BE ADMINISTERED CONCOMITANTLY WITH POLYVALENT CATIONS

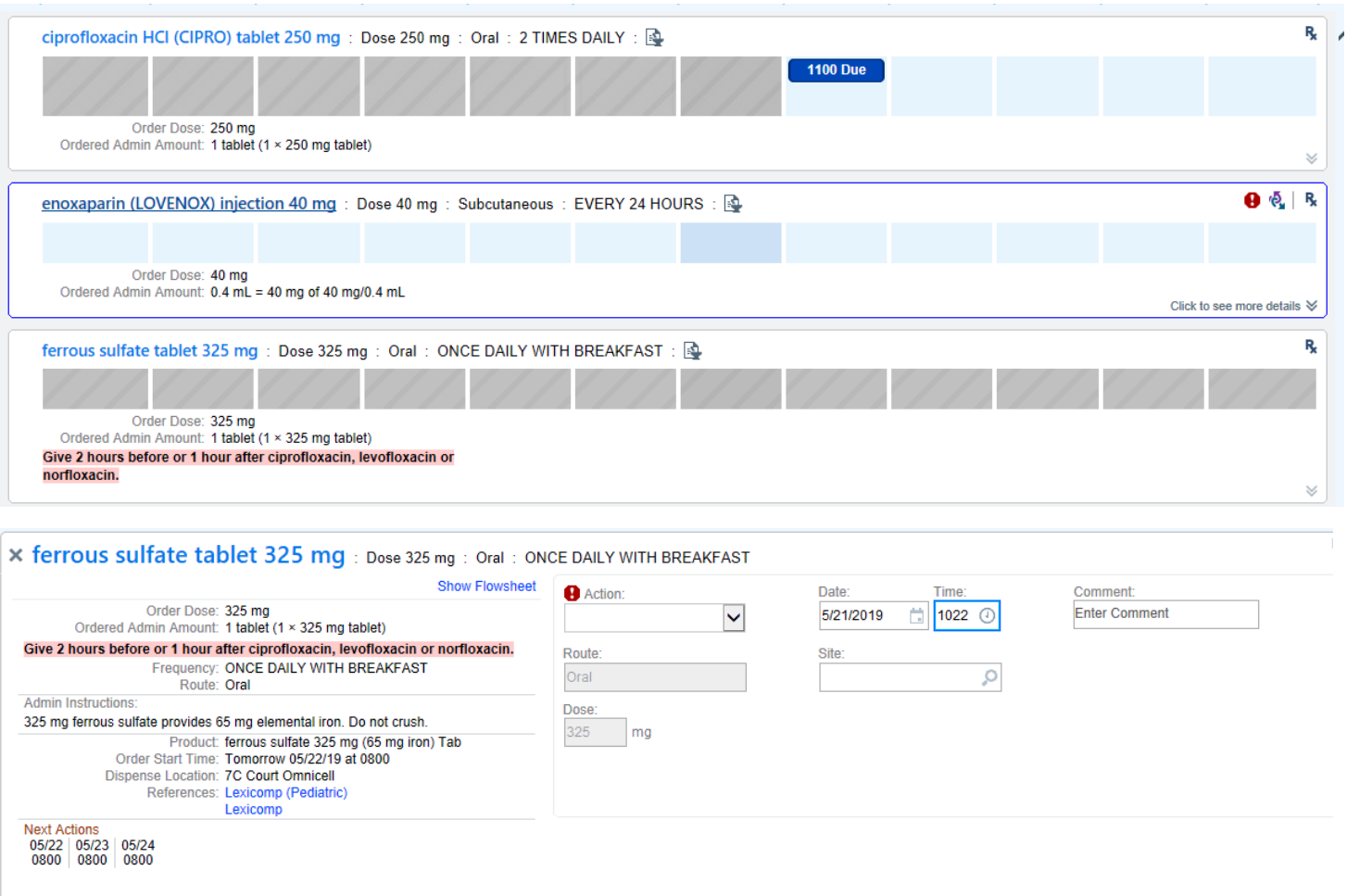
The bioavailability of certain antimicrobials is significantly reduced by co-administration with products containing di- and tri- valent cations (aluminum, calcium, iron, magnesium, and zinc). For example, co-administration of oral fluoroquinolones with such polyvalent cations has been shown to reduce the oral absorption of fluoroquinolones by 25-75%. As a result, co-administration has been shown to be a risk factor for subsequent isolation of quinolone-resistant bacteria (Cohen 2008). In the case of the HIV integrase inhibitor class, co-administration with such cations can reduce absorption by up to 80% (DHHS 2019). Of note, co-administration with enteral feedings is less well studied, but may also not be optimal. In one study, ciprofloxacin bioavailability was reduced by 27%-67% when co-administered with enteral feedings (Healy 1996).

Unfortunately, co-administration is common. In one study, 41% of quinolone prescriptions were in patients also receiving cations, and 77% of those doses were complicated by inappropriately-timed co-administration (Barton 2005).

Currently at Michigan Medicine, MiChart alerts prescribers and pharmacists of this interaction via a 'filtered' alert. Fluoroquinolones and doxycycline also have a 'special' default BID frequency for 6am and 6pm (as opposed to 9am and 9pm). In the MAR, verbiage is provided regarding these interactions via the Administration Instructions, which are not prominently displayed. Despite these steps, co-administration continues to be an issue. A two-day (9/24 and 9/28/2018) snapshot at Michigan Medicine found that of the ~30 patients on an oral quinolone/day, ~30% are also receiving a cation of some sort. In those receiving a cation, 20-40% are not being spaced appropriately to avoid the interaction.

As a result of the above, this document serves to educate clinicians on cation-medication interactions. In addition, a MAR warning (see screenshot below) has been created which will generate on cation-related drugs to warn about administration separation if there is another active (relevant) medication order which could be impacted. That warning also contains a hyperlink to this document, which will be posted on the antimicrobial stewardship web page.

Name of Medication (oral forms only)	Instructions
Recommended Instructions	
All integrase Inhibitors, whether alone or in various combination products - Bictegravir, dolutegravir, elvitegravir, raltegravir	Give 2 hours before or 6 hours after sevelamer, sucralfate, or any oral medication containing aluminum, calcium, iron, magnesium, or zinc (including antacids, sucralfate, and multivitamins). Hold enteral feeds one hour before and after administration.
Doxycycline, minocycline, tetracycline	Give 1 hour before or 2 hours after sevelamer, sucralfate, or any oral medication containing aluminum, calcium, iron, magnesium, or zinc (including antacids, sucralfate, and multivitamins). Hold enteral feeds one hour before and after administration.
Omadacycline	Give 4 hours before or 4 hours after sevelamer, sucralfate, or any oral medication containing aluminum, calcium, iron, magnesium, or zinc (including antacids, sucralfate, and multivitamins). Hold enteral feeds one hour before and after administration.
Ciprofloxacin, Levofloxacin, Norfloxacin	Give 1 hour before or 2 hours after sevelamer, sucralfate, or any oral medication containing aluminum, calcium, iron, magnesium, or zinc (including antacids, sucralfate, and multivitamins). Hold enteral feeds one hour before and after administration.
Moxifloxacin	Give 4 hours before or 8 hours after sevelamer, sucralfate, or any oral medication containing aluminum, calcium, iron, magnesium, or zinc (including antacids, sucralfate, and multivitamins). Hold enteral feeds one hour before and after administration.
Warfarin	Give 2 hours before or 6 hours after sucralfate.
Mycophenolate mofetil and Mycophenolate sodium	Separate administration from any oral medication containing magnesium or aluminum by 2 hours. Mycophenolate should be taken at least 2 hours before sevelamer.



Note: Workgroup consisted of Chris Zimmerman (MiChart), Greg Eschenauer (antimicrobial stewardship) and Katie Barwig and Pat Schmidt (nursing). New MAR process endorsed by the Nursing Documentation Committee on 2/27/2019. Approved by Antimicrobial Subcommittee on 7/2019 and MCDSS on 8/2019.

References:

- Barton TD et al. High rate of coadministration of di- or tri-valent cation-containing compounds with oral fluoroquinolones: risk factors and potential implications. Infect Control Hosp Epidemiol. 2005 Jan;26(1):93-9.
- Cohen KA et al. Coadministration of oral levofloxacin with agents that impair absorption: impact on antibiotic resistance. Infect Control Hosp Epidemiol. 2008 Oct;29(10):975-7. doi: 10.1086/590666.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.
- Healy DP et al. Ciprofloxacin Absorption Is Impaired in Patients Given Enteral Feedings Orally and via Gastrostomy and Jejunostomy Tubes. Antimicrob Agents Chemother 1996;40:6-10.

Antimicrobial Subcommittee Approval: N/A	Originated: Unknown
P&T Approval: N/A	Last Revised: 05/2023
Revision History:	