

## Implications of TIME of drug administration and FOOD

“When” a medication is given can greatly influence efficacy and/or the side effects. Additionally, the effect of administration with food can be important. While the list below is not exhaustive, it focuses on the more commonly prescribed drugs.

Administration	Medication	Notes/Reasoning
Morning	Bisphosphonates (Alendronate ( <i>Fosamax</i> ), Risedronate ( <i>Actonel</i> ) Etidronate ( <i>Didrocal</i> ) (see also “empty stomach”)	-Given first thing in the morning at least 30 minutes prior to food, drink (other than water), or other medications. (Newer formulation, Delayed-Released Risedronate (Actonel DR) is best taken with breakfast, while still avoiding calcium and iron. -Patients should avoid lying down for 60 minutes after taking the medication due to the risk of esophageal ulceration
	Corticosteroids, oral (prednisone, dexamethasone, etc.) (see also “with food”)	-Morning administration mimics natural production of steroid in the body (highest in the morning, lowest in the evening) thus minimizing suppression of the HPA (hypothalamic-pituitary-adrenal) axis -May cause insomnia if given later in the day
	Diuretics (hydrochlorothiazide, furosemide ( <i>Lasix</i> ), metolazone ( <i>Zaroxolyn</i> ) spironolactone ( <i>Aldactone</i> ))	-Given in the morning so increased urination occurs during the daytime hours -If 2 <sup>nd</sup> daytime dose is needed, best given by late afternoon -Timing may not be as important if patient is catheterized
Evening	Histamine H2-receptor antagonists (famotidine ( <i>Pepcid</i> ), nizatidine ( <i>Axid</i> ), ranitidine( <i>Zantac</i> ))	-Evening dosing reduces nocturnal symptoms as histamine is a main mediator in nighttime acid production -Can be given during the day, however, effect of decreasing daytime acid secretion is modest vs. marked effect at night
	Hormones (micronized progesterone ( <i>Prometrium</i> ), vaginal estrogen cream ( <i>Premarin</i> ))	-Oral micronized progesterone is dosed at bedtime as it may cause drowsiness -Vaginal estrogen cream is given at bedtime to increase contact time/absorption & reduce leakage
	Statins (Simvastatin ( <i>Zocor</i> ), Atorvastatin ( <i>Lipitor</i> ), Fluvastatin ( <i>Lescol</i> ), Rosuvastatin ( <i>Crestor</i> ), etc.)	-Most statins were studied and recommended for evening dosing (the body increases cholesterol production overnight) -Bedtime administration, especially for the short-acting simvastatin & fluvastatin, allows for peak drug levels to coincide with increased cholesterol production in the body
	Warfarin	-Evening administration allows for dose adjustments to occur the same day INR results are reported

Administration	Medication	Notes/Reasoning
With Food	Antibiotics-some (nitrofurantoin ( <i>Macrobid</i> ), cefuroxime ( <i>Ceftin</i> ), clarithromycin extended release ( <i>Biaxin XL</i> ))	-Taken with food to improve absorption -For many antibiotics, taking with food may decrease gastric irritation and diarrhea
	Corticosteroids, oral (prednisone, dexamethasone, etc.)	-Taken with food to decrease irritation to the gastrointestinal (GI) tract
	Dabigatran ( <i>Pradaxa</i> )	-Taken with food to reduce the side effect of dyspepsia
	Metformin	-Food decreases GI side effects (e.g. diarrhea)
	NSAIDs (naproxen ( <i>Aleve</i> ), ibuprofen ( <i>Motrin, Advil</i> ), diclofenac ( <i>Voltaren</i> ), meloxicam ( <i>Mobicox</i> ), etc.)	-Given with food or milk to decrease GI irritation -Risk of some GI side effects (i.e. ulcers) is not completely eliminated by taking with food (NSAIDs lessen pain/inflammation by decreasing prostaglandins; prostaglandins have a protective effect on the GI tract)
	Phosphate binders (Calcium carbonate ( <i>Tums</i> ), Sevelamer ( <i>Renagel, Renvela</i> ) Lanthanum ( <i>Fosrenol</i> ))	-Must be taken with meals for effectiveness to treat high phosphate levels in chronic kidney disease (drug binds with phosphate from food in the GI tract so it is not absorbed into the bloodstream and instead excreted in the feces)
	Rivaroxaban ( <i>Xarelto</i> )	-15mg & 20mg doses should be given with food for optimal bioavailability (i.e. more drug is absorbed from GI tract and available to work in body)
Empty Stomach	Antibiotics-some (Ampicillin, Penicillin VK, Cloxacillin, Doxycycline, Tetracycline, Fosfomycin ( <i>Monurol</i> ))	-Increased absorption when taken on an empty stomach. Penicillin VK absorption will be delayed but complete with food.
	Bisphosphonates (Alendronate ( <i>Fosamax</i> ), Risedronate ( <i>Actonel</i> ) Etidronate ( <i>Didrocal</i> ))	-Absorption of drug from the intestine is < 1% and is further reduced in the presence of food, calcium, iron, etc. -Note: Delayed-release risedronate (Actonel DR) is best taken with food (while still avoiding calcium, iron, etc.)
	Iron (Ferrous fumarate, ferrous gluconate, ferrous sulfate)	-Absorbed best in an empty, "mildly acidic stomach" (achieved by giving with orange juice or vitamin C) -Giving with food may decrease GI side effects, however, absorption will be decreased -Starting at a low dose and slowly titrating up and/or dosing at bedtime may improve GI tolerability -Avoid giving with milk, calcium, tea, coffee
	Gastric motility agents (domperidone ( <i>Motilium</i> ) metoclopramide ( <i>Maxeran</i> ))	-Best taken 15-30 minutes before meals to allow for peak levels of the drug to occur to improve gastric motility when eating
	Levothyroxine ( <i>Synthroid, Eltroxin</i> )	-Best absorbed on an empty stomach, separate from calcium, iron, etc. -Often suggested to be taken in the morning, but the most important thing is that it is taken the same way consistently
	Proton Pump Inhibitors (Pantoprazole ( <i>Pantoloc, Tecta</i> ), Omeprazole ( <i>Losec</i> ), Lansoprazole ( <i>Prevacid</i> ), etc)	-For best effectiveness to lessen the production of stomach acid, give 30-60 minutes before meals (typically before breakfast if once daily, before breakfast & supper if BID); if this is not possible, give at the beginning of a meal

Administration	Medication	Notes/Reasoning
Avoidance of: Calcium, Iron, Zinc Magnesium, Aluminum	Fluoroquinolones (Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin) Tetracyclines (Tetracycline, doxycycline, minocycline)	-Separate administration from the minerals listed (such as found in supplements or antacids) by at least 2 hours to ensure adequate amount of the antibiotic is absorbed to be effective
Avoidance of iron	Levodopa/carbidopa ( <i>Sinemet</i> )	-Doses should be separated by 2 hours (if given together, iron decreases the amount of levodopa available to work)

References: (1) Medication Administration Timing. *Pharmacist's Letter*, May 2016. (2) *Compendium of Therapeutic Choices*. Canadian Pharmacists Association, 2014. (3) Oral Antibiotics. *RxFiles*, Oct. 2016.

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