

## EDUCATIONAL REVIEW

# Guidelines for Administration of Cardiovascular Medications With Food and Grapefruit Juice

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In many clinics and pharmacies, patients often question whether medications should be taken with or without food. This led the authors to research recommendations for taking various cardiovascular medications with food.

The results of this search are contained within the table and are intended to be used as a quick aid for health care practitioners when they are prescribing or administering cardiovascular drugs, or are counseling patients taking these drugs.<sup>1-3</sup>

Information was collected primarily from the manufacturer-provided package inserts. In situations where the manufacturer did not provide recommendations on administration, the AHFS Drug Information online reference was used. If no information was available there, the final source consulted was Lexi-Comp's online reference.

The focus of this research was to address the effect that food has on the direct gastrointestinal absorption and tolerability of specific medications. If it is recommended that a medication be administered with food, the preferred

time (ie, before, during, or after a meal) is presented, when available. We have included the most commonly used cardiovascular medications, providing recommendations regarding administration. Specific information on the presence of a grapefruit juice interaction also is included because it can lead to variable yet significant changes in drug concentrations and effects.

## References

1. McEvoy GK, ed. *AHFS Drug Information 2012*. Bethesda, MD: ASHP; 2011.
2. Lacy CF, Armstrong LL, Goldman MP, Lance LL, eds. *Drug Information Handbook, 20th Edition*. Hudson, OH: Lexi-Comp; 2011.
3. Seden K, Dickinson L, Khoo S, Back D. Grapefruit-drug interactions. *Drugs*. 2010; 70(18):2373-2407.



**Table. Recommendations for Administration of CV Agents With Food, Grapefruit Juice**

Drug	Recommendation Regarding Food	Grapefruit Juice Interaction
Acebutolol	May be taken with or without food	No <sup>2</sup>
Aliskiren (Tekturna, Novartis)	Should be taken consistently with or without food but not with high-fat meals	Avoid combination; separation by several hours may reduce chance for interaction <sup>2</sup>
Aliskiren/Amlodipine (Tekamlo, Novartis)		Avoid combination <sup>3</sup>
Ambrisentan (Letairis, Gilead)	May be taken with or without food	No <sup>2</sup>
Amiloride	Should be taken with food	
Amiloride/HCTZ		
Amiodarone	Should be taken consistently with or without food	Avoid combination <sup>3</sup>
Amlodipine	May be taken with or without food	Avoid combination or limit consumption to small quantities <sup>2,3</sup>
Amlodipine/atorvastatin		
Amlodipine/benazepril		Avoid combination <sup>3</sup>
Amlodipine/olmesartan (Azor, Sankyo)		
Amlodipine/olmesartan/HCTZ (Tribenzor, Sankyo)		

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Drug	Recommendation Regarding Food	Grapefruit Juice Interaction
Amlodipine/telmisartan (Twynsta, Boehringer Ingelheim)	May be taken with or without food	Avoid combination <sup>3</sup>
Amlodipine/valsartan (Exforge, Novartis)	Should be taken consistently with or without food	
Aspirin	Administration with food may help prevent stomach upset <sup>1</sup>	No <sup>2</sup>
Aspirin/dipyridamole (Aggrenox, Boehringer Ingelheim)	May be taken with or without food	
Atenolol	No issue apparent regarding administration with or without food	
Atorvastatin	May be taken with or without food	Avoid combination or limit consumption to small quantities <sup>2,3</sup>
Azilsartan (Edarbi, Arbor)		No <sup>2</sup>
Benazepril		No <sup>2</sup>
Betaxolol		No <sup>2</sup>
Bisoprolol		Monitor for increased effects of bisoprolol <sup>2</sup>
Bosentan (Tracleer, Actelion)		Monitor for increased effects of bosentan <sup>2</sup>
Bumetanide		No issue apparent regarding administration with or without food
Candesartan	May be taken with or without food	No <sup>2</sup>
Captopril	Should be taken 1 h before meals	Monitor for increased effects of carvedilol <sup>2</sup>
Carvedilol	Should be taken with food to decrease risk for orthostatic hypotension	
Chlorthalidone	Should be taken as a single dose in the morning with food	No <sup>2</sup>
Cholestyramine	Should be taken with food	Monitor for increased effects of cilostazol <sup>2</sup>
Cilostazol	Should be taken consistently either 30 min before or 2 h after breakfast and dinner	
Clonidine	May be taken with or without food	
Clopidogrel		
Colesevelam (Welchol, Sankyo)	Should be taken with food	No <sup>2</sup>
Colestipol	Should be taken with plenty of fluids	
Cyclosporine	All formulations should be taken consistently with or without food, but Neoral (Novartis) should not be administered with high-fat meals	Avoid combination <sup>3</sup>
Dabigatran etexilate (Pradaxa, Boehringer Ingelheim)	May be taken with or without food	Monitor for increased effects of dabigatran <sup>2</sup>
Digoxin	May be taken with or without food; however, meals high in bran fiber should be avoided	No <sup>2,3</sup>
Diltiazem	IR product should be taken before meals; no issue with long-acting product; however, Dilacor XR (Actavis) should not be taken with high-fat meals	Monitor for increased effects of diltiazem <sup>2,3</sup>
Dipyridamole	No issue apparent regarding administration with or without food	No <sup>2</sup>
Disopyramide		Monitor for increased effects of disopyramide <sup>2</sup>
Dofetilide (Tikosyn, Pfizer)	May be taken with or without food	No <sup>2</sup>
Doxazosin		Monitor for increased effects of doxazosin <sup>2</sup>
Dronedarone (Multaq, Sanofi-Aventis)	Should be taken with food	Avoid combination <sup>3</sup>
Enalapril	May be taken with or without food	No <sup>2</sup>
Eplerenone (Inspra, Pfizer)		Dose adjustments are recommended; contact physician <sup>2</sup>
Eprosartan	Should be taken consistently with or without food	No <sup>2</sup>
Ethacrynic acid	Should be taken after meals	
Ezetimibe (Zetia, Merck/Schering)	May be taken with or without food	Avoid combination or limit consumption to small quantities <sup>2,3</sup>
Ezetimibe/simvastatin (Vytorin, Merck/Schering)		

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**Table. Recommendations for Administration of CV Agents With Food, Grapefruit Juice**

Drug	Recommendation Regarding Food	Grapefruit Juice Interaction
Felodipine	Should be taken without food or with a light meal	Moderation of grapefruit juice ingestion may be needed <sup>2</sup>
Fenofibrate	May be taken with or without food (Antara [Lupin], Fibracor [AR Scientific], TriCor [AbbVie], Triglide [Shionogi], and TriLipix [AbbVie]); should be taken with food (Fenoglide [Santarus], and Lipofen [Kowa])	No <sup>2</sup>
Flecainide		
Fluvastatin	May be taken with or without food	
Fosinopril		
Furosemide	No issue apparent regarding administration with or without food	
Gemfibrozil	Should be taken 30 min before morning and evening meals	
Guanfacine	IR and ER products may be taken with or without food, but ER products should not be taken with high-fat meals	Monitor for increased effects of guanfacine <sup>2</sup>
Hydralazine	Should be taken consistently with or without food	No <sup>2</sup>
Hydralazine/isosorbide dinitrate (BiDil, Arbor)	No issue apparent regarding administration with or without food	Monitor for increased effects of isosorbide <sup>2</sup>
Hydrochlorothiazide	May be taken with or without food; however, Microzide (Actavis) capsules should be taken consistently with or without food	No <sup>2</sup>
Indapamide	No issue apparent regarding administration with or without food	
Irbesartan	May be taken with or without food	
Isosorbide	May be taken with or without food (mononitrate); no issue apparent regarding administration with or without food (dinitrate)	Monitor for increased effects of isosorbide <sup>2</sup>
Isradipine	No issue apparent regarding administration with or without food	Monitor for increased effects of isradipine <sup>2</sup>
Labetalol	Should be taken consistently with or without food	No <sup>2</sup>
Lisinopril		
Losartan	May be taken with or without food	
Lovastatin	Should be taken with food	
Methyldopa	No issue apparent regarding administration with or without food	No <sup>2</sup>
Metolazone		
Metoprolol	Should be taken consistently with or immediately after meals	
Mexiletine	Should be taken with food	
Midodrine	May be taken with or without food	
Minoxidil	No issue apparent regarding administration with or without food	
Moexipril	Should be taken 1 h before meals	Monitor for increased effects of nadolol <sup>2</sup>
Nadolol	May be taken with or without food	
Nebivolol (Bystolic, Forest)		No <sup>2</sup>
Niacin		No <sup>2</sup>
Niacin/lovastatin (Advicor, AbbVie)	Should be taken with food	Avoid combination <sup>3</sup>
Niacin/simvastatin (Simcor, AbbVie)		Avoid combination or limit consumption to small quantities <sup>2,3</sup>
Nicardipine	To ensure constant bioavailability, do not administer with high-fat meals; SR product should be taken consistently with or without food	Avoid combination <sup>3</sup>
Nifedipine	No issue apparent regarding administration with or without food with IR products; long-acting products should be taken without food	
Nisoldipine	Should be taken either 1 h before or 2 h after a meal	
Olmesartan (Benicar, Sankyo)	May be taken with or without food	No <sup>2</sup>
Omega-3-acid ethyl esters	No issue apparent regarding administration with or without food	No <sup>2</sup>
Pentoxifylline	Should be taken with food	
Perindopril erbumine	Should be taken consistently with or without food	

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Drug	Recommendation Regarding Food	Grapefruit Juice Interaction
Pindolol	May be taken with or without food	No <sup>2</sup>
Pitavastatin (Livalo, Kowa)		
Potassium chloride		
Prasugrel (Effient, Lilly)	Should be taken with food	
Pravastatin	May be taken with or without food	Monitor for increased effects of pravastatin <sup>2</sup>
Prazosin	No issue apparent regarding administration with or without food	No <sup>2</sup>
Propafenone	May be taken with or without food	Monitor for increased effects of propafenone <sup>2,3</sup>
Propranolol	Protein-rich foods increase bioavailability, so IR product should be taken without food to ensure constant bioavailability; long-acting product has no apparent issue regarding administration with or without food	No <sup>2</sup>
Quinapril	Should be taken consistently with or without food, but not with high-fat meals	
Quinidine sulfate/quinidine gluconate	Should be taken with food	Monitor for increased effects of quinidine <sup>2</sup>
Ramipril	May be taken with or without food	No <sup>2</sup>
Rivaroxaban (Xarelto, Janssen)	When used for AF, should be taken with evening meals; when used for DVT prophylaxis after hip/knee surgery, may be taken with or without food	Monitor for increased effects of rivaroxaban <sup>2</sup>
Rosuvastatin (Crestor, AstraZeneca)	May be taken with or without food	No <sup>2</sup>
Sildenafil	May be taken with or without food, but not with high-fat meals	Monitor for increased effects of sildenafil <sup>2,3</sup>
Simvastatin	May be taken with or without food	Avoid combination or limit consumption to small quantities <sup>2,3</sup>
Sirolimus (Rapamune, Pfizer)	Should be taken consistently with or without food, but not with high-fat meals	Avoid combination <sup>3</sup>
Sotalol	Should be taken consistently with or without food	No <sup>2</sup>
Spirolactone		No <sup>2</sup>
Tacrolimus	Should be taken consistently with or without food, but not with high-fat meals	Avoid combination <sup>3</sup>
Tadalafil (Adcirca, Cialis, Lilly)	May be taken with or without food	Monitor for increased effects of tadalafil <sup>2,3</sup>
Telmisartan (Micardis, Boehringer Ingelheim)	May be taken with or without food	No <sup>2</sup>
Terazosin	No issue apparent regarding administration with or without food	No <sup>2</sup>
Ticagrelor (Brilinta, AstraZeneca)	May be taken with or without food	Monitor for increased effects of ticagrelor <sup>2</sup>
Ticlopidine	Should be taken with food	No <sup>2</sup>
Timolol	No issue apparent regarding administration with or without food	No <sup>2</sup>
Tolvaptan (Samsca, Otsuka)	May be taken with or without food	Avoid combination <sup>2</sup>
Torseamide		No <sup>2</sup>
Trandolapril		No <sup>2</sup>
Trandolapril/verapamil (Tarka, AbbVie)	Should be taken with food	Monitor for increased effects of verapamil <sup>2</sup>
Triamterene (Dyrenium, Wellspring)	Administer after meals to avoid stomach upset	No <sup>2</sup>
Triamterene/HCTZ	Administer after meals	
Valsartan	Should be taken consistently with or without food	
Verapamil	IR product has no apparent issue regarding administration with or without food; Calan SR (Pfizer) and Isoptin SR (Ranbaxy) capsules should be taken with food	Interaction unlikely to be clinically relevant <sup>3</sup> ; monitor for increased effects of verapamil <sup>2</sup>
Warfarin	Should be taken consistently with or without food; efforts should be made to maintain a consistent dietary vitamin K intake	No <sup>2</sup>

AF, atrial fibrillation; CV, cardiovascular; DVT, deep vein thrombosis; ER, extended-release; HCTZ, hydrochlorothiazide; IR, immediate-release; SR, sustained-release

Based on manufacturers' package inserts unless otherwise noted.