

DRUG-DRUG INTERACTIONS IN **NEPHROLOGY**



In Management of Hyperphosphatemia in CKD



✓ 10 fold reduction in CV deaths¹

✓ Two million Patient-Years of Combined Experience²

✓ Robust Efficacy and Safety in all Dosing forms^{*3}



* Data on file for both Renvela and Rengel. 1. Di-Lorio, B, Molony, Bell C et al Sevelamer versus Calcium carbonate in incident hemodialysis. Patients:Results of an open label 24 Month Randomized Clinical Trial. Am J KIDNEY Dis;2013 May 20;62(4):771-77 2. Data on file - 3. Fan S, Ross C, Mitra S, Kalra P et al A randomized,cross over design study of sevelamer carbonate powder and sevelamer hydrochloride tablets in chronic kidney disease patients on haemodialysis. Nephrol Dial Transplant. 2009 Dec; 24(12):3794-9

Abridged Prescribing Information

Sevelamer Carbonate Tablets and Powder for Oral Suspension. **Renvela® THERAPEUTIC CATEGORY** Phosphate Binder. **COMPOSITION** Renvela Tablets : Each film coated tablet contains 800 mg of sevelamer carbonate on an anhydrous basis. **Renvela Sachets** : Each sachet contains 0.8 g of sevelamer carbonate for oral suspension on an anhydrous basis. **THERAPEUTIC INDICATIONS** Renvela is indicated for the control of serum phosphorus levels in patients with chronic kidney disease (CKD) on hemodialysis. **DOSAGE AND ADMINISTRATION** Starting dose is 2.4 to 4.8 g per day based on clinical needs and phosphorus level. Renvela must be taken three times per day with meals. For patients previously on phosphate binders (sevelamer hydrochloride or calcium based) Renvela should be given on a gram for gram basis with monitoring of serum phosphorus levels to ensure optimal daily doses. Titration and Maintenance Serum phosphorus levels must be monitored and the dose of sevelamer carbonate titrated every 2-4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring thereafter. Patients taking Renvela should adhere to their prescribed diets. **Special Populations** Children The safety and efficacy of Renvela has not been established in children below the age of 18 years. Renvela is not recommended for use in children below the age of 18 years. **Elderly** There is no evidence for special considerations when Renvela is administered to elderly patients. **Route of administration** is oral. Renvela is available as tablets or powder for oral suspension. Renvela 800 mg tablets can be taken three times per day with meals at a dose based on individual patient requirements to control phosphate levels. Tablets should be swallowed intact and should not be crushed, chewed, or broken into pieces prior to administration. Renvela 800 mg powder sachet can be taken three times per day with meals individually or in combination at a dosage based on individual patient requirements to control phosphate levels. The powder should be dispersed in water (30 mL for 0.8 g powder sachet) prior to administration. Multiple sachets may be mixed together, as long as an appropriate amount of water is used. Patient should drink the preparation within 30 minutes. **Safety-Related INFORMATION** **CONTRAINDICATIONS** Renvela is contraindicated in patients with hypophosphatemia or bowel obstruction and in patients with hypersensitivity to the active substance or to any of the excipients. **WARNINGS AND PRECAUTIONS** The safety and efficacy of Renvela in patients with dysphagia, swallowing disorders, severe gastrointestinal motility disorders including severe constipation or major gastrointestinal tract surgery have not been established. Consequently, caution should be exercised when Renvela is administered in patients with these disorders. Renvela treatment should be reevaluated in patients who develop severe constipation or other severe gastrointestinal symptoms. Use of Renvela may be difficult, especially in older patients. Clinical experience suggests that use of Renvela may be associated with an increased risk of difficulty swallowing. **PREGNANCY** Pregnancy Category C. The safety of Renvela has not been established in pregnant or lactating women. Renvela should only be given to pregnant or lactating women if clearly needed and after careful risk/benefit analysis has been conducted for both the mother and fetus or infant. Studies in animals have shown minimal reproductive toxicity when sevelamer was administered to rats at high doses (see section "Impairment of Fertility" in section Reproduction toxicity). There have been no adequate well controlled studies in women undergoing labor and delivery. **ADVERSE REACTIONS** The most frequently occurring adverse reaction for Renvela 800 mg tablets and 800 mg powder sachet are hypersensitivity, nausea, vomiting, constipation, diarrhea, dyspepsia, abdominal pain, flatulence, constipation, pruritis, abdominal distention and anorexia.

For full prescribing information, please write to: Sanofi-Synthelab (India) Private Ltd., Sanofi House, CT Survey No 117-B, L&T Business Park, Saket Vihar Road, Powai, Mumbai 400072

Source: CCDS version No 4 dated 18 August 2015 Updated: November 2015

DRUG-DRUG INTERACTIONS IN NEPHROLOGY

The drugs referred to in this booklet are discussed under following sections:

- Interacting Category/Drugs
- Effects of Interaction
- Consequences/Signs/Symptoms Subsequent to Interaction
- Severity of Interactions
- Time of Onset of Effects
- Section Excerpts and Recommendations

© All rights reserved.

No part of this publication can be reused or stored in a retrieval system in any form without written permission from the publisher.

Care has been taken to confirm the accuracy of the information present. However, the authors, editors and publisher are not responsible for errors or omissions or from any consequences from the application of the information in this booklet. Application of this information in a particular situation remains the professional responsibility of the practitioner.

The authors, editors and publisher have exerted every effort to ensure drug selection in accordance with the current recommendations and practice at the time of preparing/publishing this booklet. However, in view of ongoing research, changes in government regulations and constant flow of information relating to drug therapy and drug-drug interactions, the readers are urged to check the package insert for each drug for any change/modification in the information.

INTRODUCTION

Concurrent administration of two or more drugs may cause interaction between each other. This interaction may be potentiation or antagonism of the drugs concerned and may cause unexpected toxicity. As newer and more potent drugs become available, the number of serious drug-drug interactions is likely to increase.

Drug interaction series is a handy, pocket-sized book that presents a quick glance of the drug-drug interactions during administration of most used drugs in nephrology,* through pictorial representation.

*Mentioned in ATC codes B01-B03, C01-C04, C07-C09, G04, H02, J01-J02, J04-J07, L01-L04; also from the National List of Essential Medicines of India, 2011.

GUIDE TO READ

The heading on each page represents individual drug or the class of drugs commonly used in nephrology.*

The **first column** lists the commonly used category/drugs in nephrology.

The **second column** lists the category/drugs that interact with the given category/drugs used in nephrology.

The **third column** shows, in brief, the pharmacological effects of the interaction *in vivo*.

The **fourth column** shows the consequences/signs/symptoms of the patient due to the effects of drug-drug interaction. It is presented through the symbols and each symbol depicts a series of clinical signs/symptoms as mentioned in Table 1.

The **fifth column** defines the severity of interaction and these may be:

- 👉 **Major (!!!):** This defines potentially fatal effects of interaction that can cause permanent damage to the patient.
- 👉 **Moderate (!!):** The effects may cause a deterioration in patient's clinical condition, that may require hospitalization.
- 👉 **Minor (!):** The effects are mild and tolerable.

The **last column** is the pictorial representation of the time of onset of clinical effects, as shown below.



Fast (occur within 24 hr)



Slow (may occur in days to weeks)



Not known/not available

*Mentioned in ATC codes B01-B03, C01-C04, C07-C09, G04, H02, J01-J02, J04-J07, L01-L04; also from the National List of Essential Medicines of India, 2011.

GUIDE TO READ

Table 1: Symbols used may refer to the following consequences/signs/symptoms

	Low blood pressure and resulting syncope, dizziness or fainting. Orthostatic hypotension.
	High blood pressure and resulting headache, dizziness and shortness of breath.
	Irregularity in rate and rhythm of the heart beat. May include tachycardia or bradycardia.
	Immunological disorders including fever/chills, hypersensitivity, allergy, skin rashes or infection in any part of the body.
	Respiratory disorders such as difficulty in breathing, cough, bronchospasm.
	Neurological disorders, may include confusion, impaired concentration, delirium and dizziness, lethargy, sedation, visual disturbances, headache, anxiety. Paralysis, muscle weakness, loss of sensation, ataxia and seizures.
	Diarrhea, stomach pain, nausea, vomiting, mild metabolic acidosis. GI ulceration.
	Electrolyte imbalance, may result in weakness, muscle pains or cramps, nausea, anorexia, visual disturbances, increased thirst, sweating, irritability.
	Hepatic disorders resulting in nausea, vomiting, abdominal pain, loss of appetite, diarrhea, weakness, pale skin and jaundice.
	Hemorrhage, easy bruising, prolonged bleeding from cuts. May include GI bleeding, vaginal bleeding, nosebleeds, bleeding of gums from brushing associated with pain.
	Blood clot resulting in chest pain, hemoptysis, shortness of breath, sudden loss of vision, pain, redness or swelling in extremity. Decreased anticoagulant effect.
	Methemoglobinemia, causing slate-grey cyanosis in buccal mucous membranes, lips and nail beds.

GUIDE TO READ

	Increase in blood sugar level resulting in frequent urination, dry mouth, increased thirst.
	Decrease in blood sugar level causing headache, dizziness, drowsiness, hunger, tremor, weakness, sweating, palpitations.
	Ototoxicity causing partial or profound loss of hearing, tinnitus, vertigo.
	Myopathy causing muscle pain, fatigue, muscle tenderness and weakness, nocturnal cramping, tendon pain.
	Renal disorders, nephrotoxicity
	Hematologic toxicity including anemia, leukopenia, thrombocytopenia. Bone marrow suppression
	Vasospasm, thrombosis, cerebral ischemia, ischemia of extremities
	Miscellaneous (patients may show any of the above mentioned signs/symptoms; may also include whole body).

CONTENTS

1.	Antihypertensive and cardiovascular agents	11
	• ACE inhibitors	
	• Angiotensin receptor blockers	
	• Beta blockers	
	• Calcium channel blockers	
	• Diuretics	
2.	Anticoagulants	23
	• Direct thrombin inhibitors	
	• Heparin and low molecular weight heparins	
	• Warfarin	
3.	Antimicrobial agents	27
	• Antibacterial agents	
	• Antifungal agents	
	• Antiviral agents	
4.	Antineoplastic agents	34
5.	Antiplatelet agents	35
6.	Drugs in hyperkalemia	38
7.	Drugs in hyperphosphatemia	39
8.	Erythropoietin stimulating agents	41
9.	Immunosuppressants	42
10.	Iron salts	48
11.	Urinary alkalisers	49
	INDEX	50
	BIBLIOGRAPHY	56

LIST OF ABBREVIATIONS

ACE	Angiotensin converting enzymes
ACTH	Adrenocorticotrophic hormone
ARB	Angiotensin receptor blocker
BP	Blood pressure
BZD	Benzodiazepines
CAIs	Carbonic anhydrase inhibitors
CCBs	Calcium channel blockers
CHF	Congestive heart failure
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CV	Cardiovascular
CVEs	Cardiovascular events
eATG	Antithymocyte globulin equine
5-FU	5-Fluorouracil
GI	Gastrointestinal
GU	Genitourinary
HD	Hemodialysis
HF	Heart failure
INH	Isoniazid
INR	International normalized ratio
IV	Intravenous
LMWH	Low molecular weight heparin
MAO	Monoamine oxidase
MAOIs	Monoamine oxidase inhibitors
NSAIDs	Non-steroidal anti-inflammatory drugs
PPIs	Proton pump inhibitors
rATG	Antithymocyte globulin rabbit
RBC	Red blood cell
SRIss	Serotonin reuptake inhibitors
SSRIs	Selective serotonin reuptake inhibitors
T2DM	Type 2 diabetes mellitus
TCAs	Tricyclic antidepressants
TdP	Torsades de pointes

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS					
Angiotensin converting enzyme inhibitors[#]					
Captopril Enalapril Fosinopril Lisinopril Perindopril Quinapril Ramipril	Aliskiren	Increased risk of hypotension and hyperkalemia; may cause acute renal failure, particularly in patients with type 2 diabetes and renal impairment	  	!!!	-
	Allopurinol	Increased risk of severe hypersensitivity reactions, neutropenia, agranulocytosis, and serious infections		!!!	-
	Antacids: Aluminum hydroxide/ Magnesium carbonate	Antacids may decrease the oral bioavailability of ACE inhibitors		!	
	Lithium	Concomitant administration may attenuate the vasodilator and hypotensive effects of ACE inhibitors	 	!!	
	NSAIDs: Celecoxib, Diclofenac, Flurbiprofen, Indomethacin, Mefenamic acid	NSAIDs may attenuate antihypertensive effects of ACE inhibitors Deterioration of renal function in patients taking diuretics, or with compromised renal function*	 	!!	
	Phenothiazines: Chlorpromazine, Fluphenazine, Methotrimeprazine, Promethazine, Trifluoperazine	Phenothiazines may potentiate the antihypertensive effect of given ACE inhibitors	 	!!	
	Potassium sparing diuretics: Amiloride, Spironolactone, Triamterene	Increased risk of hyperkalemia		!!!	
	Potassium salts: Potassium chloride				

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Captopril Enalapril Fosinopril Lisinopril Perindopril Quinapril Ramipril	Probenecid	Duration of action of ACE inhibitors may be prolonged		!	
	Thiazide diuretics: Hydrochlorothiazide	Thiazide diuretics potentiate hypotensive effects of ACE inhibitors**		!!	-
	Tizanidine	Increased risk of hypotension		!!!	
	Vasodilators: Nitroglycerin or other nitrates	ACE inhibitors may increase vasodilator and hypotensive effects of nitroglycerin		!!	-
Enalapril	Rifampin	Rifampin may decrease the hypotensive effects of enalapril		!	
Benazepril	Beta-blockers, Calcium channel blockers	Beta-blockers and calcium channel blockers may potentiate the antihypertensive effect of benazepril	-	-	-
	Warfarin	Decreased anticoagulant effect of warfarin		-	-

SECTION EXCERPTS AND RECOMMENDATIONS

- * ACE inhibitors majorly interact with aliskiren (a direct rennin inhibitor), potassium sparing diuretics, potassium salts, allopurinol and tizanidine.
- * The adverse effects may be reversed after the discontinuation of concomitant administration of drugs
- ** Discontinue diuretic or increase salt intake one week before initiating ACE inhibitors or start therapy with ACE inhibitors in small doses (6.25 or 12.5 mg)

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS					
Angiotensin receptor blockers*					
Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan	Aliskiren	Increased risks of hypotension and hyperkalemia, including acute renal failure, in patients with T2DM and renal impairment		!!!	-
	Corticosteroids: Cortisone, Hydrocortisone, Prednisolone	Corticosteroids may antagonize the effects of antihypertensive medications by inducing sodium and fluid retention		!!	-
	Lithium	May increase serum lithium levels, thus increasing associated toxicity		!!	
	Acetaminophen NSAIDs: Aspirin, Ibuprofen, Indomethacin, Ketoprofen	Deterioration of renal function and acute renal failure in patients who are elderly, taking diuretics, or with compromised renal function. Antihypertensive effects of ARBs may be decreased by NSAIDs	 	!!	
	Phenothiazines and neuroleptic agents: Aripiprazole, Promethazine	These agents may potentiate the antihypertensive effect of ARBs		!!	-
	Potassium sparing diuretics: Amiloride, Spironolactone*, Triamterene Potassium salts: Potassium phosphate, Potassium iodide, Potassium gluconate, Potassium bicarbonate	Increased risk of hyperkalemia	  	!!!	

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan	Ramipril	ARBs increase concentration of ramipril; thus may increase the risk of hyperkalemia, hypotension and renal dysfunction	  	!!	-
	Tadalafil	Tadalafil may potentiate the hypotensive effect of ARBs	 	!	-
Losartan	Azole antifungal agents: Fluconazole, Ketoconazole	Concomitant use may increase losartan concentration; thus antihypertensive effects of losartan may increase	  	!!	
	Hydantoins: Fosphenytoin, Phenytoin	Hydantoins may decrease the antihypertensive effects of losartan	  	!!	
	Rifampin	Serum levels of losartan may be reduced; thus decrease in the antihypertensive effects	  	!!	
Telmisartan	Digoxin	Telmisartan may increase serum concentration of digoxin; increased risk of toxicity	  	!!	

SECTION EXCERPTS AND RECOMMENDATIONS

- * ARBs should not be administered with aliskiren, potassium sparing diuretics and potassium salts.
- * If spironolactone is prescribed with an ARB, its dosage should not exceed 25 mg/day in high-risk patients

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS					
Beta-blockers*					
Acebutolol Atenolol Betaxolol Bisoprolol Esmolol Metoprolol Nadolol Nebivolol Penbutolol Pindolol Propranolol Sotalol Timolol Carvedilol Labetalol	Aminophylline, Theophylline	High doses of beta-blockers may cause severe or fatal bronchospasm, opposing the bronchodilator effects of the interacting drugs.		!!!	-
	Calcium channel blocker: Nifedipine	Additive reductions in heart rate, cardiac conduction, and cardiac contractility, resulting in CHF, severe hypotension, and/or exacerbation of angina.	 	!!	
	Calcium channel blockers: Diltiazem, Verapamil	Additive reductions in heart rate, cardiac conduction, and cardiac contractility, resulting in potentially serious CVE.		!!!	
	Digoxin	Concomitant use may increase the risk of bradycardia.		!!	-
	Diphen- hydramine	Diphenhydramine may potentiate the hypotensive effect of beta blockers.	 	!!	
	Disopyramide	Coadministration may result in severe hypotension, syncope, severe bradycardia, asystole, and heart failure.	 	!!!	-
	H₂ antagonist: Cimetidine	Cimetidine increases plasma concentrations of beta blockers.		!!	
	Lidocaine	Coadministration may result in lidocaine toxicity.	 	!!	

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Acbutolol Atenolol Betaxolol Bisoprolol Esmolol Metoprolol Nadolol Nebivolol Penbutolol Pindolol Propranolol Sotalol Timolol Carvedilol Labetalol	NSAIDs: Ibuprofen, Indomethacin, Piroxicam	NSAIDs may decrease the antihypertensive effect of beta blockers.		!!	
	Reserpine, Guanethidine, MAO inhibitors	Additive effect may result in hypotension, orthostasis, bradycardia and HF.		!!	
	Sympatho- mimetics: Dobutamine, Dopamine, Metaraminol, Norepinephrine, Phenylephrine	Beta-blockers may antagonize the cardiostimulatory effects of pressor agents.		!!	-
	Tizanidine	Tizanidine may potentiate the hypotensive effect of beta blockers. ⁵		!!!	-
Acbutolol Atenolol Betaxolol Bisoprolol Esmolol Metoprolol Nadolol Nebivolol Penbutolol Pindolol Propranolol Timolol Carvedilol Labetalol	Amiodarone	Additive effects of severe bradycardia, cardiac arrest, and ventricular fibrillation may occur.		!!	
	Epinephrine	Beta-blockers may antagonize the cardiostimulatory effects of epinephrine.		!!	-
Nadolol Penbutolol Pindolol Propranolol Sotalol Timolol Carvedilol Labetalol	Epinephrine	Enhanced pressor response to epinephrine. Concomitant administration may result in severe hypertension accompanied by bradycardia.		!!!	-

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Acebutolol Atenolol Betaxolol Bisoprolol Esmolol Penbutolol Nadolol Nebivolol Carvedilol Labetalol	Phenothiazines: Chlorpromazine, Thioridazine	Phenothiazines may potentiate the hypotensive effect.		!!	
Pindolol Propranolol Sotalol	Phenothiazines: Chlorpromazine, Thioridazine	Coadministration may increase the plasma concentrations of thioridazine, increasing the risk of ventricular arrhythmias, cardiac arrest and sudden death.*		!!!	
Bisoprolol Penbutolol Propranolol Metoprolol Timolol Carvedilol Labetalol	Rifampin	Concurrent use of rifampin may decrease serum levels and effects of some oral beta-blockers.		!!	
Metoprolol Propranolol	Sodium channel blockers: Flecainide, Propafenone	Serum levels and effects of some beta-blockers may increase significantly. Negative inotropic effects may also be potentiated.	 	!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

- # Concomitant administration of almost all the cardioselective and non-selective beta-blockers with aminophylline and theophylline, calcium channel blockers (verapamil, diltiazem), sodium channel blocker (disopyramide), and tizanidine may prove to be fatal.
- \$ Initiate tizanidine treatment with 4 mg doses and gradually increase in 2 to 4 mg increments until optimum effect is achieved. The dose can be repeated at 6 to 8 hour intervals as needed, up to a maximum of three doses in 24 hours and a total daily dosage of 36 mg.
- * Concurrent use is contraindicated.

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS					
Calcium channel blockers					
Amlodipine S-Amlodipine	Simvastatin	Coadministration may significantly increase the plasma concentrations of simvastatin and its active metabolite, simvastatin acid, and potentiate the risk of statin-induced myopathy. [#]		!!!	-
Amlodipine S-Amlodipine Felodipine Nicardipine Nifedipine Nimodipine Nisoldipine Diltiazem Verapamil	Azole antifungal: Itraconazole	Dose-related negative inotropic effects of itraconazole may be increased. ^{\$}		!!!	-
	Dolasetron	Coadministration may result in additive effects and increased risk of bradycardia and heart block.		!!!	-
	Nitroglycerin	Concurrent administration may cause symptomatic orthostatic hypotension.		!!	-
Amlodipine S-Amlodipine Felodipine Nicardipine Nifedipine Nisoldipine Diltiazem Verapamil	Protease inhibitors: Indinavir, Lopinavir/ Ritonavir	Coadministration may increase the plasma concentrations and pharmacologic effects of CCBs.		!!	
	Rifamycins: Rifabutin, Rifampin, Rifapentine	Rifamycins may decrease the bioavailability, plasma levels, and pharmacological effects of CCBs.		!!	-
	SRIs: Fluoxetine, Fluvoxamine	SRIs may increase the serum concentration of calcium channel blockers.		!!	-
Amlodipine S-Amlodipine Felodipine Nicardipine Nisoldipine	Barbiturates: Phenobarbital, Butabarbital, Amobarbital, Secobarbital	Coadministration may have additive effects on blood pressure and orthostasis.		!!	-

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Diltiazem Verapamil	Dofetilide	Significant increase in dofetilide plasma concentrations and/or C_{max} .*			-
	Benzo-diazepines: Midazolam, Triazolam	Diltiazem and verapamil increase peak plasma concentration and prolong the elimination half-life of midazolam.		!!	-
	Erythromycin	Coadministration may increase the plasma concentrations of erythromycin.		!!!	-
	Lovastatin, Simvastatin	Coadministration may significantly increase the plasma concentrations of simvastatin and lovastatin and potentiate the risk of statin-induced myopathy. ^s		!!!	-
Nifedipine	Cyclosporine/ ciclosporine	Cyclosporine may increase serum concentrations of some dihydropyridine CCBs.		!!	-
Nimodipine	Phenobarbital	Coadministration may significantly reduce the plasma concentrations and pharmacologic effects of oral nimodipine.		!!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

- # Simvastatin dosage should not exceed 20 mg daily when used in combination with amlodipine. Fluvastatin, pravastatin, and rosuvastatin are probably safer alternatives in patients receiving amlodipine, since they are not metabolized by CYP450 3A4.
- ^s Coadministration of CCBs and itraconazole may potentiate the risk of ventricular dysfunction, CHF, peripheral and pulmonary edema, particularly in patients with preexisting risk factors, such as patients having history of CHF, cardiac disease such as ischemic and valvular disease, significant pulmonary disease such as COPD, and edematous disorders such as renal failure.
- * Verapamil has shown severe interaction as compared to diltiazem with dofetilide.
- ^s Simvastatin dosage should not exceed 10 mg daily and lovastatin dosage not to exceed 20 mg daily when used in combination with diltiazem/verapamil.

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS					
Diuretics					
Carbonic anhydrase inhibitors: Acetazolamide Methazolamide	Aspirin	Large doses of aspirin with CAIs may result in severe metabolic acidosis and/or salicylate toxicity.		!!!	-
	Quinidine	Coadministration may decrease the urinary excretion of quinidine, resulting in quinidine toxicity.		!!	
Carbonic anhydrase inhibitors: Acetazolamide Methazolamide Loop diuretics: Bumetanide Furosemide Torsemide Thiazide diuretics: Chlorothiazide Chlorthalidone Hydrochlorothiazide Indapamide Metolazone	Amiodarone	Coadministration may increase QT interval.		!!!	-
	Dofetilide	Coadministration may increase the plasma concentrations and pharmacodynamic effects of dofetilide.		!!!	-
	Droperidol	Concurrent administration may increase the QT interval.		!!!	-
	Sulfonylureas: Glimepiride, Glipizide, Glyburide, Tolazamide, Tolbutamide	The efficacy of oral hypoglycemic agents may be decreased by diuretics.		!!	-
Carbonic anhydrase inhibitors: Acetazolamide Methazolamide Thiazide diuretics: Chlorothiazide Chlorthalidone Hydrochlorothiazide Indapamide Metolazone	Calcium salts: Calcium acetate, Calcium carbonate, Calcium citrate, Calcium gluconate, Calcium lactate	Coadministration may result in hypercalcemia.		!!	-
	And/or Vitamin D supplements			!!	-

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Carbonic anhydrase inhibitors: Acetazolamide Methazolamide Thiazide diuretics: Chlorothiazide Chlorthalidone Hydrochlorothiazide Indapamide Metolazone	Corticosteroids: Hydrocortisone, Prednisolone	Coadministration may result in increased risk of hypokalemia.		!!	-
	SNRIs: Desvenlafaxine, Sibutramine, Venlafaxine SSRIs: Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Sertraline	Coadministration may potentiate the risk of hyponatremia, especially in elderly. Diuretics may potentiate the orthostatic effects of SSRIs and SNRIs.	 	!!	-
Loop diuretics: Bumetanide Furosemide Torsemide	Aminoglycoside antibiotics: Amikacin, Gentamicin, Streptomycin (parenteral preparations), Tobramycin, Neomycin (oral)	Coadministration may potentiate the risk of oto- and nephro-toxicity due to their additive or synergistic pharmacologic effects.	 	!!!	
	Skeletal muscle relaxant: Atracurium, Pancuronium, Tubocurarine	Enhanced or decreased effect of nondepolarizing neuromuscular blockers.		!!	-
Loop diuretics: Bumetanide Furosemide Torsemide Potassium sparing diuretics: Amiodarone Spironolactone Triamterene Thiazide diuretics: Chlorothiazide Chlorthalidone Hydrochlorothiazide Indapamide Metolazone	Lithium	Coadministration may cause a rapid increase in serum lithium levels and potentiate the risk of lithium toxicity.	 	!!!	-
	NSAIDs: Ibuprofen, Ketoprofen	Concomitant administration may adversely affect renal function. Hypotensive effect of the diuretics may be reduced. NSAIDs may also increase the risk of hyperkalemia.	 	!!	-

ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Potassium sparing diuretics: Amiodarone Eplerenone Spironolactone Triamterene	Potassium preparations: Potassium chloride, Potassium citrate, Potassium guaiacol-sulfonate	Concurrent administration may result in hyperkalemia.			
Thiazide diuretics: Chlorothiazide Chlorthalidone Hydrochlorothiazide Indapamide Metolazone	Allopurinol	Thiazide diuretics may increase the risk of allopurinol-induced hypersensitivity reactions, especially in patients with renal insufficiency.			-
	Antineoplastic agents: Cyclophosphamide, Fluorouracil, Methotrexate	Antineoplastic-induced bone marrow suppression may be prolonged with concomitant thiazide administration.			
	Diazoxide	Coadministration may result in profound and prolonged hyperglycemia.			
	Skeletal muscle relaxant: Atracurium, Pancuronium, Tubocurarine	Thiazide diuretics may induce hypokalemia and prolong the neuromuscular blocking effects of nondepolarizing muscle relaxants.			
	Warfarin	Concurrent administration may decrease the anticoagulant effect.			

SECTION EXCERPTS AND RECOMMENDATIONS

- Concurrent administration of CAs with aspirin, amiodarone, dofetilide and droperidol should be avoided.
- Loop diuretics interact majorly with amiodarone, dofetilide, droperidol, aminoglycoside antibiotics, lithium and dolasetron.
- Potassium sparing diuretics should not be given with lithium, ACE inhibitors, ARBs and potassium preparations.
- Coadministration of thiazide diuretics with dofetilide is contraindicated. Thiazide diuretics should also be avoided in patients taking amiodarone, droperidol, dolasetron and lithium.

ANTICOAGULANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTICOAGULANTS					
Direct thrombin inhibitors					
Argatroban Bivalirudin Dabigatran Lepirudin	Alteplase	Risk of bleeding complication increases.		!!!	-
	Aspirin	Aspirin may increase the risk of bleeding.		!!	-
	NSAIDs: Ibuprofen, Ketoprofen, Naproxen, Diclofenac, Celecoxib	Anticoagulants may potentiate the risk of GI bleeding complications associated with NSAIDs.		!!	-
Heparin and low molecular weight heparins					
Heparin Low molecular weight heparins: Dalteparin Enoxaparin Tinzaparin	Aspirin	Coadministration may increase the risk of bleeding.		!!	
	Nitroglycerin	Concurrent administration of heparin and intravenous nitroglycerin may lead to a decreased anticoagulant effect.		!!	
	NSAIDs: Ibuprofen, Ketoprofen, Naproxen, Diclofenac, Celecoxib	Coadministration may increase the risk of bleeding.		!!	-
Heparin Low molecular weight heparins: Dalteparin Enoxaparin Tinzaparin	Alteplase	Alteplase may potentiate the risk of bleeding complications associated with the use of a low molecular weight heparin or its derivative. ^Ω		!!!	-
	SSRIs: Fluoxetine, Fluvoxamine	Serotonin reuptake inhibitors on coadministration may potentiate the risk of bleeding.		!!	-

ANTICOAGULANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Low molecular weight heparins: Dalteparin Enoxaparin Tinzaparin	Aspirin	Coadministration may increase the risk of bleeding. ^s		!!!	-
	NSAIDs: Ibuprofen, Ketoprofen, Naproxen, Diclofenac, Celecoxib	NSAIDs may potentiate the risk of bleeding complications associated with LMWH, while NSAIDs dose-related gastrointestinal bleeding may be complicated by anticoagulant therapy. ^s		!!!	-
Warfarin					
Warfarin	Allopurinol	Allopurinol may inhibit warfarin metabolism, thus increasing its anticoagulant effects.		!!	
	Alteplase	Oral anticoagulants may increase the risk of serious bleeding when administered before, during, or after fibrinolytic agents. ^o		!!!	-
	Androgens and anabolic steroids: Danazol, Fluoxymesterone, Methyltestosterone, Testosterone	Androgens and anabolic steroids may potentiate the hypo-prothrombinemic response to warfarin and thus increase the risk of bleeding.		!!!	
	Anti-neoplastic agents: Capecitabine, Fluorouracil	Fluorouracil and its prodrug capecitabine may significantly potentiate the hypo-prothrombinemic effect of warfarin.		!!!	
	Aspirin	Aspirin, even in small doses, may increase the risk of bleeding in patients on oral anticoagulants.		!!!	
	Azole antifungals: Fluconazole, Miconazole, Voriconazole	Coadministration may significantly increase the hypo-prothrombinemic effect of warfarin.		!!!	

ANTICOAGULANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Warfarin	Barbiturates: Amobarbital, Butabarbital, Mephobarbital, Phenobarbital, Secobarbital	Barbiturates reduce the effects of oral anticoagulants.*		!!!	
	Cyclosporine	Increased level or effect of warfarin		!!!	
	Fibric acid derivatives: Clofibrate, Fenofibrate, Gemfibrozil	Fibric acid derivatives may enhance the hypoprothrombinemic effect of warfarin.#		!!!	
	Lovastatin, Rosuvastatin	Rosuvastatin and lovastatin may enhance the hypoprothrombinemic effect of warfarin.		!!	
	Macrolide antibiotics: Clarithromycin, Erythromycin	Coadministration with interacting macrolides may infrequently but significantly increase the hypo- prothrombinemic effect of warfarin.†		!!!	
	Metronidazole	Coadministration may increase the plasma concentrations and hypoprothrombinemic effect of warfarin.		!!!	
	Nalidixic acid	Nalidixic acid potentiates the hypoprothrombinemic effect of warfarin.		!!!	
	NSAIDs: Diclofenac, Diflunisal, Ibuprofen, Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Piroxicam	NSAIDs may potentiate the hypoprothrombinemic effect and bleeding risk associated with oral anticoagulants.		!!!	
	Penicillins: Ampicillin, Penicillin G, Piperacillin, Ticarcillin	Penicillins may occasionally increase the risk of bleeding in patients on oral anticoagulants.		!!	

ANTICOAGULANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Warfarin	Protease inhibitors: Indinavir	Altered plasma concentration/ pharmacological effects of warfarin.		!!	
	Quinolones: Ciprofloxacin, Levofloxacin, Norfloxacin, Ofloxacin	Some quinolone antibiotics potentiate the hypoprothrombinemic effect of warfarin.		!!!	
	Rifamycins: Rifabutin, Rifampin, Rifapentine ^f	Rifampin may decrease the anticoagulant effect of warfarin.		!!!	
	Sulfonamides: Sulfamethizole, Sulfa-methoxazole, Sulfasalazine, Sulfa-methoxazole/ Trimethoprim	Coadministration with a sulfonamide may increase the plasma concentrations and hypoprothrombinemic effects of coumarin anticoagulants.		!!!	
	Tamoxifen	Enhanced hypoprothrombinemic response to warfarin.		!!!	
	Tetracyclines	Increases action of oral anticoagulants.		!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

- Ω Alteplase is contraindicated in patients with acute ischemic stroke who have received heparin within the last 48 hours and have an elevated activated partial thromboplastin time. It is also contraindicated in patients taking oral anticoagulants and having an INR greater than 1.7.
- § In patients receiving neuraxial anesthesia or spinal puncture, the risk of developing an epidural or spinal hematoma during low molecular weight heparin therapy may be increased by the concomitant use of other drugs that affect coagulation, including NSAIDs. The development of epidural and spinal hematoma can lead to long-term or permanent paralysis.
- ¥ Excessive anticoagulation and bleeding may occur if the anticoagulant dose is not reduced after discontinuation of barbiturates.

Therefore, concomitant administration of oral anti-coagulants with alteplase, aspirin and NSAIDs should be avoided. High caution is recommended when warfarin is administered with amiodarone, androgens, anabolic steroids, antineoplastic agents, barbiturates, macrolides (especially clarithromycin and erythromycin), metronidazole and nalidixic acid, quinolones, rifamycins, sulfonamides and tamoxifen.

- # Warfarin dose be reduced by approximately one-third to one-half initially, then gradually adjusted as necessary according to INR monitoring. Frequent prothrombin determinations are recommended till prothrombin level stabilizes.
- ♦ Interaction of warfarin with azithromycin is moderate in severity, thus it can be used as a substitute for clarithromycin and erythromycin.
- £ The interaction between warfarin and rifapentine is reported to be moderate in severity.

ANTIMICROBIAL AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIMICROBIAL AGENTS					
Antibacterial agents					
Amikacin*	Botulinum toxin	Increased risk of neurotoxicity including systemic neuromuscular blockade		!!	-
	Ciclosporine, Tacrolimus	Increased risk of nephrotoxicity		!!!	-
	Cytotoxics	Increased risk with platinum compounds of nephrotoxicity and possibly of ototoxicity		!	-
	Diuretics	Increased risk of ototoxicity with loop diuretics		!!	-
Amoxicillin	Methotrexate	Amoxicillin can reduce the excretion of methotrexate; potential increase in hematologic and gastrointestinal toxicity		!!	-
	Allopurinol	Increased risk of allergic skin reactions		!	-
Capreomycin**	Amino-glycosides, Vancomycin	Increased risk of nephrotoxicity, neurotoxicity and ototoxicity		!!	
Cephalexin	Metformin	May result in accumulation of metformin and could result in fatal lactic acidosis		!!!	-
	Anticoagulants	Combined use of cephalexin and oral anticoagulants may prolong prothrombin time		!!	

ANTIMICROBIAL AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Ciprofloxacin	Analgesics	Increased risk of CNS stimulation and convulsive seizures with NSAIDs		!!	-
	Anticoagulants	Increased prothrombin time		!!	
	Antipsychotics^s	Increased serum concentration of olanzapine and clozapine; QT prolongation, TdP, cardiac arrest		!!	
	Tizanidine^{ss}	Increased serum tizanidine concentration; potentiated hypotensive and sedative effect		!!!	
	Theophylline	Increased plasma levels of theophylline; risk of cardiac arrest, seizure, status epilepticus, and respiratory failure		!!!	-
Clarithromycin	Cisapride, Pimozide, Astemizole, Terfenadine[#]	Elevated levels of these drugs; QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and TdP		!!!	
	Ergotamine	Acute ergot toxicity; vasospasm, and ischemia of the extremities and other tissues including the central nervous system		!!!	-
	Statins^{##}	Increased plasma concentration of statins; increased risk of myopathy, including rhabdomyolysis		!!	
	Antidiabetic agents	Increased risk of hypoglycemia		!	-

ANTIMICROBIAL AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Clarithromycin	Rifabutin	Increased serum levels of rifabutin; increased risk of uveitis and neutropenia		!!	-
Clindamycin	Erythromycin	Antagonism demonstrated in vitro; the two drugs should not be administered concurrently		!!	-
	Muscle relaxants	Enhanced neuromuscular blockade		!	-
	Oral typhoid vaccine®	Oral typhoid vaccine is inactivated by coadministered clindamycin		!!	
Doxycycline	Warfarin	Prolonged prothrombin time		!!	
	Ciclosporine	Increased plasma concentration of ciclosporine		!!	-
	Methoxyflurane	May result in fatal renal toxicity		!!!	-
	Retinoids	Increased risk of benign intracranial hypertension; avoid concomitant use		!!!	
Isoniazid (INH)	Carbamazepine, E ethosuximide, Primidone, Phenytoin, Diazepam, Triazolam, Chlorzoxazone, Theophylline, Disulfiram,	INH inhibits the hepatic metabolism of these drugs; may lead to increased toxicity		!!	-
	Rifampicin	Concurrent administration may induce abnormalities in liver function		!!	-

ANTIMICROBIAL AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Metronidazole	Warfarin	Enhanced anticoagulant effect		!!	
	Phenobarbital, Phenytoin	Increased metabolism of metronidazole		!!	-
	5-fluorouracil	Metronidazole reduces the clearance of 5-Fluorouracil and can therefore result in increased toxicity		!	-
	Busulfan	Increased serum levels of busulfan; may lead to severe busulfan toxicity		!!!	-
Rifampicin/ Rifampin	Antacids	Concomitant antacid administration may reduce the absorption of rifampicin ^y		!!	-
	Anti-arrhythmics: Disopyramide, Mexiletine, Propafenone	Rifampicin accelerates metabolism of anti-arrhythmics		!!	-
	Antibacterials: Chloramphenicol, Clarithromycin, Dapsone, Trimethoprim	Reduces the concentration of antibacterials		!	-
	Antidiabetics	Reduced antidiabetic effect of sulphonylureas, meglitinides and thiazolidinediones		!!!	-
	Anti-epileptics	Reduced concentration of phenytoin and lamotrigine; decreased anticonvulsant efficacy		!!	-
	Antipsychotics	Reduced concentration of haloperidol, aripiprazole and clozapine		!	-
	Saquinavir, Ritonavir	Increased potential for hepatotoxicity		!!!	-
	Cyclosporine, Tacrolimus	Markedly reduced levels of cyclosporine; increased risk of transplant rejection		!!!	-

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Streptomycin	Cyclosporine, Tacrolimus	Increased risk of nephrotoxicity		!!!	-
	Cytotoxics	Increased risk of nephrotoxicity and ototoxicity with platinum compounds		!!	-
	Loop diuretics	Increased risk of ototoxicity		!!	-
Trimethoprim	Antiarrhythmics	Increased risk of ventricular arrhythmias with amiodarone; avoid concomitant use		!!!	-
	Antimalarials	Increased risk of hematologic toxicity		!!	
	Cytotoxics	Increased risk of hematological toxicity with azathioprine and mercaptopurine		!!	
Vancomycin	Anesthetic agents	Erythema, histamine-like flushing and anaphylactoid reactions		!!!	
	Cyclosporine, Tacrolimus	Increased risk of nephrotoxicity		!!!	-
	Diuretics	Increased risk of ototoxicity with loop diuretics		!!	

SECTION EXCERPTS AND RECOMMENDATIONS

- * Amikacin affects auditory function to a greater extent than gentamicin
- ** Frequent monitoring of serum potassium concentrations is recommended during capreomycin therapy for the risk of hypokalemia
- ** Simultaneous administration of other drugs which have ototoxic or nephrotoxic potential (e.g. polymyxin, colistin sulphate, amikacin, gentamicin, tobramycin, vancomycin, kanamycin and neomycin) should be undertaken only with great caution
- \$ Ciprofloxacin, similar to other fluoroquinolones should be used with caution in patients receiving drugs known to prolong QT interval (e.g. Class IA or III antiarrhythmics, tricyclic antidepressants, macrolides, and antipsychotics)
- \$\$ Tizanidine must not be administered along with ciprofloxacin
- # Coadministration of these drugs with clarithromycin is contraindicated
- ## Concomitant use of clarithromycin with lovastatin or simvastatin is contraindicated. In cases where the coadministration of clarithromycin with statins cannot be avoided, it is recommended to prescribe the lowest registered dose of the statin
- @ Clindamycin should be avoided for 3 days before and after oral typhoid vaccination
- ¥ Daily doses of rifampicin should be administered at least 1 hour before the ingestion of antacids

ANTIMICROBIAL AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIMICROBIAL AGENTS					
Antifungal agents					
Amphotericin-B	Cyclosporine, Aminoglycosides, Polymyxins, Tacrolimus, Pentamidine	Increased risk of drug-induced nephrotoxicity		!!!	
	Corticosteroids, Corticotropin, (ACTH), Diuretics	Increased risk of hypokalemia		!!	
	Cardiac glycosides	Increased toxicity if hypokalemia occurs		!!	
	Flucytosine	Impaired renal excretion of flucytosine; reduction in renal functions; may increase bone marrow toxicity	 	!!	-
	Antineoplastic agents	Increased potential for renal toxicity, bronchospasm and hypotension	 	!!	-
Fluconazole Itraconazole Voriconazole	Anticoagulants	Potentiates effect of coumarin-type anticoagulants		!!	
	Antidiabetics, Nateglinide, Repaglinide	Enhanced hypoglycemic effect		!	-
	Anti-epileptics	Increased levels of phenytoin and carbamazepine		!!	-
	Calcium channel blockers*	Increased risk of CHF		!!!	
	Diuretics	Increased levels of eplerenone; risk of developing hyperkalemia and hypotension- avoid concomitant use. Hydrochlorothiazide increases concentration of fluconazole	 	!!	-

ANTIMICROBIAL AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Fluconazole Itraconazole Voriconazole	Ergot alkaloids	Increased risk of ergot-related side effects (e.g., vasospasm leading to cerebral ischemia, peripheral ischemia, and/or other serious effects); avoid concomitant use		!!!	
	Statins	Increased risk of myopathy with atorvastatin or simvastatin		!!	
Fluconazole Voriconazole	Cyclosporine, Tacrolimus	Increased levels of cyclosporine and tacrolimus; risk of nephrotoxicity, QTc prolongation, TdP		!!	
Voriconazole	Benzodiazepines, Midazolam, Estazolam, Flurazepam	Reduced metabolism of benzodiazepines; risk of BZD-toxicity		!!	-
	Antilulcer drugs	Increased levels of omeprazole; reduce omeprazole dose by one-half		!	-

Antiviral agents

Acyclovir Valaciclovir	Cyclosporine, Tacrolimus	Increased risk of nephrotoxicity		!!!	-
	Mycophenolate	Higher concentrations of both acyclovir and mycophenolic acid on concomitant administration		!!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

- * CCBs can have negative inotropic effects which may be additive to those of itraconazole. Caution should be exercised when co-administering itraconazole with calcium channel blockers due to an increased risk of CHF

ANTINEOPLASTIC AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTINEOPLASTIC AGENTS					
Azathioprine	Allopurinol*	Increased azathioprine activity and toxicity (e.g., bone marrow suppression, leukopenia, pancytopenia)		!!!	
	Antibacterials	Increased risk of hematological toxicity with cotrimoxazole		!!!	
	Anticoagulants: Heparin, Warfarin	Reduced anticoagulant effects		!!	
	Captopril, Enalapril, Fosinopril	Pharmacodynamic synergism; risk of anemia and leukopenia		!!!	
Methotrexate	Analgesics**	Increased risk of hematologic and gastrointestinal toxicity with NSAIDs		!!!	
	Antibacterials: Neomycin, Cotrimoxazole, Trimethoprim, Penicillins, Doxycycline, Tetracycline	Reduced excretion of methotrexate; increased antifolate effect; increased risk of hematological toxicity		!!!	
	Antimalarials	Antifolate effect enhanced by pyrimethamine; risk of bone marrow suppression		!!!	
Methotrexate	Corticosteroids	Increased risk of hematological toxicity		!!!	
	Cisplatin	Increased systemic and renal toxicity of methotrexate		!!!	
	Probenecid	Reduced excretion of methotrexate; increased risk of uric acid neuropathy		!!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

* When possible, this drug combination should be avoided. If avoidance of coadministration is not possible, reduce azathioprine dose by 50-75% of the original dose

** NSAIDs should not be administered prior to, concomitantly, or following intermediate or high doses of methotrexate. Caution should be used when NSAIDs are administered concurrently with lower doses of methotrexate

ANTIPLATELET AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ANTIPLATELET AGENTS					
Aspirin	Antacids: Aluminum carbonate, Aluminum hydroxide, Calcium carbonate, Magnesium carbonate	Chronic administration of antacids may reduce serum salicylate concentrations in patients receiving large doses of aspirin.		!!	-
	Ibuprofen	The antiplatelet and cardioprotective effect of low-dose aspirin may be antagonized by ibuprofen. [#]		!!!	-
	Methotrexate	Aspirin may increase the pharmacologic effect and toxicity of methotrexate.		!!!	-
	SRIs: Fenfluramine, Fluoxetine TCA: Clomipramine	SRIs or clomipramine may potentiate the risk of bleeding in patients taking aspirin.		!!	-
	Urinary alkalinizers: Potassium citrate, Sodium bicarbonate, Sodium citrate	Urinary alkalinizers can reduce serum salicylate concentrations in patients taking large doses of aspirin.		!!	
	Valproic acid	Aspirin may increase the serum concentration of valproic acid. Large doses of aspirin may cause valproate toxicity and hepatotoxicity.		!!	-
	Zafirlukast	Aspirin may increase the plasma concentrations of zafirlukast.		!!	-
Glycoprotein IIb/IIIa inhibitors: Abciximab Eptifibatide Tirofiban	Fibrinolytic agents: Alteplase, Reteplase, Tenecteplase, Streptokinase	Increased frequency of major bleeding complications, including intracranial hemorrhage, retroperitoneal bleeding, spontaneous GI and GU bleeding.		!!!	-

ANTIPLATELET AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Glycoprotein IIb/IIIa inhibitors: Abciximab Eptifibatide Tirofiban	Heparin, Low molecular weight heparin, Warfarin	Coadministration increases risk of bleeding complications.		!!!	-
	NSAIDs: Ibuprofen, Ketoprofen	Risk of bleeding increases on coadministration.		!!	-
Cilostazol	Macrolide antibiotics: Clarithromycin, Erythromycin	Coadministration may increase the plasma concentrations of cilostazol and or its pharmacologically active metabolites. ⁵		!!	
	SRIs: Citalopram, Escitalopram	SRIs may potentiate the risk of bleeding in patients.		!!	-
Cilostazol Clopidogrel Ticagrelor Ticlopidine	NSAIDs: Ibuprofen, Ketoprofen, Naproxen	Coadministration may increase the risk of bleeding.		!!	-
Clopidogrel	Atorvastatin	Concomitant administration may reduce the metabolic activation of clopidogrel and its antiplatelet effects. ⁶		!!	-
	Azole antifungals: Fluconazole, Ketoconazole	Coadministration may reduce the efficacy of clopidogrel.		!!!	-
	Bupropion	Clopidogrel may increase the plasma concentrations of bupropion.		!!	
Clopidogrel	Macrolide antibiotics: Clarithromycin, Erythromycin	Some macrolide antibiotics may reduce the metabolic activation of clopidogrel and its antiplatelet effects.		!!	-
	PPIs: Omeprazole, Rabeprazole	PPI may reduce the cardioprotective effects of clopidogrel. ⁵		!!!	-
Clopidogrel Prasugrel	SRIs: Venlafaxine, Fluoxetine, Fluvoxamine	SRIs may potentiate the risk of bleeding when used in patients treated with prasugrel and clopidogrel.		-	-
	Vitamin E	Vitamin E may potentiate the effects of platelet inhibitors. ⁷		!!	-

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Dipyridamole	Low molecular weight heparins: Dalteparin, Enoxaparin, Tinzaparin	Dipyridamole may potentiate the risk of bleeding complications associated with LMWHs.		!!!	-
	Adenosine	Dipyridamole potentiates the effects of adenosine.		!!	
Prasugrel	NSAIDs: Ibuprofen, Ketoprofen, Naproxen	The risk of bleeding increases. ^e		!!!	-
Ticagrelor	Carbamazepine, Phenytoin, Fosphenytoin	Coadministration may significantly decrease the plasma concentrations of ticagrelor.		!!!	-
	Clarithromycin	Coadministration may significantly increase the plasma concentrations of ticagrelor.		!!!	-
	Dexamethasone	Coadministration may significantly decrease the plasma concentrations of ticagrelor.		!!!	-
Ticlopidine	Cimetidine	Cimetidine may reduce the clearance of ticlopidine by up to 50%.		!!	-
	Theophylline	Ticlopidine interferes with theophylline metabolism, may cause theophylline toxicity.		!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

- # For patients requiring routine NSAID therapy with concomitant low-dose aspirin, diclofenac may be considered as a suitable alternative.
- \$ Fifty percent dosage reduction of cilostazol (i.e., 50 mg twice a day) has been recommended in patients receiving erythromycin.
- ^a Pravastatin, fluvastatin, and rosuvastatin are not metabolized by CYP450 3A4 and are theoretically not expected to interact with clopidogrel.
- ^s PPIs should only be considered in high-risk patients such as those receiving dual antiplatelet therapy, those with a history of gastrointestinal bleeding or ulcers, and those receiving concomitant anticoagulant therapy.
- ^v If vitamin E supplementation dosages greater than 400 units/day are initiated in patients stabilized on anticoagulant or antiplatelet therapy, hematological complications may occur and the patient should be monitored closely.
- ^e Prasugrel may be used with aspirin, heparin, or glycoprotein IIb/IIIa inhibitors.

DRUGS IN HYPERKALEMIA

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
DRUGS IN HYPERKALEMIA					
Calcium gluconate	Digitalis	Potentially life-threatening digitalis-induced cardiac arrhythmias		!!!	-
	Ceftriaxone®	Concurrent use potentiates risk of fatal particulate precipitation in lungs and kidneys		!!!	-
	Amlodipine	Calcium gluconate antagonizes the effect of amlodipine		!!	-
Salbutamol	Diuretics, Theophylline, Corticosteroids	Increased risk of hypokalemia with high doses of salbutamol		!!	
	Digitalis	Risk of hypokalemia, which could lead to the development of digitalis toxicity		!!	-
	Atomoxetine	Increased heart rate and blood pressure		!!!	
	Sulfamethoxazole	QT prolongation resulting in ventricular tachycardia and TdP		!!	
Sodium bicarbonate*	Acetazolamide	Risk of development of renal calculi		!!	
Sodium polystyrene sulfonate	Meloxicam, Sorbitol\$	Increased risk of upper gastrointestinal injury and colonic necrosis with coadministered meloxicam oral suspension		!!!	

SECTION EXCERPTS AND RECOMMENDATIONS

- ® Ceftriaxone should not be coadministered with calcium gluconate
- * In order to minimise the risk of interactions affecting pharmacokinetics of coadministered products, drug administration should be separated by approximately 2 to 3 hours
- \$ Coadministration of sorbitol and sodium polystyrene sulfonate is not recommended due to cases of intestinal necrosis and other serious gastrointestinal adverse reactions, which may be fatal

DRUGS IN HYPERPHOSPHATEMIA

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
DRUGS IN HYPERPHOSPHATEMIA					
Calcium acetate Calcium carbonate	Ceftriaxone	Concomitant use of calcium acetate (IV) and ceftriaxone potentiates risk of fatal particulate precipitation in lungs and kidneys		!!!	
	Thiazide diuretics	Concomitant administration of thiazides results in an increased risk of hypercalcemia		!!	-
	Tetracyclines, Doxycycline, Quinolones, Bisphosphonates, Fluorides Anticholinergics	Calcium salts May reduce the absorption of these drugs*		!!	-
	Systemic corticosteroids	Reduced calcium absorption in patients receiving systemic corticosteroid therapy		!	-
Ferric citrate*	Ciprofloxacin, Gemifloxacin, Levofloxacin, Moxifloxacin, Ofloxacin,	Decreased bioavailability of these drugs		!	-
Magnesium hydroxide	ACE inhibitors, Antibacterials, Antifungals, Antivirals, Antihistamines, Bisphosphonates, Corticosteroids, Digoxin, Dipyridamole, Iron preparations, Chloroquine, Penicillamine	Magnesium salts reduce the absorption of various other coadministered drugs		!	-

DRUGS IN HYPERPHOSPHATEMIA

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Sevelamer carbonate	Digoxin, Warfarin	No effect on bioavailability	-	-	-
Sevelamer hydrochloride	Ciprofloxacin ^s	Bioavailability of ciprofloxacin is reduced by almost 50% when coadministered with sevelamer carbonate/sevelamer hydrochloride	M	-	-
	Cyclosporine, Mycophenolate mofetil, Tacrolimus [®]	Reduces the levels of cyclosporine, mycophenolate mofetil and tacrolimus	M	-	-

SECTION EXCERPTS AND RECOMMENDATIONS

- * It is recommended that there should be an interval of 1-2 hours between the intake of calcium salts and tetracyclines
- # The oral absorption of fluoroquinolone antibiotics is significantly reduced by orally administered ferric citrate
Ciprofloxacin should be administered either 2 hours before or 6 hours after the administration of iron containing products
Moxifloxacin should be administered at least 4 hours before or 8 hours after iron administration
Gemifloxacin should be administered at least 3 hours before or 2 hours after iron administration
Ofloxacin and levofloxacin administration is recommended either 2 hours before or 2 hours after iron administration
- \$ Sevelamer hydrochloride/sevelamer carbonate should not be coadministered with ciprofloxacin.
- @ Serum concentrations of cyclosporine, mycophenolate mofetil and tacrolimus should be closely monitored during the use of any of these agents concurrently with sevelamer hydrochloride/sevelamer carbonate.
When the reduced drug absorption of an oral medication coadministered with sevelamer may have a clinically significant effect on its safety or efficacy, drug administration should be separated by at least one hour before or three hours after sevelamer administration.

ERYTHROPOIETIN STIMULATING AGENTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
ERYTHROPOIETIN STIMULATING AGENTS					
Darbepoetin alfa	Cyclosporine, Tacrolimus	These drugs are highly bound to red blood cells, hence, there is a potential risk of drug interaction as hemoglobin concentration rises		-	-
	Androgens: Danazol, Nandrolone, Oxandrolone,	Androgens stimulate erythropoiesis. Concurrent administration of androgens can increase the patient's response to darbepoetin alfa, reducing the amount required to treat anemia		-	-
Darbepoetin alfa Epoetin alpha	Lenalidomide	Increased risk of thrombosis in patients with multiple myeloma who are also receiving dexamethasone		!!!	
Darbepoetin alfa Epoetin alpha Epoetin beta	ACE inhibitors, Angiotensin-II antagonists	Increased risk of hyperkalemia		!!!	

SECTION EXCERPTS AND RECOMMENDATIONS

- Treatment with ESA may necessitate concomitant iron therapy (200-300 mg elemental oral iron)
- For serum transferrin saturation of less than 20%, IV Iron is mandatory when ESA is used
- Heparin requirement may be increased during HD

IMMUNOSUPPRESSANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
IMMUNOSUPPRESSANTS					
Antithymocyte globulin equine (eATG) Antithymocyte globulin rabbit (rATG)	Cyclosporine, Tacrolimus, Mycophenolate mofetil	Risk of over- immunosuppression with a risk of lymphoproliferation	 	-	-
	Live attenuated vaccines ^s	Risk of systemic infection due to the vaccine; may potentially be fatal	 	!!!	-
Basiliximab	Cyclosporine Tacrolimus	May alter the dose requirements of cyclosporine and tacrolimus	 	!!	-
	Analgesics	Increased risk of bleeding with NSAIDs such as diclofenac; monitor closely for bleeding		!!	
Cyclo- phosphamide	Antipsychotics	Increased risk of agranulocytosis; avoid concomitant use with clozapine		!!!	
	Cytotoxics	Increased risk of cardiotoxicity with high-dose cyclophosphamide and pentostatin; avoid concomitant use		!!!	-
Cyclosporine	ACE inhibitors, Angiotensin-II antagonists, Potassium- sparing diuretics, Potassium salts	Increased risk of hyperkalemia		!!!	
Cyclosporine	Aciclovir Aminoglyco- sides Amphotericin Colchicine Disopyramide Foscarnet Melphalan NSAIDs Polymyxins Quinolones Sulfonamides Trimethoprim Vancomycin	Increased risk of nephrotoxicity		!!!	-

IMMUNOSUPPRESSANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Cyclosporine	Antibacterials	Increased risk of myopathy with daptomycin; avoid concomitant use		!!	-
	Calcium channel blockers	Increased concentration of nifedipine; increased toxicity		!!	-
	Cardiac glycosides	Increased digoxin concentration and toxicity		!!!	-
	Colchicine	Risk of myopathy or rhabdomyolysis; also increased blood-cyclosporine concentrations and nephrotoxicity		!!!	-
	Cytotoxics	Increased risk of neurotoxicity and seizures		!!!	-
	Statins*	Increased risk of myopathy with statins		!!!	-
	Fenofibrate	Increased risk of nephrotoxicity		!!!	-
Everolimus	Antifungals: Fluconazole Ketoconazole Itraconazole	Increased everolimus blood levels	 	-	-
	Antibacterials	Erythromycin, clarithromycin increase everolimus levels. Rifampicin reduces the bioavailability and increases the clearance of everolimus	 	-	-
Everolimus	Anti-convulsants: Carbamazepine, Phenobarbital, Phenytoin	Decreased everolimus blood levels	 	-	-
Leflunomide	Hepatotoxic or Hemotoxic drugs	Increased risk of toxicity	 	-	-
	Colestyramine	Rapid and significant decrease in plasma concentration of leflunomide		-	-

IMMUNOSUPPRESSANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Methyl prednisolone	Antibacterials	Rifampicin accelerates the metabolism of methylprednisolone, whereas erythromycin and clarithromycin inhibit it	M	-	-
	Anti-epileptics	Metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone	M	!!	-
Methyl prednisolone	Antifungals	Increased risk of hypokalemia with amphotericin; avoid concomitant use		!!	
	Cytotoxics	Increased risk of hematological toxicity with methotrexate		!!!	
	Diuretics	Enhanced hypokalemic effects of acetazolamide, loop diuretics and thiazide diuretics		!!	
Mycophenolate mofetil Mycophenolate sodium	Antipsychotics	Increased risk of agranulocytosis with clozapine		!!!	
	Antivirals	Increased concentrations of both mycophenolate acid and acyclovir or ganciclovir when the two are coadministered	M	!!	
	Antacids*	Decreased bioavailability of mycophenolate in presence of magnesium and aluminum salts	M	!!	

IMMUNOSUPPRESSANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Mycophenolate mofetil Mycophenolate sodium	Colestyramine	40% decrease in oral bioavailability of mycophenolate	M	!!	
	Sevelamer	Reduced levels of mycophenolate	M	!!	
Sirolimus	Antibacterials: Clarithromycin, Telithromycin, Erythromycin	Sirolimus concentration increased by clarithromycin and telithromycin. Coadministration of erythromycin and sirolimus increases systemic exposure of both drugs. Avoid coadministration.	M	!!	
	Antifungals: Itraconazole, Ketoconazole, Miconazole, Posaconazole, Voriconazole	Increased concentration of sirolimus	M	!!	
	Antivirals	Concentration increased by atazanavir and lopinavir	M	!!	
	Calcium channel blockers	Concentration increased by diltiazem. Coadministration of CCB and verapamil increases concentration of both drugs	M	!!	
	Cyclosporine	Increased absorption of sirolimus; administer sirolimus 4 hours after cyclosporine. Long-term coadministration may cause deterioration in renal function	M 	!!	

IMMUNOSUPPRESSANTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
Sirolimus	Mycophenolate	Coadministration of mycophenolate and sirolimus increases plasma levels of both sirolimus and mycophenolic acid		!!	
Tacrolimus**	Atazanavir, Basiliximab, Bromocriptine, Chloramphenicol, Cimetidine, Dapsone, Diltiazem, Felodipine, Lansoprazole, Nicardipine, Nifedipine, Omeprazole, Pantoprazole, Quinidine, Ritonavir, Telithromycin, Theophylline, Verapamil, Voriconazole	Increased levels of tacrolimus; risk of nephrotoxicity and QT prolongation	 	!!!	
	Carbamazepine, Caspofungin, Ergotamine, Isoniazid, Phenobarbital, Phenytoin, Rifampicin,	Decreased levels of tacrolimus; associated toxicity		!!	
	Aciclovir, Amino-glycosides, Amphotericin, Cotrimoxazole, Ganciclovir, NSAIDs, Vancomycin	Increased nephrotoxicity		!!!	-
	Potassium sparing diuretics, Potassium salts	Increased risk of hyperkalemia		!!!	

SECTION EXCERPTS AND RECOMMENDATIONS

- \$ The risk of systemic infection is increased in patients who are already immunocompromised due to the underlying disease, such as aplastic anemia.
Live vaccines: patients taking immunosuppressive drugs such as cyclosporine, methotrexate, cyclophosphamide, leflunomide, and cytokine inhibitors should not be administered live vaccines during or for up to 6 months after treatment has stopped, as they can cause severe or potentially fatal infections.
- # Statin therapy should be temporarily withheld or discontinued in patients with signs and symptoms of myopathy
- * Antacids and mycophenolate should be administered at separate times; do not give simultaneously
- ** Tacrolimus and cyclosporine should not be prescribed concomitantly. Caution should be taken when converting from cyclosporine to tacrolimus

IRON SALTS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
IRON SALTS					
Ferrous fumarate Ferrous gluconate Ferrous sulfate	Antacids: Calcium, carbonate, Magnesium, hydroxide, Aluminum, hydroxide	The bioavailability of orally administered iron may be reduced by concomitant administration of antacids. [#]		!!	-
	Methyldopa, Levodopa, Carbidopa	Iron salts may decrease the oral bioavailability and pharmacologic effects of methyldopa.		!!	-
	Dimercaprol	Dimercaprol can form nephrotoxic chelates with iron salts.*		!!!	-
Ferrous fumarate Ferrous gluconate Ferrous sulfate Iron dextran	Vitamin E	Vitamin E may diminish the therapeutic response to iron therapy in patients with iron deficiency anemia.		!!	-
Iron dextran	ACE inhibitors: Benazepril, Captopril, Enalapril, Perindopril, Quinapril, Ramipril	Increased risk of systemic adverse effects. Anaphylaxis may occur on parenteral administration.		!!!	
	Chloramphenicol	Chloramphenicol can cause bone marrow depression and inhibit RBC maturation, which may interfere with the therapeutic effects of iron preparation in the treatment of anemia. [§]		!!	-

SECTION EXCERPTS AND RECOMMENDATIONS

- # Oral iron preparations should be administered at least two hours apart from antacids or other agents with acid-neutralizing effects.
- * Iron preparations should not be administered during chelation therapy with dimercaprol and also before 24 hours of the last dose of dimercaprol.
- § Chloramphenicol should not be given in patients with preexisting anemia due to the drug's depressive effect on bone marrow and reticulocytes.

URINARY ALKALISERS

Category/ Drugs	Interacting Category/Drugs	Effects of Interaction	Consequences/ Signs/ Symptoms	Level of Effects	Onset
URINARY ALKALISERS					
Potassium citrate	Methenamine*	Potassium citrate inhibits the activation of methenamine		!!	-
	Aluminum hydroxide	Risk of metabolic alkalosis; potentially fatal		!!!	
	Potassium sparing diuretics	Increased risk of hyperkalemia, especially in elderly patients or patients with impaired renal function		!!!	
Sodium citrate/ Citric acid	Aluminum hydroxide	Increases aluminum absorption, potentially fatal		!!!	

SECTION EXCERPTS AND RECOMMENDATIONS

- * Urinary alkalinizers, such as potassium or sodium citrate and those antacids that can raise the urinary pH above 5.5 should not be used during treatment with methenamine because acidic urine is required for methenamine therapeutic efficacy

INDEX OF INTERACTING DRUGS/CLASS

SYMBOLS

5-fluorouracil 30

A

Abciximab 35, 36
Acebutolol 15, 16, 17
ACE inhibitors 39, 41, 42, 48
Acetaminophen 13
Acetazolamide 20, 21, 38
Aciclovir 42, 46
Acyclovir 33
Adenosine 37
Aliskiren 11, 13
Allopurinol 11, 22, 24, 27, 34
alteplase 23, 24, 35
Aluminum carbonate 35
Aluminum hydroxide 11, 35, 48, 49
Amikacin 21, 27
Amiloride 11, 13
Aminoglycoside antibiotics 21
Aminoglycosides 27, 32, 42, 46
Aminophylline 15
Amiodarone 16, 20, 21, 22
Amlodipine 18, 38
Amobarbital 18, 25
Amoxicillin 27
Amphotericin 42, 46
Amphotericin-B 32
Ampicillin 25
Analgesics 28, 34, 42
Androgens 41
Androgens and anabolic steroids 24
Anesthetic agents 31
Angiotensin converting enzyme inhibitors 11
Angiotensin-II antagonists 41, 42
Angiotensin receptor blockers 13
Antacids 11, 30, 35, 44, 48
Antiarrhythmics 30, 31
Antibacterial agents 27
Antibacterials 30, 34, 39, 43, 44, 45

Anticholinergics 39
Anticoagulants 27, 28, 32, 34
Anticonvulsants 43
Antidiabetic agents 28
Antidiabetics 30, 32
Anti-epileptics 30, 32, 44
Antifungal agents 32
Antifungals 39, 43, 44, 45
Antihistamines 39
Antimalarials 31, 34
Antimicrobial Agents 27, 32
Antineoplastic agents 22, 24, 32
Antipsychotics 28, 30, 42, 44
Antithymocyte globulin equine (eATG) 42
Antithymocyte globulin rabbit (rATG) 42
Antulcer drugs 33
Antivirals 39, 44, 45
Argatroban 23
Aripiprazole 13
Aspirin 13, 20, 23, 24, 35
Astemizole 28
Atazanavir 46
Atenolol 15, 16, 17
Atomoxetine 38
Atorvastatin 36
Atracurium 21, 22
Azathioprine 34
Azole antifungal 18
Azole antifungal agents 14
Azole antifungals 24, 36

B

Barbiturates 18, 25
Basiliximab 42, 46
Benazepril 12, 48
Benzodiazepines 19, 33
Beta-blockers 12, 15
Betaxolol 15, 16, 17
Bisoprolol 15, 16, 17
Bisphosphonates 39

Bivalirudin 23
Botulinum toxin 27
Bromocriptine 46
Bumetanide 20, 21
Bupropion 36
Busulfan 30
Butabarbital 18, 25

C

Calcium acetate 20, 39
Calcium carbonate 20, 35, 39, 48
Calcium channel blocker 15
Calcium channel blockers 12, 18, 20, 32, 43, 45
Calcium citrate 20
Calcium gluconate 20, 38
Calcium lactate 20
Calcium salts 20
Candesartan 13, 14
Capecitabine 24
Capreomycin 27
Captopril 11, 12, 34, 48
Carbamazepine 29, 37, 43, 46
Carbidopa 48
Carbonic anhydrase inhibitors 20, 21
Cardiac glycosides 32, 43
Carvedilol 15, 16, 17
Caspofungin 46
Ceftriaxone 38, 39
Celecoxib 11, 23, 24
Cephalexin 27
Chloramphenicol 30, 46, 48
Chloroquine 39
Chlorothiazide 20, 21, 22
Chlorpromazine 11, 17
Chlorthalidone 20, 21, 22
Chlorzoxazone 29
Ciclosporine 19, 27, 29
Cilostazol 36
Cimetidine 15, 37, 46
Ciprofloxacin 26, 28, 39, 40
Cisapride 28
Cisplatin 34
Citalopram 21, 36

Clarithromycin 25, 28, 29, 30, 36, 37, 45
Clindamycin 29
Clofibrate 25
Clomipramine 35
Clopidogrel 36
Colchicine 42, 43
Colestyramine 43, 45
Corticosteroids 13, 21, 32, 34, 38, 39
Corticotropin (ACTH) 32
Cortisone 13
Cotrimoxazole 34, 46
Cyclophosphamide 22, 42
Cyclosporine 19, 25, 30, 31, 32, 33, 40, 41, 42, 43, 45
Cytotoxics 27, 31, 42, 43, 44

D

Dabigatran 23
Dalteparin 23, 24, 37
Danazol 24, 41
Dapsone 30, 46
Darbepoetin alfa 41
Desvenlafaxine 21
Dexamethasone 37
Diazepam 29
Diazoxide 22
Diclofenac 11, 23, 24, 25
Diflunisal 25
Digitalis 38
Digoxin 14, 15, 39, 40
Diltiazem 15, 18, 19, 46
Dimercaprol 48
Diphenhydramine 15
Dipyridamole 37, 39
Direct thrombin inhibitors 23
Disopyramide 15, 30, 42
Disulfiram 29
Diuretics 27, 31, 32, 38, 44
Dobutamine 16
Dofetilide 19, 20
Dolasetron 18
Dopamine 16
Doxycycline 34, 39
Droperidol 20

E

- Enalapril 11, 12, 34, 48
- Enoxaparin 23, 24, 37
- Epinephrine 16
- Eplerenone 22
- Epoetin alpha 41
- Epoetin beta 41
- Eprosartan 13, 14
- Eptifibatide 35, 36
- Ergot alkaloids 33
- Ergotamine 28, 46
- Erythromycin 19, 25, 29, 36, 45
- Escitalopram 21, 36
- Esmolol 15, 16, 17
- Estazolam 33
- Ethosuximide 29
- Everolimus 43

F

- Felodipine 18, 46
- Fenfluramine 35
- Fenofibrate 25, 43
- Ferric citrate 39
- Ferrous fumarate 48
- Ferrous gluconate 48
- Ferrous sulfate 48
- Fibrin acid derivatives 25
- Fibrinolytics 35
- Flecainide 17
- Fluconazole 14, 24, 32, 33, 36, 43
- Flucytosine 32
- Fluorides 39
- Fluorouracil 22, 24
- Fluoxetine 18, 21, 23, 35, 36
- Fluoxymesterone 24
- Fluphenazine 11
- Flurazepam 33
- Flurbiprofen 11
- Fluvoxamine 18, 21, 23, 36
- Foscarnet 42
- Fosinopril 11, 12, 34
- Fosphenytoin 14, 37
- Furosemide 20, 21

G

- Ganciclovir 46
- Gemfibrozil 25
- Gemifloxacin 39
- Gentamicin 21
- Glimepiride 20
- Glipizide 20
- Glyburide 20
- Glycoprotein IIb/IIIa inhibitors 35, 36
- Guanethidine 16

H

- H2 antagonist 15
- Hemotoxic drugs 43
- Heparin 23, 34, 36
- Hepatotoxic or hemotoxic drugs 43
- Hydantoins 14
- Hydrochlorothiazide 12, 20, 21, 22
- Hydrocortisone 13, 21

I

- Ibuprofen 13, 16, 21, 23, 24, 25, 35, 36, 37
- Indapamide 20, 21, 22
- Indinavir 18, 26
- Indomethacin 11, 13, 16, 25
- Irbesartan 13, 14
- Iron dextran 48
- Iron preparations 39
- Isoniazid 46
- Isoniazid (INH) 29
- Itraconazole 18, 32, 33, 43, 45

K

- Ketoconazole 14, 36, 43
- Ketoprofen 13, 21, 23, 24, 25, 36, 37
- Ketoconazole 45

L

- Labetalol 15, 16, 17
- Lansoprazole 46
- Leflunomide 43
- Lenalidomide 41
- Lepirudin 23
- Levofloxacin 26, 39

Lidocaine 15
Lisinopril 11, 12
Lithium 11, 13, 21
Live attenuated vaccines 42
Loop diuretics 20, 21, 31
Lopinavir 18
Losartan 13, 14
Lovastatin 19, 25
Low molecular weight heparin 36
Low molecular weight heparins 23, 24, 37

M

Macrolide antibiotics 25, 36
Magnesium carbonate 11, 35
Magnesium hydroxide 39, 48
MAO inhibitors 16
Mefenamic acid 11, 25
Meloxicam 38
Melphalan 42
Mephobarbital 25
Metaraminol 16
Metformin 27
Methazolamide 20, 21
Methenamine 49
Methotrexate 22, 27, 34, 35
Methotrimeprazine 11
Methoxyflurane 29
Methyldopa 48
Methyl prednisolone 44
Methyltestosterone 24
Metolazone 20, 21, 22
Metoprolol 15, 16, 17
Metronidazole 25, 30
Mexiletine 30
Miconazole 24, 45
Midazolam 19, 33
Moxifloxacin 39
Muscle relaxants 29
Mycophenolate 33, 46
Mycophenolate mofetil 40, 42, 44, 45
Mycophenolate sodium 44, 45

N

Nadolol 15, 16, 17
Nalidixic acid 25

Nandrolone 41
Naproxen 23, 24, 25, 36, 37
Nateglinide 32
Nebivolol 15, 16, 17
Neomycin 34
Neomycin (oral) 21
Nicardipine 18, 46
Nifedipine 15, 18, 19, 46
Nimodipine 18, 19
Nisoldipine 18
Nitroglycerin 12, 18, 23
Norepinephrine 16
Norfloxacin 26
NSAIDs 11, 13, 16, 21, 23, 24, 25, 36, 37, 42, 46

O

Ofloxacin 26, 39
Olmesartan 13, 14
Omeprazole 36, 46
Oral typhoid vaccine 29
Oxandrolone 41

P

Pancuronium 21, 22
Pantoprazole 46
Penbutolol 15, 16, 17
Penicillamine 39
Penicillin G 25
Penicillins 25, 34
Pentamidine 32
Perindopril 11, 12, 48
Phenobarbital 18, 19, 25, 43, 46
Phenobarbital Phenytoin 30
Phenothiazines 11, 13, 17
Phenylephrine 16
Phenytoin 14, 29, 30, 37, 43, 46
Pimozone 28
Pindolol 15, 16, 17
Piperacillin 25
Piroxicam 16, 25
Polymyxins 32, 42
Posaconazole 45
Potassium bicarbonate 13
Potassium chloride 11, 22

Potassium citrate 22, 35, 49
Potassium gluconate 13
Potassium guaiacolsulfonate 22
Potassium iodide 13
Potassium phosphate 13
Potassium preparations 22
Potassium salts 11, 13, 42, 46
Potassium-sparing diuretics 11, 13, 21, 42, 46, 49
PPIs 36
Prasugrel 36, 37
Prednisolone 13, 21
Primidone 29
Probenecid 12, 34
Promethazine 11, 13
Propafenone 17, 30
Propranolol 15, 16, 17
Protease inhibitors 18, 26

Q

Quinapril 11, 12, 48
Quinidine 20, 46
Quinolones 26, 39, 42

R

Rabeprazole 36
Ramipril 11, 12, 14, 48
Repaglinide 32
Reserpine 16
Reteplase 35
Retinoids 29
Rifabutin 18, 26, 29
Rifampicin 29, 46
Rifampicin/Rifampin 30
Rifampin 12, 14, 17, 18, 26
Rifamycins 18, 26
Rifapentine 18, 26
Ritonavir 18, 30, 46
Rosuvastatin 25

S

Salbutamol 38
S-Amlodipine 18
Saquinavir 30
Secobarbital 18, 25

Sertraline 21
Sevelamer 45
Sevelamer carbonate 40
Sevelamer hydrochloride 40
Sibutramine 21
Simvastatin 18, 19
Sirolimus 45, 46
Skeletal muscle relaxant 21, 22
SNRIs 21
Sodium bicarbonate 35, 38
Sodium channel blockers 17
Sodium citrate 35
Sodium citrate/Citric acid 49
Sodium polystyrene sulfonate 38
Sorbitol 38
Sotalol 15, 16, 17
Spironolactone 11, 13, 21, 22
SRIs 18, 35, 36
SSRIs 21, 23
Statins 28, 33, 43
Streptokinase 35
Streptomycin 31
Streptomycin (parenteral preparations) 21
Sulfamethizole 26
Sulfamethoxazole 26, 38
Sulfamethoxazole/Trimethoprim 26
Sulfasalazine 26
Sulfonamides 26, 42
Sulfonylureas 20
Sympathomimetics 16
Systemic corticosteroids 39

T

Tacrolimus 27, 30, 31, 32, 33, 40, 41, 42, 46
Tadalafil 14
Tamoxifen 26
TCA 35
Telithromycin 45, 46
Telmisartan 13, 14
Tenecteplase 35
Terfenadine 28
Testosterone 24
Tetracycline 34
Tetracyclines 26, 39
Theophylline 15, 28, 29, 37, 38, 46

Thiazide diuretics 12, 20, 21, 22, 39
Thioridazine 17
Ticagrelor 36, 37
Ticarcillin 25
Ticlopidine 36, 37
Timolol 15, 16, 17
Tinzaparin 23, 24, 37
Tirofiban 35, 36
Tizanidine 12, 16, 28
Toberamycin 21
Tolazamide 20
Tolbutamide 20
Torsemide 20, 21
Triamterene 11, 13, 21, 22
Triazolam 19, 29
Trifluoperazine 11
Trimethoprim 30, 31, 34, 42
Tubocurarine 21, 22

U

Urinary alkalinizers 35

V

Valaciclovir 33
Valproic acid 35
Valsartan 13, 14
Vancomycin 27, 31, 42, 46
Vasodilators 12
Venlafaxine 21, 36
Verapamil 15, 18, 19, 46
Vitamin D supplements 20
Vitamin E 36, 48
Voriconazole 24, 32, 33, 45, 46

W

Warfarin 12, 22, 24, 25, 26, 29, 30, 34, 36, 40

Z

Zafirlukast 35

BIBLIOGRAPHY

- <http://www.pdr.net/>
- <http://www.fda.gov/>
- <https://www.medicines.org.uk/emc/>
- <http://reference.medscape.com/>
- <http://www.ncbi.nlm.nih.gov/pubmed>
- <https://pubchem.ncbi.nlm.nih.gov/>
- British National Formulary No. 57. London: BMJ Publishing Group/RPS Publishing; 2009.
- Martindale: The Complete Drug Reference. 37th edition, 2011. Pharmaceutical Press.
- National List of Essential Medicines of India 2011. Central Drugs Standard Control Organization. Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India
- National Formulary of India. 4th Edition 2011. Indian Pharmacopoeia Commission. Ministry of Health & Family Welfare. Government of India
- Lange Current Medical Diagnosis and Treatment. 43rd Edition, 2004. Large Medical Books/McGraw-Hill.
- Marie A. Chisholm-Burns et al, editors. Pharmacotherapy Principles & Practice. USA: The McGraw-Hill Companies, Inc; 2010. 2nd ed.
- Tripathi KD. Essentials of Medical Pharmacology. 6th edition. Jaypee Brothers Medical Publishers (P) Ltd.
- Drug Index. Passi HealthCom Pvt Ltd. New Delhi. 2015; 19(2).

NOTES

NOTES

Disclaimer: This is an independent publication owned by Passi HealthCom Pvt. Ltd. The contents are summarized, validated and referenced from various authentic sources. The contents including text and graphics of the drug index are meant for educational and informational purposes only. Although great care has been taken in compiling and checking the information, the publisher shall not be responsible/liable in any way for the present and/or continued accuracy of the information or for any errors, omissions or inaccuracies in this publications whether arising from negligence or otherwise howsoever, or for any consequences arising therefrom. Any unauthorized reproduction or distribution of this publication is illegal. Please read the full prescribing information before prescribing any of the products mentioned in this booklet. Prescribing information is continually updated.

In Patients **At Risk** of Rejection



93.6% Freedom from acute rejection through 5 years¹

Excellent graft and patient survival¹

Well-tolerated¹

Minimises post transplant immunosuppression²

References: * Data on file. 1. Gaber AO, Matas AJ, Henry ML, Brennan DC, et al. Antithymocyte globulin induction in living donor renal transplant recipients: final report of the "TAILOR" registry. *Transplantation*. 2012 Aug 27;94(4):331-7. 2. Gaber AO et al, Rabbit Antithymocyte Globulin (Thymoglobulin) 25 Years and New Frontiers in Solid Organ Transplantation and aematology. *Drugs* 2010; 70 (6): 691-732.

Abridged Prescribing Information

THYMOGLOBULINE*

Rabbit antihuman thymocyte immunoglobulin Powder for concentrate for a solution for infusion Injection

COMPOSITION:Powder for concentrate for solution for infusion Rabbit antihuman thymocyte immunoglobulin: 25 mg/5ml. **THERAPEUTIC INDICATIONS:** Immunosuppression in transplantation: prophylaxis and treatment of graft rejection. Prophylaxis of acute and chronic graft versus host disease in haematopoietic stem cell transplantation. Treatment of steroid-resistant, acute graft versus host disease. Haematology: treatment of aplastic anaemia. **DOSAGE AND ADMINISTRATION:** The dosing depends on the indication, the administration regimen and the possible combination with other immunosuppressive agents. Recommendations may be used as reference. The treatment may be discontinued without gradual reduction of dose. Administer doses of corticosteroids and aminosterines are required prior to infusion of rabbit anti-human thymocyte immunoglobulin. **SAFETY-RELATED INFORMATION:****Contraindications:** Acute or chronic infections, which would contraindicate any additional immunosuppression. Hypersensitivity to rabbit proteins or to any product excipients. **Pregnancy and Lactation:** Thymoglobulin should not be given unless absolutely required. Breast feeding should be discontinued. **Warnings and Precautions:** Must be used in a hospital setting. Acute infusion-associated reaction (IARs) may occur following the administration of Thymoglobulin and may occur as soon as the first or second infusion during a single course of Thymoglobulin treatment. In the event of an anaphylactic shock, the infusion has to be stopped immediately and any further administration must not be carried out after the benefits and the risks have been carefully weighed up. Thrombocytopenia and/or leucopenia have been identified: white blood cell and platelet count must be monitored during and after the treatment. Infections, reactivation of infection, and sepsis have been reported after administration of Thymoglobulin in association with several immunosuppressive agents. The use of immunosuppressive agents, including Thymoglobulin may increase the incidence of malignancies. Reactions at the infusion site may occur and may include pain, swelling, and erythema. Immunization with attenuated live vaccines is contraindicated for patients who have received Thymoglobulin. **ADVERSE REACTIONS:** Infection (including reactivation of infection), Sepsis, Lymphoproliferative disorder, Lymphomas (which may be virally mediated), Neoplasms malignant (Solid tumors), Febrile neutropenia, Disseminated intravascular coagulopathy, Coagulopathy, Cytokine release syndrome (CRS), Anaphylactic reaction , Serum Sickness (including reactions such as fever, rash, urticaria, arthralgia, and/or myalgia). Transaminases increased, Hepatotoxicity, Hepatic Failure, Infusion related reactions (Infusion associated Reactions (IARs)

For full prescribing information please contact: Sanofi-Synthelabo (India) Private Limited., Sanofi House, CTS No. 117-B, L&T Business Park, Saki Vihar Road, Powai 400072

Updated: October 2015

Source: 1)CCDS version no. 2 dated 16 July 2015. 2) UK Summary of Product characteristics dated 03 May 2015.

