



# DRUG INTERACTIONS

 NOVARTIS

# 2004 Cyclosporine Manual

NEORAL<sup>®</sup>  
cyclosporine capsules and  
oral solution, USP [MODIFIED]



**Protect Your Choice**

 SANDIMMUNE<sup>®</sup>  
(cyclosporine capsules and oral solution, USP)

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## Letter from the Editor...

Since 1983, when Sandimmune® (cyclosporine) was approved, we have witnessed a medical miracle: the transition of organ transplantation from a desperate, experimental gamble to a procedure that is so much a part of medical therapy that our greatest problem today is supplying sufficient donor organs to meet the enormous demand. Transplant recipients are to be found at every age and in every walk of life, not simply existing, but living full, fulfilling and lengthy lives. Over the years, the Sandimmune Drug Interaction book has been in great demand, and we have been honored to provide it to the medical community as a service.

A new formulation of cyclosporine, Neoral® (cyclosporine capsules and oral solution, USP) MODIFIED became available in 1995; indications for treatment resistant rheumatoid arthritis and recalcitrant psoriasis were obtained soon after, and the transition to a new company, Novartis Pharmaceuticals Corporation occurred over the course of 1997. Our commitment to providing this service is, however, unchanged, and we are pleased to provide this valuable aid to providing the highest level of care to your patients receiving Sandimmune or Neoral. You will notice, if you are familiar with the older versions of our manual, that we have changed the format in order to make the booklet easier to use. It is our intention to provide updated versions on a yearly basis, unless a new, serious interaction is described in the literature, in which case we intend to provide a supplement to the current manual.

Though many interacting drugs are described, the extent and clinical significance of a given interaction will be variable and may be dependent on numerous other factors such as the patient's condition, drug dosage, and mode of administration. In the majority of cases, concomitant administration of interacting drugs would not be contraindicated and may, in fact, be unavoidable. In such cases, consideration should be given to the potential for interaction and any compensatory action (such as dosage adjustment or additional monitoring) which may be appropriate.

Naturally, Novartis is interested in obtaining information regarding any cyclosporine drug interactions of which you are aware. We encourage you to report these to us on the self-addressed, prepaid report form provided at the end of this booklet. In addition to compiling this information for future revisions of this booklet, appropriate follow-up reporting to the FDA will be made.

I would like to acknowledge the following individuals, without whom this interaction manual could not have been prepared: Kwakye Acheampong, Vidhu Bansal, Kelly Celuch, May Chan, Greta Chen, Abraham Choi, Rebecca Doyle, Rebecca Enright, Rebecca Florez, Joseph Frey, Suzanne Jahng, Barbara Landis, Ellaria Lee, Maria T. Leibfried, Wen Luan, Emily Luk, Mendy McGuire, Lauren Min, Neema Modi, Michael Morozewicz, Lisa Munch, Sekayi Mushonga, Raymond Pak, Swati Patel, Brian Raineri, Charles Rembert, Debra Scherb, Angie Sgro, Jasmine Singh, Ramon Tantalean, Jennifer Tilli, Elsa Tsang, Windy Wang, and all the dedicated people of Novartis Electronic Publishing and Printing.

We thank you for your interest in Neoral and Sandimmune, and hope you will continue to rely upon the Medical Information and Communication section of Novartis Transplantation & Immunology, and our highly trained specialists for any assistance you may require with our products.

For full prescribing information for Neoral please refer to page 70.  
For full prescribing information for Sandimmunne please refer to page 86.



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Director, Medical Information & Communication  
Novartis Transplantation and Immunology

# CYCLOSPORINE DRUG INTERACTIONS

## INTRODUCTION

This manual primarily describes the impact of various pharmaceutical agents on cyclosporine, regardless of whether cyclosporine is being used in or out of label. If a pharmaceutical agent is itself impacted by cyclosporine, *it is not the intention of this manual to provide comprehensive information on such effects.* Nevertheless, if, in the opinion of the editor, an effect of cyclosporine on a given drug has been extensively documented in the literature as having major clinical ramifications in humans, **and/or that drug interaction is listed in the approved prescribing information for Sandimmune or Neoral** (included in this manual), then that aspect of the interaction has been documented under "additional effects." There are additional effects of cyclosporine on other pharmaceutical agents that are either not extensively documented, or not listed in the approved label, and these effects will thus not appear in this manual. The decision regarding whether or not to administer cyclosporine and another pharmaceutical agent concomitantly in a given situation is ultimately the responsibility of the prescribing physician.

For your convenience, the information contained in the manual has been divided into two sections. The first section is a categorization of drugs, according to generic name, with listings for brand names, effects of the drug on cyclosporine blood levels (if any), effects on the nephrotoxic potential of cyclosporine (if any), additional effects, and reference number(s). The effects on blood levels and nephrotoxicity are listed as either well-substantiated or isolated reports which have yet to be substantiated or refuted. There are three minimum criteria used to establish well-substantiated status: (1) the reported agent must have clear documentation in at least one patient of the effect, resolution and return of effect on challenge, dechallenge and rechallenge respectively; (2) at least three patients are clearly documented to have exhibited the interaction followed by resolution upon withdrawal of the interacting agent (rechallenge not required); (3) the described interaction has been established in a prospective, crossover trial involving the interacting agent and cyclosporine. Each criterion assumes the absence of equal or stronger conflicting data. Where any conflicting reports exist, these have been noted.

The second section contains the source articles referenced in the first section. Each citation is followed by a document number which will assist you should you need to order it from us. It is always advised that literature references be viewed in light of current evidence and medical opinion with respect to the individual patient. Appropriate monitoring of cyclosporine levels should always be performed and consideration given to laboratory parameters (especially those reflecting renal and hepatic function). These tests have increased relevance when new medications are added or dosages are changed.

It is not possible to report the potential interaction for every existing or new drug. When such combinations are being considered, it will be helpful to realize that cyclosporine is a highly lipid soluble drug with a large volume of distribution which is extensively bound to plasma lipoproteins and erythrocytes. Ninety-nine percent of cyclosporine is metabolized, primarily in the liver, and this is thought to involve the Cytochrome P-450 3A4 gene family of microsomal enzymes. The primary route of excretion of cyclosporine and its metabolites is biliary, with about 6% excreted in the urine. Therefore, drugs which are known to alter gastrointestinal transit time, the excretion of bile, the absorption of lipids, or the hepatic microsomal enzyme systems should be considered with a higher index of suspicion for potential interactions.

Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>ACE inhibitors</b> (refer to individual agents for effects)	various		enhanced/additive nephrotoxicity		1
<b><i>acenocoumarol</i></b>	Sintrom			CsA inhibited the biotransformation of acenocoumarol	2
<b>acetazolamide</b>	Diamox	↑	nephrotoxic (isolated reports)		3
<b>acyclovir</b>	Zovirax	↑ †	nephrotoxic (isolated reports)	CsA levels may be falsely decreased due to interference of acyclovir with the assay	4-7
<b>alendronate</b>	Fosamax	↑		Alendronate use suggests a diagnosis of osteoporosis; that medical condition may alter cyclosporine pharmacokinetics	576
<b>allopurinol</b>	Zyloprim	↑ ↑	increase serum creatinine levels	Increased CsA toxicity	8-10
<b>alprostadil</b>	Caverject	↑			11, 12
<b>Aluminum</b> (see Antacids)	Domeboro Basaljel Amphojel Maalox	↑	nephrotoxic (isolated reports)	Aluminum significantly increases the nephrotoxicity and bioavailability of cyclosporine, due to excessive generation of free radicals.	525
<b>amikacin sulfate</b>	Amikin	↑	nephrotoxic (isolated reports)		13, 14
<b>amiloride</b> (see Diuretics)	Midamor, Moduretic		nephrotoxic (isolated reports)	Possible hyperkalemia	15
<b>Aminoglycosides</b> (refer to individual agents for effects)	various	↑	nephrotoxic† (isolated reports)		16
<b>amiodarone</b>	Cordarone	↑	nephrotoxic (isolated reports)		17-20
<b>amlodipine</b> (see Calcium Antagonists)	Norvasc	↑ ↑ †		Increases gingival overgrowth† Ameliorates post-transplant hypertension	21-23, 415, 601, 627
<b><i>amoscanate</i></b>				Additive effects in the treatment of schistosomiasis	24
<b>amoxicillin</b>	Amoxil, Augmentin, Wymox	↑			25, 26
<b>amphotericin B</b>	Fungizone, Abelcet AmBisome (liposomal amphotericin B)	↑	nephrotoxic (well-substantiated)	Conflicting reports of nephrotoxicity with liposomal amphotericin B	27-30
<b>ampicillin</b>	Omnipen (PO), Unasyn (inj)	↑			25, 26

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>Anabolic Steroids</b>	various	↑			31
<b>Androgens</b> (refer to individual agents for effects)		↑			32, 33
<b><i>ansamycin</i></b> (see rifabutin)					
<b>Antacids</b>	Maalox, Rolaids, Tums, etc			Neurotoxic effects associated with increased aluminum concentration	35, 36
<b>Anti-CD45RB</b> (Monoclonal antibody)				CsA inhibits longterm graft survival	510
<b>Anticoagulants</b> (see EDTA, heparin, warfarin)				Variations in CsA levels	1, 14, 37-41
<b>Anticonvulsants</b> (refer to individual agents for effects)		↓		May induce CsA metabolism	42, 43
<b>Antithymocyte Globulin</b>	Thymoglobulin ATGAM			Synergistic capacity with cyclosporine in immunosuppressive therapy	527
<b>Antitubercular Agents</b> (refer to individual agents for effects)		↓			44, 45
<b>aspirin</b> (see NSAIDs)	Bayer, Ecotrin, Excedrin, Norgesic, etc		nephrotoxic (isolated reports)		46, 47
<b>atracurium</b>	Tracrium			Prolonged neuromuscular blockade	48
<b>atorvastatin</b>	Lipitor			Increased levels of HMG-CoA reductase inhibitory activity: risk of rhabdomyolysis	509, 602
<b><i>azapropazon</i></b> (see NSAIDs)			nephrotoxic (well-substantiated)		38, 49
<b>azathioprine</b>	Imuran	↓		Concomitant use may allow lower CsA dose to be used	50, 473
<b>azithromycin</b> (see Macrolides)	Zithromax	↑ †		May decrease gingival hyperplasia caused by CsA Azithromycin may increase cyclosporine concentrations	51-53, 181, 603, 628
<b>azodicarbonamides</b>				Synergistically inhibits CD4 <sup>+</sup> T cell proliferation	577
<b>Azole Antifungals</b> (refer to individual agents for effects)	various	↑		Inhibits CsA metabolism	43, 54, 55
<b>bactobolamine</b>				Inhibit the mixed-lymphocyte reaction synergistically rather than additively	578
<b>Barbiturates</b>	various	↓			56

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>basiliximab</b>	Simulect	↑		Interleukin-2 receptor-mediated alteration of the Cytochrome P-450 system may cause this interaction. Initial cyclosporine doses may need to be lower if used in combination with basiliximab.	579
<b>Beta-Blockers</b> <small>(refer to individual agents for effects)</small>	various			Hyperlipidemia	57
<b>bezafibrate</b>	Bezalip	↑	nephrotoxic <small>(isolated reports)</small>		216
<b>Bile Acid</b> <small>(tablet)</small>	various			Increases the bioavailability of CsA	58, 59
<b>Bile Acid and/or Dietary Fat</b>				Increases bioavailability of CsA†	59
<b><i>bosentan</i></b>			Attenuates the CsA induced fall of effective renal plasma flow	Sodium retention	280, 571
<b>bromocriptine</b>	Parlodel	↑ ↑		Regulates CsA immunosuppression through inhibition of prolactin (with concomitant dopamine use)	60, 61, 285
<b>bupropion</b>	Wellbutrin, Zyban	↓		Bupropion decreased cyclosporine levels in one subject	580
<b>buspirone</b>	Buspar	↑			62
<b>busulfan</b>	Myleran			CsA-associated seizures (seen in combination with cyclophosphamide)	63
<b>calcitriol</b>	Rocaltrol	↑			629
<b>Calcium Antagonists</b> <small>(refer to individual agents for effects)</small>	various			Decreases acute allograft rejection; protective renal effect	64-71
<b>captopril</b> <small>(see ACE inhibitors)</small>	Capoten		nephrotoxic <small>(isolated reports)</small>	Slightly increases renal blood flow (RBF) and glomerular filtration rate (GFR)	66, 72
<b>carbamazepine</b> <small>(see anticonvulsants)</small>	Tegretol, Atretol	↓ ↓		Increases the metabolism of CsA through enzyme induction	36, 57, 61, 73, 74
<b>carvedilol</b>	Coreg	↑		Beneficial acute hemodynamic effects	75, 483
<b>caspofungin</b>	Cancidas			Cyclosporine may increase caspofungin bioavailability and may elevate ALT (alanine transaminase) and AST (aspartate transaminase) levels	581
<b>cefamandole</b> <small>(see Cephalosporins)</small>	Mandol			Possible interaction with the alcohol contained in Sandimmune/Neoral®	1

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>cefoperazone sodium</b> (see Cephalosporins)	Cefobid			Possible interaction with the alcohol contained in Sandimmune/Neoral®	1
<b>cefotaxime sodium</b> (see Cephalosporins)	Claforan		nephrotoxic (isolated reports)		1, 76
<b>ceftazidime</b> (see Cephalosporins)	Ceptaz, Fortaz, Tazicef, Tazidime		nephrotoxic (isolated reports)		14
<b>ceftriaxone</b> (see Cephalosporins)	Rochephin	↑			77
<b>cefuroxime</b> (see Cephalosporins)	Ceftin (PO) Kefurox, Zinacef (inj)		nephrotoxic (isolated reports)		1, 76
<b>celecoxib</b>	Celebrex		nephrotoxic (isolated reports)	As seen with other NSAIDs	582
<b>Cephalosporins</b> (refer to individual agents for effects)	various	↑	nephrotoxic (isolated reports)		1, 38, 78
<b>cephradine</b> (see Cephalosporins)	Velosef		nephrotoxic (isolated reports)		1, 76
<b>cerivastatin</b>	Baycol			Combination well tolerated in kidney transplant patients. Increase in level of cervistatin and metabolites	495, 530, 630
<b>chlorambucil</b>	Leukeran	↓			79
<b>chloramphenicol</b>	Chloromycetin	↑		Inhibition of Cytochrome P-450	80, 81, 496
<b>chloroquine</b>	Aralen HCl Injection, Aralen Phosphate tablets	↑ ↑		Synergistic effects in combination with CsA in the treatment of rheumatoid arthritis	82, 83, 534 564
<b>chlorpropamide</b>	Diabenese			Possible interaction with the alcohol contained in Sandimmune/Neoral®	1
<b>cholestyramine</b>	Questran	↓		May alter the absorption of CsA	31, 35, 84, 85
<b>cidofovir</b>	Vistide		nephrotoxic (isolated reports)		583

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>cimetidine</b> (see H <sub>2</sub> -Receptor Antagonists)	Tagamet	↑ †	nephrotoxic (well-substantiated) †; effects on renal function may be due to competitive inhibition of renal tubular secretion of creatinine and true nephrotoxicity	May delay absorption	86-93
<b>ciprofloxacin</b> (see Fluoroquinolones)	Cipro	↑ †	nephrotoxic (isolated reports)	May counter suppressive effect of CsA by increasing IL-2 and INF-γ Marked increase in incidence of rejection when ciprofloxacin used with CsA	94-102, 604, 605
<b>cisapride</b>	Propulsid	↑		Enhances absorption	103, 104
<b>cisplatin</b>	Platinol			CsA reverses resistance of nephrons to cisplatin	105
<b>clarithromycin</b> (see Macrolides)	Biaxin	↑	increases serum creatinine levels	Inhibits CsA metabolism; has been reported to cause hand tremors in combination with CsA (may be due to increased levels of CsA)	53, 57, 106-108, 314, 355
<b>clindamycin</b>	Cleocine	↓			497
<b>clonidine</b>	Catapres	↑			109, 110
<b>colchicine</b>	Col-BENEMID	↑	nephrotoxic (isolated reports)	May potentiate CsA muscle toxicity; additional toxicities noted with this combination include diarrhea, increased LDH, increased ALT, hyperbilirubinemia, and multiple organ failure; cyclosporine may inhibit metabolism of colchicine	39, 111-113, 456, 532, 631
<b>Contraceptives</b> (refer to individual ingredients for effects)	various	↑			38, 57
<b>Cox-2 inhibitors</b> (refer to individual agents for effects)	Various		nephrotoxic (isolated reports)	As seen with other NSAIDs	582
<b>cyclophosphamide</b>	NEOSAR, Cytosan			Increases potential for hepatotoxicity; CsA associated seizures (seen in combination with Busulfan). CsA neurotoxicity reported in spite of normal CsA level	63,115, 498
<b>cytosine</b> (Cytarabine; Ara-C)	Cytosar-V			Increases pain associated with acral erythema	116
<b>danazol</b>	Danocrine	↑ ↑	nephrotoxic (isolated reports)	May inhibit the metabolism or increase the absorption of CsA	117-119, 308
<b>daunorubicin</b>	Cerubidine			CsA increases daunorubicin levels; also increased leukopenia and bilirubin seen with this combination	120

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>desogestrol</b>	Desogen, Ortho-Cept	↑			121
<b>dexamethasone</b>	Decadron	↓		Increases metabolism of CsA; synergistic inhibition of T-cell function	114, 122, 123
<b>diclofenac</b> <small>(see NSAIDs)</small>	Cataflam (potassium), Voltaren (sodium)		nephrotoxic <small>(well-substantiated) †</small>	CsA coadministration increases the systemic exposure to diclofenac. Drug induced colitis when both diclofenac and CsA are given orally concomitantly; symptoms resolved with IV CsA administration	38, 57, 124, 125, 416, 437, 499
<b>digoxin</b>	Lanoxin		nephrotoxic (isolated reports)	Decreased volume of distribution and clearance of digoxin; digoxin toxicity may be precipitated by CsA administration	126
<b>diltiazem</b> <small>(see Calcium Antagonists)</small>	Cardizem, Dilacor XR	↑ ↑	nephrotoxic <small>(isolated reports) †</small>	Decreases CsA-induced nephrotoxicity (but not chronic nephrotoxicity); prevents delayed graft function and rejection; reduces ATN; significant gingival enlargement; sharp increase in CsA AUC	127-140, 417-419, 500, 546, 547, 606
<b><i>diphenyl-dimethyl-dicarboxylate</i></b>		↓			455
<b><i>dipyrrone</i></b> <small>(see NSAIDs)</small>		↓ †		CsA peak not altered, but delayed time to peak	14, 35, 567
<b>dirithromycin</b> <small>(see Macrolides)</small>	Dynabac	↑ †		Dirithromycin decreased clearance of cyclosporine, increasing steady state concentrations and trough concentrations	141, 598
<b>disopyramide</b>	Norpace		nephrotoxic <small>(isolated reports)</small>		14, 57
<b>disulfiram</b> <small>(see Ethanol)</small>	Antabuse			Possible interaction with the alcohol contained in Sandimmune/Neoral®	37
<b>Diuretics</b> <small>(refer to individual agents for effects)</small>	various				15, 38, 556
<b>docetaxel</b>				Coadministration with CsA leads to a pronounced increase in systemic exposure of oral docetaxel	511, 512
<b>docusate</b>	Colace, Dialose, Fleet Sof-Lax, Peri-Colace, etc.	↑			142

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
dopamine	Inotropin		↓ nephrotoxicity		143-146
doxorubicin	Adriamycin, Rubex		nephrotoxic (isolated reports)	CsA increases doxorubicin and doxorubicinol (metabolite) levels; enhances cytotoxicity; possible synergistic deleterious effects on the central nervous system	147-153, 454 513
doxycycline	Doryx, Monodox, Vibramycin	↑			14, 35
<b>EDTA</b> (see Anticoagulants)				Variation of CsA levels in vitro due to anticoagulant in the collecting tubes	40
eletriptan	Relpax			Decreased eletriptan metabolism	632
enalapril (see ACE inhibitors)	Vasotec, Vasoretic		nephrotoxic (isolated reports)	May have protective renal effect also seen when enalapril is used in combination with furosemide	154-156
enisoprost		↓		Decreases CsA AUC and C <sub>max</sub>	157, 158
<b>Ergot Alkaloids</b>	Cafergot, Ergomar, etc.		decreases renal dysfunction†		159
erythromycin (see Macrolides)	E-Mycin, Ery-tab, ERYC, PCE, etc.	↑ ↑	nephrotoxic (well-substantiated) (secondary to increased CsA levels)	Increased hepatotoxicity	53, 160-166 536
estradiol	Climara, Estrace, Estraderm, Vivelle	↑		Increased/additive hepatotoxicity; antagonizes immunosuppressive activity in animals	113, 115
ethambutol (see Antitubercular Agents)	Myambutol	↓			44, 45
ethanol (see Disulfiram)		↑ ↑ † or ↓ ↓ †		Hyperlipidemia	167, 168
etoposide	VePesid	↓	nephrotoxic (isolated reports)	Increases cytotoxicity; increases toxicity (isolated reports) and antineoplastic effects; decreases clearance, and increases mean AUC, of etoposide and prolongs retention in mdrl expressing cells in vivo. Concomitant CsA with etoposide resulted in an average increase in etoposide plasma levels, 50% decrease in median etoposide clearance, and decrease in median WBC count nadir	169-171, 420 484, 538, 607
<b>everolimus</b> (formerly RAD 001)				Increases AUC and C <sub>max</sub> of everolimus	520, 521, 608, 633

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>famotidine</b> <small>(see H<sub>2</sub>-Receptor Antagonists)</small>	Pepcid	↑ †		May inhibit CsA metabolism	87, 88, 90, 172-176
<b>fat</b>				High fat meals may increase the AUC of Sandimmune, but may decrease the AUC of Neoral. Therefore, it is important that dosing is kept consistent with regard to timing and content of meals	59, 476-482
<b>felodipine</b> <small>(see Azole Antifungals)</small>	Plendil	↑ †	Renoprotective (increases GFR and renal plasma flow) nephrotoxic <small>(isolated reports) †</small>	Increases gingival hyperplasia in susceptible patients, AUC and C <sub>max</sub> of felodipine increased with CsA; combination may result in a renoprotective effect	22, 177-180, 421, 422, 554, 555, 609
<b>fenofibrate</b>	Tricor				610
<b>fish oil</b>			protective renal effect		182-185
<b>FK 506</b> <small>(see tacrolimus)</small>					
<b>fluconazole</b>	Diflucan	↑	nephrotoxic <small>(isolated reports) †</small>	No clinically significant interactions when given with I.V. fluconazole Oral fluconazole may increase bioavailability of CsA	186-194, 423, 501, 539, 611
<b>Fluoroquinolones</b> <small>(refer to individual agents for effects)</small>	various	↑	nephrotoxic†		55, 195
<b>fluoxetine</b>	Prozac	↑ †		May inhibit Cytochrome P-450 2D6	196-199
<b>fluvastatin</b> <small>(see HMG CoA Reductase Inhibitors)</small>	Lescol			Increased risk of myopathy and rhabdomyolysis; increases AUC of fluvastatin <sup>†</sup>	200-205
<b>fluvoxamine</b>	Luvox			Associated with CsA toxicity; reaction possibly due to inhibition of CYP3A3/4 by fluvoxamine	612
<b>Food</b> <small>(see fat, grapefruit juice, olestra)</small>				Variable effects on bioavailability	58, 206-210
<b>foscarnet</b>	Foscavir		nephrotoxic <small>(isolated reports) †</small>	Reversible acute renal failure due to the synergistic toxic effect of the combination	424
<b>framycetin</b>		↑	nephrotoxic <small>(isolated reports)</small>		39
<b>FTY720</b>				Synergistic effect with cyclosporine	526
<b>furosemide</b> <small>(see Diuretics)</small>	Lasix	↑	nephrotoxic <small>(isolated reports) †</small>	Decreases nephrotoxicity <sup>†</sup>	38, 155, 211

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<i>gallopamil</i>		↑	improves renal tubular function	Decreases the CsA dose needed to maintain immunosuppressive blood levels	458
<b>ganciclovir</b>	Cytovene	↑	nephrotoxic <small>(isolated reports)</small>	Increased absorption and decreased elimination of CsA	14, 35, 212, 502
<b>gemfibrozil</b>	Lopid	↓ †		Decrease in gemfibrozil plasma level occurs with Sandimmune®, but may not occur with Neoral®	213, 485
<b>gentamicin</b> <small>(see Aminoglycosides &amp; Antibiotics)</small>	Garamycin		nephrotoxic <small>(well-substantiated)</small>		14, 573
<b>ginkgolide B</b>				Possible synergism with cyclosporine to inhibit pathogenic immune activation in asthmatics	529
<b>glibenclamide</b> <small>(glyburide)</small>	Danolin, Euglucon, Glimel	↑		May inhibit metabolism of CsA	425
<b>glipizide</b>	Glucotrol	↑		May inhibit metabolism of CsA	214
<b>Glucocorticoids</b> <small>(refer to individual agents for effects)</small>	various	↑ † <small>(high dose)</small> or ↓ †		Shortens the CsA half life; increases risk of hypertension; seizures with high-dose glucocorticoids	1, 32, 33, 42, 109, 114, 167
<b>glutethimide</b>	Doriden	↓			24
<b>grapefruit juice</b>		↑ ↑		Inhibits Cytochrome P-450 metabolism of CsA in the intestinal mucosa	215, 217-225, 574, 613
<b>grepafloxacin</b>				Cyclosporine decreased secretory-directed transport by inhibiting P-glycoprotein	584
<b>griseofulvin</b>	Fulvicin P/G, Grifulvin V, Gris-PEG, Grisactin	↓			39, 226
<b><i>Helleborus sp.</i> extract</b>	veratrum			Strongly potentiates the T-cell suppressive effects of Cyclosporine A	524
<b>heparin</b> <small>(see Anticoagulants)</small>	Liquaemin Sodium	↓			1, 39
<b>H<sub>2</sub>-Receptor Antagonists</b> <small>(refer to individual agents for effects)</small>	various		nephrotoxic <small>(isolated reports)</small>		87, 88, 172, 227, 426
<b>HMG CoA Reductase Inhibitors</b> <small>(refer to individual agents for effects)</small>	various		nephrotoxic <small>(isolated reports - possibly secondary to myoglobin toxicity)</small>	Risk of myopathy; possible inhibitor of metabolism of HMG CoA Reductase Inhibitors	228-230, 427, 634-639, 661
<b>hydroxychloroquine</b>	Plaquentil		nephrotoxic		585

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>ICAM-1</b>				Together showed a potent synergistic interaction on allograft survival	586
<b>idarubicin</b>	Idamycin			CsA increases idarubicin levels in mdr1 expressing cells	428, 503
<b><i>iloprost</i></b>			Protective renal effect		231, 232
<b>imipenem/Cilastatin</b>	Primaxin	↑ † or ↓ †	The cilastatin component decreases CsA-induced nephrotoxicity	Increases CNS toxicity.	42, 233, 234, 429
<b>indomethacin</b> <small>(see NSAIDs)</small>	Indocin		nephrotoxic <small>(isolated reports)</small>	Induces salt and water retention; decreases GFR and effective renal plasma flow Drug induces colitis when both Indomethacin and CsA are given orally concomitantly	235-237, 499
<b>interferon gamma</b>				CsA induces apoptosis in human gastric carcinoma cells. Cyclosporine accelerates the activation of caspase induced by interferon gamma	587
<b>intravenous fat emulsion</b>	Liposyn, Intralipid	↑			238, 239
<b>irinotecan</b>	Camptosar			CsA reduces irinotecan clearance by decreasing biliary excretion	588
<b>isoflurane</b>	Forane			Decreases CsA absorption	240
<b>isoniazid</b> <small>(see Antitubercular Agents)</small>	Nydrazid, Rifamate, Rifater	↓ †	nephrotoxic <small>(isolated reports)</small>		44, 45, 241
<b>isotretinoin</b>	Accutane			Hyperlipidemia	57, 242
<b>isradipine</b> <small>(see Calcium Antagonists)</small>	DynaCirc	↑ †		Reduces CsA induced side effects on renal hemodynamics and the proximal tubule	243-250, 555
<b>itraconazole</b> <small>(see Azole Antifungals)</small>	Sporanox	↑ ↑ †	nephrotoxic <small>(isolated reports) †</small>	Inhibits Cytochrome P-450 metabolism; CsA administered in a fed state with a cola resulted in greater random levels of itraconazole	56, 251, 560 614
<b>ivermectin</b>				Increased neurotoxicity with CsA in mice	514
<b><i>josamycin</i></b> <small>(see Macrolides)</small>		↑ ↑		Inhibits Cytochrome P-450 metabolism	162, 252, 253, 430

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>ketoconazole</b> <small>(see Azole Antifungals)</small>	Nizoral	↑ ↑	nephrotoxic <small>(well-substantiated)</small> (secondary to increased CsA levels)	Hepatotoxicity; CNS toxicity; glucose intolerance; worsening of gingival hyperplasia; gastrointestinal adverse effects; grand mal seizures	28, 130, 164, 254-270, 431, 461, 570, 640
<b>ketoprofen</b> <small>(see NSAIDs)</small>	Orudis, Oruvail		nephrotoxic <small>(isolated reports)</small>		271
<b>lacidipine</b> <small>(see Calcium Antagonists)</small>	Lacipil		Protective renal effect		272
<b>latamoxef disodium</b>		↑	nephrotoxic <small>(isolated reports)</small>		1, 14, 76
<b>leflunomide</b>	Arava			Additive interaction between metabolite of leflunomide and cyclosporine in preventing T cell proliferation	589
<b>levofloxacin</b>	Levaquin			Cyclosporine decreases secretory-directed transport of levofloxacin due to inhibition of P-glycoprotein	488, 584
<b>levonorgestrel</b> <small>(see Contraceptives)</small>	Levlen, Levora, Nordette, Tri-Levlen, Triphasil	↑		Hepatotoxicity when used in combination with ethinyl estradiol	14, 39, 115
<b>loop diuretics</b>	various			Magnesium levels and requirements unchanged when loop diuretics. Calcineurin inhibitors and loop diuretics may have similar site of action	615
<b>loperamide</b>	Imodium			Alters CsA absorption	273
<b>losartan</b>	Cozaar, Hyzaar	↑		Cyclosporine & Losartan may have competition for catalysis by Cytochrome P-450 3A4	576
<b>lovastatin</b> <small>(see HMG CoA Reductase Inhibitors)</small>	Mevacor			Increased risk of myopathy and rhabdomyolysis; CsA may inhibit the metabolism of lovastatin	274-277, 565
<b>Macrolides</b> <small>(refer to individual agents for effects)</small>	various	↑ ↑			16, 162
<b>mannitol</b> <small>(see Diuretics)</small>	Osmitrol		Decreased nephrotoxicity; in large doses it can aggravate the occurrence of toxic tubulopathy with isomeric vacuolization		278
<b>mefenamic</b> <small>(see NSAIDs)</small>	Ponstel	↑	nephrotoxic <small>(isolated reports)</small>		279
<b>melphalan</b>	Alkeran		nephrotoxic <small>(well-substantiated)</small>	CsA can help overcome melphalan resistance	33, 38, 57, 109, 548

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b><i>metamizole</i></b> (see dipyrone)					
<b>methsuximide</b>		↓			35
<b>methylphenidate</b>	Concerta, Metadate, Methylin, Ritalin	↑		Methylphenidate increased cyclosporine levels in one subject	580
<b>methotrexate</b>	Rheumatrex, etc.	↑		Methotrexate and CsA can inhibit each other's elimination. This may result in an elevation in the levels of both†	39, 281, 549
<b>methylprednisolone</b> (see Glucocorticoids)	Medrol	↑		Grand mal seizures with high doses†	282-284, 550
<b>methyltestosterone</b> (see Androgens)	Android, Oreton Methyl, Testred, Virilon	↑	nephrotoxic (isolated reports)	Hepatotoxicity; increases in serum bilirubin and alanine amino-transferase	14, 39, 285, 286
<b>metoclopramide</b>	Reglan	↑ ↑		May increase the absorption of CsA	234, 287
<b>metolazone</b> (see Diuretics)	Diulo, Mykrox, Zaroxolyn,		nephrotoxic (isolated reports)		14, 35
<b>metoprolol</b> (see Beta Blockers)	Lopressor	↓		Beneficial hemodynamic effects	39, 75
<b>metronidazole</b>	Flagyl	↑		Possible interaction with the alcohol contained in Sandimmune/Neoral®	1, 14, 39, 504, 568
<b>mibefradil</b>	Posicor	↑	Nephrotoxic (isolated report)	Rhabdomyolysis and acute renal failure in combination with simvastatin	505, 616, 641
<b>miconazole</b> (see Azole Antifungals)	Monistat, Fungoid	↑ †			39, 288
<b>midecamycin</b> (see Macrolides)		↑	Increased serum creatinine levels	Edema; tremor; gingival pain; elevation of blood pressure	289, 432
<b>minoxidil</b>	Loniten, Rogaine			Potentialiation of hirsutism	57, 290
<b>miocamycin</b> (see Macrolides)		↑			162, 506
<b>misoprostol</b>	Cytotec	↓	Protective renal effect	Decreased incidence of acute rejection	291-293

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>mitoxantrone</b>	Novantrone			CsA decreases clearance and increases the mean AUC of mitoxantrone	459, 607
<b><i>mizorbine</i></b>				Enhanced immunosuppression	35
<b>modafinil</b>	Modiodal	↓		50% decrease in CsA level	463, 507, 642
<b>morphine</b>				Post-transplant neuropsychosis	515
<b><i>moxalactam</i></b> (see latamoxef disodium)					
<b>mycophenolic acid</b>				Cyclosporine can cause a significant reduction in mycophenolic acid trough levels	590, 591, 644, 645
<b>mycophenolate mofetil</b>	Cellcept			Decreased MMF levels	516, 643
<b>muromonab-CD3</b> (OKT3)	Orthoclone	↑			313
<b>nafcillin</b>	Unipen	↓	Increased nephrotoxicity (isolated reports)	May interfere with assay, resulting in an underestimation of CsA levels	16, 39, 294
<b>naproxen</b> (see NSAIDs)	Naprosyn		nephrotoxic (isolated reports); reduces GFR and RBF		295, 296
<b>nefazodone</b>	Serzone	↑		Reaction possibly due to inhibition of CYP3A3/4 by nefazodone	433, 551, 612
<b>nicardipine</b> (see Calcium Antagonists)	Cardene	↑ ↑	nephrotoxic (isolated reports)		139, 297-299, 434, 435
<b>nifedipine</b> (see Calcium Antagonists)	Adalat, Procardia	↑	Decreased nephrotoxicity; increased RBF	Enhanced immunosuppression; increased gingival hyperplasia	22, 300-304, 436, 546, 619
<b>nisoldipine</b>	Sular	↑			561
<b>nitrendipine</b> (see Calcium Antagonists)	Baypress			Improved liver function; shortened t <sub>max</sub> for CsA	305, 306
<b>Non-steroidal Anti-inflammatory Drugs</b> (NSAIDs- refer to individual agents for effects)	various		nephrotoxic (isolated reports)  may be due to inhibition of renal prostaglandin synthesis	Drug induced colitis	89, 307, 437, 545

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>norethindrone</b> (see Contraceptives)	Brevicon, Jenest, Micronor, Modicon, Norethin, Norinyl, Nor-Q.D., Ortho-Novum, Orvette, Ovcon, Tri-Norinyl	↑ †			308
<b>norethisterone</b> (see Contraceptives)		↑ †			35
<b>norfloxacin</b>	Chibroxin, Noroxin	↑ †		Norfloxacin may inhibit Cytochrome P-450 3A4 enzymes	39, 95, 99, 438
<b>octreotide</b>	Sandostatin	↓	nephrotoxic (isolated reports) †	May decrease the absorption and bioavailability of CsA	39, 57, 309
<b>ofloxacin</b> (see Fluoroquinolones)	Floxin	↑ †			45, 99, 310-312
<b>OKT3</b> (see Muromonab-CD3)					
<b>olestra</b>		↓		Inhibits CsA absorption	314
<b>omeprazole</b>	Prilosec	↑ † or ↓ †		May delay the absorption of CsA	88, 91, 315-322 620
<b>orlistat</b>	xenical	↓		Interferes with CsA absorption	517, 646
<b>oxandrolone</b>	Oxandrin	↑			323
<b>oxcarbazepine</b>	Trileptal	↓		Addition of oxcarbazepine decreased cyclosporine trough levels, by inducing Cytochrome P-450 3A enzyme	592
<b>oxycodone</b>		↓		Oxycodone may slow gastric emptying and reduce Cytochrome P-450 3A4 saturation, which may increase the metabolism and decrease the bioavailability of cyclosporine	576
<b>oxymetholone</b>				Hepatotoxicity	324

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>paclitaxel</b>	Taxol			CsA may enhance the in vivo efficacy of paclitaxel <sup>†</sup> . CsA increases oral absorption of paclitaxel by inhibiting the multidrug transporter P-glycoprotein in the GI tract	325, 326, 457, 489, 540, 541, 647
<b>pancuronium</b>	Pavulon			Prolongation of pancuronium blockade	327, 453
<b>pantoprazole</b>	Protonix	↓		Has a lower affinity for Cytochrome P-450 3A4 than omeprazole and lansoprazole	593
<b>PEG-3350 and electrolytes for oral solution</b>	GoLYTELY	↓		Decreases the absorption of CsA	328
<b>pentazocine</b>	Talacen, Talwin	↑			35
<b>pentoxifylline</b>	Trental			Additive inhibition of tissue necrosis factor activities; Selective potentiation of CsA-mediated suppression of cell-mediated lymphocytotoxicity. Potentiation of CsA-mediated suppression of lymphocyte proliferation	329, 330, 562
<b>phenobarbital</b> <small>(see Anticonvulsants &amp; Barbiturates)</small>	Arco-Lase, Bellatal, Bellergal-S, Donnatal, Quadrinal, Mudrane, Rexetal, Solfoton	↓ ↓		May induce Cytochrome P-450 3A4 metabolism of CsA	39, 331
<b>phenytoin</b> <small>(see Anticonvulsants)</small>	Dilantin	↓ ↓		May induce Cytochrome P-450 3A4 metabolism of CsA; increased gingival hyperplasia	39, 331, 332
<b>picotamide</b> <small>(see Anticoagulants)</small>			Protective renal effect		231
<b>piroxicam</b> <small>(see NSAIDs)</small>	Feldene		nephrotoxic <small>(isolated reports)</small>		333
<b>pomelo</b> <small>(citrus fruit)</small>		↑		Inhibits Cytochrome P450 metabolism of CsA	648
<b>ponsinomycin</b> <small>(see miocamycin)</small>					

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>pravastatin</b> <small>(see HMG CoA Reductase Inhibitors)</small>	Pravachol			Increased risk of myopathy and rhabdomyolysis; CsA may inhibit the metabolism of pravastatin. However, compared to lovastatin, the interaction between pravastatin and CsA is clinically insignificant. No changes in CsA Pharmacokinetics	335, 336, 440-442, 490, 531
<b>prazosin</b>	Minipress, Minizide		Protective renal effect; increases RBF; small reduction in GFR	Decreases arterial blood pressure	14, 337
<b>prednisolone</b> <small>(see Glucocorticoids)</small>	Prelone, Hydeltrasol Inj, Hydeltra-T.B.A.	↑		Increased AUC and $t_{1/2}$ of CsA; decreased clearance of CsA may decrease metabolism and clearance of prednisolone†. Synergistic immunosuppressive effect when given with CsA	14, 338, 339, 469-472, 491, 518
<b>prednisone</b> <small>(see Glucocorticoids)</small>	Deltasone, Liquid Pred Syrup, Prednicen-M, Sterapred			Increased liver enzymes; hirsutism; hyperlipidemia	14, 57, 340
<b>prenylamine</b>		↑			39
<b>primidone</b> <small>(see Anticonvulsants &amp; Barbiturates)</small>	Mysoline	↓		Induces metabolism of CsA	39, 57
<b>pristinamycin</b> <small>(see Macrolides)</small>		↑	nephrotoxic <small>(isolated reports)</small>	Inhibits Cytochrome P-450 3A4 metabolism of CsA	16, 39, 53
<b>probucol</b>	Lorelco	↓ ↓		Increases clearance of CsA	341-343, 443
<b>progesterone</b>	Progestasert System			Inhibits CsA metabolism	122
<b>propafenone</b>	Rythmol	↑	Decreased renal function		39, 344
<b>propionyl carnitine</b>			Protective against CsA nephrotoxicity		519
<b>propranolol</b> <small>(see Beta-Blockers)</small>	Inderal			Antagonizes the immunosuppressive effects of CsA. CsA increases the elimination of propranolol and also reduces first pass effects and increases propranolol GI absorption	35, 542
<b>prostaglandins</b>			Protective renal effect		345
<b>purified helleborus species extract</b>	See <i>Helleborus</i>				

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>pyrazinamide</b> <small>(see Antitubercular Agents)</small>	Rifater	↓ †			45, 346
<b>quinupristin/ dalfopristin</b>	Synercid	↑ ↑		Inhibits Cytochrome P-450 3A4; May have a 2-5x increase in cyclosporine levels	444, 563, 599
<b>quinine</b>	Legatrin, Q-Vel, etc	↓			347
<b>rabeprazole</b>	Aciphex	↑		Induces Cytochrome P-450 3A4 but less than omeprazole; At doses greater than 20mg inhibits Cytochrome P-450 3A4 mediated cyclosporine metabolism	594
<b>ranitidine</b> <small>(see H2-Receptor Antagonists)</small>	Zantac	↑ †	<b>nephrotoxic</b> <small>(well-substantiated)</small>	Hepatotoxicity; thrombocytopenia	93, 142, 227, 348, 349
<b>red yeast rice</b> <small>(Monascus purpureus)</small>				Rhabdomyolysis possibly due to interference of CsA with metabolism of statins	652
<b>repaglinide</b>	Prandin			CsA may increase repaglinide levels by inhibiting CYP450 3A4	595
<b>rifabutin</b> <small>(see Antitubercular Agents)</small>	Mycobutin	↓		Induces Cytochrome P-450 3A4 metabolism of CsA. This effect is less than that seen with rifampicin; increases clearance of CsA	34, 350, 351
<b>rifampicin</b> <small>(see Antitubercular Agents)</small>		↓		Induces CsA metabolism	57, 161, 164, 356, 357, 430
<b>rifampin</b> <small>(see Antitubercular Agents)</small>	Rifadin, Rifamate, Rifater, Rimactane	↓ ↓	<b>nephrotoxic</b> <small>(isolated reports)</small>	Induces CsA metabolism and decreases bioavailability (F) Cytochrome P-450 induction	34, 352-355 552
<b>rifamycin SV</b> <small>(see Antitubercular Agents)</small>		↓			358
<b>rofecoxib</b>	Vioxx		<b>nephrotoxic</b> <small>(isolated reports)</small>	As seen with other NSAIDs	582
<b>roxithromycin</b> <small>(see Macrolides)</small>		↑		Insignificant rise in CsA levels; rise in levels due to inhibition of Cytochrome P-450 3A4 metabolism of CsA	162, 359-362
<b>sertraline</b>	Zoloft			May inhibit enzymes responsible for CsA metabolism	198
<b>sibutramine</b>	Meridia	↑		Both sibutramine and cyclosporine undergo P450 3A4 metabolism	649

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>sildenafil</b>	Viagra			Cyclosporine and sildenafil may have competition for catalysis by Cytochrome P-450 3A4	596, 650
<b>simvastatin</b> <small>(see HMG CoA Reductase Inhibitors)</small>	Zocor			CsA may inhibit the metabolism of simvastatin resulting in increased levels of simvastatin, CsA free fraction and clearance may be increased by simvastatin. No changes in CsA Pharmacokinetics	276, 363-366, 462, 531, 651
<b>sirolimus</b> <small>(Rapamycin)</small>	Rapamune®	↑		Impact on the immune system may be additive when given with CSA; increases in serum creatinine and decreases in GFR and CsA clearance may be seen. Simultaneous administration of Neoral® increases sirolimus C <sub>max</sub> and AUC, but this effect is mitigated if the medications are given four hours apart; and simultaneous administration with Sandimmune® may cause smaller increases in sirolimus trough concentrations. Sirolimus and CsA compete for P-450 3A4 enzyme and multidrug-resistant P-glycoprotein.	475, 558, 559, 575, 621, 633
<b>sparfloxacin</b>	Zagam			Cyclosporine decreases secretory-directed transport due to inhibition of P-glycoprotein	584
<b>spiramycin</b> <small>(see Macrolides)</small>		↑ †			367
<b>spironolactone</b> <small>(see Diuretics)</small>	Aldactazide, Aldactone			Hyperkalemia	78
<b>St. John's wort</b> <small>(<i>Hypericum perforatum</i>)</small>		↓ ↓			522, 523, 533, 535, 537, 553, 557, 617-618, 622-626, 653-655
<b>sucralfate</b>	Carafate			Neurotoxic effects associated with the elevated aluminum levels from the sucralfate	14, 36
<b>sulfadiazine</b>		↓			368
<b>sulfamethoxazole</b>	Gantanol	↑ † ↓ †		Use of HPLC assay may result in increased CsA levels	369, 474
<b>sulfamethoxazole/trimethoprim</b> <small>(see Sulfonamides &amp; Antibiotics)</small>	Bactrim, Cotrim, Septra, Sulfatrim	↑ † or ↓ †	nephrotoxic <small>(well-substantiated)</small>	Use of HPLC assay may result in increased CsA levels due to interference by the sulfamethoxazole component.	370, 474, 486
<b>Sulfasalazine</b>		↓		Possible induction of Cytochrome P-450 metabolism	508

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>sulfinpyrazone</b>	Anturane	↓		Interference with assay results	14, 35, 39, 566
<b>Sulfonamides</b> (refer to individual agents for effects)	various	↓ † ↑ †		Must monitor renal function	42, 372, 474
<b>sulindac</b> (see NSAIDs)	Clinoril	↑	nephrotoxic (isolated reports); decreases GFR and RBF	Inhibits Cytochrome P-450 3A4 metabolism of CsA	295, 296, 371
<b>sulphadimidine</b> (see Sulfonamides)		↓			14, 16, 55
<b>sulphadimidine/ trimethoprim</b> (see Sulfonamides)		↓		Decreases in CsA levels seen only with the IV form	33, 413, 414
<b>tacrolimus</b> (FK-506)	Prograf	↑	nephrotoxic (isolated reports)	Decreases metabolism of CsA; increases cellular uptake of CsA; increases toxicities, including muscle and joint aches and lower limb paresthesia	57, 373, 374 451
<b>tamoxifen</b>	Nolvadex	↑			35
<b>teniposide</b> (VM26)	Vumon			CsA has been reported to increase the bioavailability of VM26	375, 572
<b>terbinafine</b>	Lamisil	↓ †		Terbinafine may induce the metabolism of CsA	446-448
<b>terfenadine</b>	Seldane			Competitive inhibition of the formation of the alcohol metabolite	376
<b>thalidomide</b>				Prevents graft versus host disease (GVHD); acts synergistically to create a tolerance to GVHD	24
<b>theophylline</b>	Slo-bid, Slo-phylline, Theo-dur, Uni-dur, etc.		Protective renal effect		120, 345, 377
<b>thiazides</b> (see Diuretics)	various	↑		Hyperlipidemia	38, 57, 89
<b>ticarcillin</b>	Ticar, Timentin	↑			14, 35
<b>ticlopidine</b>	Ticlid	↓ ↓		Alters metabolism of CsA. Produces a decrease in the concentration/dose ratio of CsA after introduction of ticlopidine	378-381, 449 543, 569

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
<b>tobramycin</b> (see Aminoglycosides)	Nebcin	↑	nephrotoxic (well-substantiated)		14, 39
<b>tresperimus</b>				Together have synergistic activity	597
<b>triamterene</b> (see Diuretics)	Dyazide, Dynerium, Maxide			Hyperkalemia	382
<b>trifluoperazine</b>	Stelazine			Additive immunosuppression	383
<b>trimethoprim</b>	Bactrim (DS), Proloprim, Septra (DS), Trimplex, Sulfatrim	↓	nephrotoxic (well-substantiated)	Induces metabolism of CsA	55, 57, 369
<b><i>Tripterygium wilfordii</i></b>				Concomitant therapy with CsA successfully suppressed immune system in cardiac transplant rats	528
<b>troglitazone</b>	Rezulin	↓		Moderate inducer of Cytochrome P-450 3A4	494, 600
<b>troleandomycin</b> (see Macrolides)	Tao Capsules	↑		Increase in CsA levels has not been widely reported, but should be expected	16, 384
<b>ursodeoxycholic acid</b> (ursodiol)	Actigall	↑ †		Shortened t <sub>max</sub>	59, 385-388, 452
<b>Vaccines</b>				CsA decreased the efficacy of vaccine prophylaxis; it also increased the patients' vulnerability to active infection if immunized with live vaccines	389-391
<b>valproate sodium</b> (see Anticonvulsants)	Epilim	↓		This depression in CsA levels is not very significant	42
<b>valproic acid</b> (see Anticonvulsants)	Depakene	↓		This depression in CsA levels is not very significant; monitor for hepatotoxicity	14, 38, 39 372
<b>valsartan</b>	Diovan	↑		May be due to both drugs being excreted in the bile	576
<b>vancomycin</b>	Vancocin	↑	nephrotoxic (well-substantiated)		38, 39, 231

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Drug Name	Brand Name	CsA Level	Renal Effects	Additional Effects‡	Citations
vasopressin				Vasopressin's antidiuretic effects are enhanced by CsA	392
vecuronium	Norcuron			Prolonged neuromuscular block	48, 393, 394
verapamil <small>(see Calcium Antagonists)</small>	Calan, Isoptin, Verelan	↑ ↑	Protective renal effect; decreased nephrotoxicity	Gingival hyperplasia; enhanced immunosuppression; decreased early graft non-function or rejection	139, 395-402, 450, 555, 619
vinblastine	Velban, Velsar			CsA dose is correlated with degree of leucopenia produced by vinblastine	460
Vitamin A		↑			242, 403
Vitamin D <sub>3</sub>				Additive effects on T-cell proliferation; additive suppressive effects on the secretion of IL-2, TNF-α, and IFN-γ	37, 404, 544,
Vitamin E, water soluble <small>(d-alpha-tocopherol polyethylene glycol 1000 succinate; TPGS)</small>		↑		TPGS may enhance CsA absorption due to micelle formation and increase its solubility	405-412
warfarin <small>(see Anticoagulants)</small>	Coumadin	↑ † or ↓ †			14, 38, 40, 41

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