

Potential Part D Drug-Drug Interactions

The Centers for Medicare & Medicaid Services developed performance and quality measures to help Medicare beneficiaries make educated decisions about their health care when choosing a Part D plan. As part of these measures, CMS analyzes drug-drug interactions that overlap by one day. CMS supplies Part D sponsors (i.e., contracts) with monthly reports about the DDI measure calculated with the Medicare prescription drug event data.

The following drug interaction pairs are measured by CMS for each health plan that offers a PDP or MA-PD Plan. The DDI rate is defined as the percentage of Medicare beneficiaries who received at least one of the target medications with at least one day overlap with a contraindicated medication during the measuring period.

If any of the potential DDI listed below exist please contact the member’s physician to discuss.

Target medication	Contraindicated medication	Clinical significance
Acitretin (Soritane [®])	Norethindrone (0.35mg) <ul style="list-style-type: none"> • Camila[®] • Errin[®] • Jolivette[®] • Nor-QD[®] • Nora-BE[®] • Ortho-Micronor[®] 	Use of acitretin with norethindrone oral has been reported by the manufacturer of acitretin (Soritane [®]) to interfere with the contraceptive effects of low dose progestin contraceptives (microgestin “minipill” preparations).
Itraconazole (Sporanox [®])	Pimozide (Orap [®])	Itraconazole may increase the plasma concentrations of pimozide that can lead to cardiovascular toxicity. Use of these two drugs is contraindicated. Itraconazole inhibits CYP 3A and decreases the elimination of pimozide.
Itraconazole (Sporanox [®])	Dofetilide (Tikosyn [®])	Official package labeling for itraconazole and ketoconazole contraindicates their use with dofetilide. The pharmacologic effects and concentrations of dofetilide may be increased. Cardiovascular toxicity, including torsades des pointes, may occur. Itraconazole inhibits CYP3A4 and decreases the metabolic elimination of dofetilide.
Itraconazole (Sporanox [®])	Tricyclic antidepressants <ul style="list-style-type: none"> • Clomipramine (Anaphanil[®]) • Imipramine (Tofranil[®]) • Doxepin (Sinequan[®]) • Amitriptyline (Elavil[®]) 	The use of TCAs and MAOIs may lead to severe and sometimes lethal toxicity. This may be due to additive or synergistic pharmacologic action due to excessive neurotransmitters at the receptor sites. Serotonin syndrome has also been reported (somnolence, confusion, fever, myoclonus, intermittent convulsions and elevated serum creatine kinase

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		concentrations).
MAO inhibitors <ul style="list-style-type: none"> • Isocarboxazid (Marplan[®]) • Phenelzine (Nardil[®]) • Tranylcypromine (Parnate[®]) 	Serotenergic medications <ul style="list-style-type: none"> • Buspirone (Buspar[®]) • Citalopram (Celexa[®]) • Dextromethorphan • duloxetine (Cymbalta[®]) • Escitalopram (Lexapro[®]) • Fluoxetine (Prozac[®]) • Fluvoxamine (Luvox[®]) • Meperidine (Demerol[®]) • Mirtazapine (Remeron[®]) • Paroxetine (Paxil[®]) • Sertraline (Zoloft[®]) • Sirbutramine (Meridia[®]) • Tramadol (Ultram[®]) • Trazodone (Desyrel[®]) • Venlafaxine (Effexor[®]) 	<p>Concomitant use of MAOI and SSRI / serotenergic medications are usually contraindicated in most patients. Serious, sometimes fatal reactions may occur, including fever (hyperthermia), rigidity, myoclonus, autonomic instability with possible rapid fluctuation of vital signs and mental status changes that include extreme agitation progressing to delirium and coma (citalopram, escitalopram, fluoxetine, fluvoximine, paroxetine, sertraline).</p> <p>MAOI + buspirone – Elevated blood pressure</p> <p>MAOI + dextromethorphan – Hyperpyrexia (high fever), abnormal muscle movement, psychosis, hypotension, coma and death have been associated with combination. Co-Administration is contraindicated.</p>
MAO inhibitors <ul style="list-style-type: none"> • Isocarboxazid (Marplan[®]) • Phenelzine (Nardil[®]) • Tranylcypromine (Parnate[®]) 	Sympathomimetics <ul style="list-style-type: none"> • Amphetamines (Adderall[®]) • Benzphetamine (Didrex[®]) • Cocaine • Dextroamphetamine (Dexedrine[®]) • Diethylpropion (Tenuate[®]) • Dopamine • Ephedrine • Isometheptene (Midrin[®]) • Methylphenidate (Ritalin[®]) • Phentermine (Adipex-P[®]/ Ionamin[®]) • Phenylephrine • Pseudoephedrine 	Sympathomimetic drugs with indirect activity can release large quantities of norepinephrine, which accumulates during monoamine oxidase inhibition and produces excessive noradrenergic stimulation. The potential danger of this interaction has been well documented. Hyperpyrexia (high fever), cardiac arrhythmias and severe hypertension including hypertensive crisis may result.
Nitrates <ul style="list-style-type: none"> • Isosorbide dinitrate (Isordil[®]) 	ED drugs <ul style="list-style-type: none"> • Sildenafil (Viagra[®]) • Tadalafil (Cialis[®]) • Vardenafil (Levitra[®]) 	The risk of nitrate-induced hypotension may be increased by co-administration of phosphodiesterase inhibitors (sildenafil, tadalafil and vardenafil). Concurrent use

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<ul style="list-style-type: none"> • Nitroglycerin (Nitrostat[®]) • Isosorbide mononitrate (Imdur[®]) 		of these agents is contraindicated in official package labeling for these agents.
Pimozide (Orap [®])	Azole antifungals <ul style="list-style-type: none"> • Fluconazole (Diflucan[®]) • Itraconazole (Sporanox[®]) • Ketoconazole • Voriconazole (Vfend[®]) 	Pharmacologic effects of pimozide oral may be increased by azole antifungals. Elevated plasma concentrations with cardiovascular toxicity may occur. Concomitant use is contraindicated in manufacturer's literature for pimozide oral and azole antifungals. Voriconazole has the potential for QT interval prolongation and rare occurrences of torsades de pointes.
Pimozide (Orap [®])	Macrolide antibiotics <ul style="list-style-type: none"> • Clarithromycin (Biaxin[®]) • Erythromycin • Azithromycin (Zithromax[®]) 	Macrolide antibiotics may increase plasma concentrations and pharmacologic effects of pimozide oral. Additive cardiotoxicity may occur when pimozide oral and macrolides are co-administered; concomitant use is contraindicated in manufacturer labeling for pimozide oral.
Pimozide (Orap [®])	<ul style="list-style-type: none"> • Amprenavir (Agenerase[®]) • Atazanavir (Reyataz[®]) • Cyclosporine (Neoral[®]) • Delaviradine (Rescriptor[®]) • Diltiazem (Cardizem[®]) • Fluvoxamine (Luvox[®]) • Grapefruit • Indinavir (Crixivan[®]) • Nelfinavir (Viracept[®]) • Quinupristin/dalfopristin (Synercid[®]) • Ritonovir (Norvir[®]) • Saquinavir (Invirase[®]) • Sertraline (Zoloft[®]) • Telithromycin 	<p>Protease Inhibitors — Pharmacologic effects of pimozide oral may be increased by protease inhibitors. Elevated plasma concentrations with cardiovascular toxicity may occur. Concomitant use is contraindicated in manufacturer's literature.</p> <p>SSRIs — Plasma concentrations of pimozide oral may be increased by SSRIs. Co-administration of pimozide oral with SSRIs is contraindicated in official package labeling for SSRIs.</p> <p>Grapefruit/grapefruit juice — Pharmacologic effects of pimozide oral may be increased by grapefruit juice. Elevated plasma concentrations with cardiovascular toxicity may occur. Concomitant use is contraindicated in manufacturer's literature for pimozide oral.</p> <p>Quinupristin/dalfopristin (Synercid[®]) — The risk of QT-interval prolongation and cardiac arrhythmias caused by pimozide</p>

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	(Ketek [®]) <ul style="list-style-type: none"> • Verapamil (Calan[®]) • Fluoxetine (Prozac[®]) 	oral may be increased by co-administration of quinupristin-dalfopristin intravenous.
Rifampin (Rifadin [®])	Anti-arrhythmic medications <ul style="list-style-type: none"> • Amiodarone (Cordarone[®]) • Flecainide (Tambocor[®]) • Propafenone (Rythmol[®]) • Quinidine 	Serum concentrations of antiarrhythmics may be decreased because of CYP3A4 induction by rifampin. Closely monitor serum concentrations when starting or stopping rifampin.
Rifampin (Rifadin [®])	Sedative/hypnotics <ul style="list-style-type: none"> • Midazolam (Versed[®]) • Triazolam (Halcion[®]) • Diazepam (Valium[®]) 	The pharmacologic effects of midazolam, triazolam and diazepam may be decreased because of increased metabolism of benzodiazepines. Monitor clinical response when starting or stopping rifampin.
Tizanidine (Zanaflex [®])	Fluvoxamine (Luvox [®])	Plasma concentrations of tizandidine may be increased by fluvoxamine. These increased plasma concentrations many lead to significant hypotension. Concomitant use is contraindicated.
Tizanidine (Zanaflex [®])	Ciprofloxacin (Cipro [®])	Ciprofloxacin may increase the plasma concentrations of tizandidine. This can cause hypotension and dizziness. Concomitant use is contraindicated.
Voriconazole (Vfend [®])	Ritonavir (Norvir [®])	Plasma concentrations and pharmacologic effects of voriconazole may be decreased by ritonavir. According to the official package labeling, concomitant use of voriconazole and ritonavir (at doses of 400 mg every 12 hours or greater) is contraindicated. Also, co-administration of voriconazole and low-dose ritonavir should be avoided unless the potential benefits outweigh the associated risks.

If you have any questions about this, please call Mary Kay Cutler, Pharm.D., at 248-448-5230