Worst Pills, Best Pills Public Citizen

Muscle Damage from Interactions Between Statins and Other Commonly Prescribed Drugs

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Some of the widely used class of cholesterol-lowering drugs called statins may cause rhabdomyolysis (severe, sometimes fatal, muscle damage) when taken with many other commonly used drugs, such as clopidogrel (PLAVIX) and trimethoprim and sulfamethoxazole (BACTRIM).

What is rhabdomyolysis?

Rhabdomyolysis is the rapid breakdown of muscle tissue, resulting in the release of broken-down muscle tissue into the bloodstream. The broken-down tissue can cause kidney failure, requiring temporary or ongoing dialysis.

What are the symptoms of rhabdomyolysis?

Muscle pain and weakness are the most common signs of statin-induced muscle damage. Sometimes these are signals of only mild to moderate muscle damage, but a person on a statin should consult their prescriber if they have such symptoms.

In some people, a darkening of the urine from broken-down muscle tissue is the first sign of muscle damage, and people who develop this should immediately contact their prescriber.

All statin drugs can cause rhabdomyolysis, even when used alone. But the risk of rhabdomyolysis varies depending on the statin. For instance, we list rosuvastatin (CRESTOR) as a Do Not Use drug due to its increased risk of rhabdomyolysis and kidney damage.

What drugs interact with statins?

For some statins, the risk of rhabdomyolysis is increased when combined with certain other drugs.

CYP3A4 inhibitors

Simvastatin (ZOCOR), lovastatin (MEVACOR) and atorvastatin (LIPITOR) are all metabolized by the enzyme CYP3A4. Taking these statins with other drugs that inhibit CYP3A4, such as

tamoxifen (NOLVADEX) and verapamil (CALAN), can result in rhabdomyolysis because these latter drugs can increase the blood levels of the three statins (See the list of CYP3A4 inhibitors, page 7).

A recent epidemiologic study looked at the risk of rhabdomyolysis in patients taking either simvastatin or pravastatin with and without drugs that inhibit CYP3A4. Rhabdomyolysis was rare with both drugs, but in patients who took no drugs that inhibited CYP3A4, the risk of rhabdomyolysis was higher in patients using simvastatin than in those using pravastatin.

People taking simvastatin with one or more CYP3A4 inhibitors experienced a six-fold increase in the risk rhabdomyolysis, but the use of CYP3A4 inhibitors did not increase the risk of rhabdomyolysis in people who used pravastatin. This is because pravastatin (PRAVACHOL) is not metabolized by the enzyme CYP3A4 or other cytochrome P450 enzymes, so compared to other statins it appears to have the lowest risk of adverse drug interactions such as rhabdomyolysis.

CYP2C9 inhibitors

Fluvastatin (LESCOL) is metabolized by the enzyme CYP2C9, so, theoretically, drugs that inhibit this enzyme,could increase the risk of muscle damage by increasing blood levels of fluvastatin (See the list of CYP2C9 inhibitors, page 7).

What You Can Do

You should only take a statin if diet and exercise have failed to bring your cholesterol to the desired level. Some people can avoid the expense, bother and risk of statins through changes in lifestyle.

Do not use rosuvastatin (CRESTOR) because it has a greater risk of muscle damage and kidney problems than other statins.

If you must take a statin, consider using pravastatin (PRAVACHOL), now available in generic form, because it has the lowest risk of drug interactions among the statins. There is also some evidence to suggest that in addition to having less of a chance of interacting with other drugs, pravastatin has a lower overall risk of muscle damage than other statins.

If you are taking simvastatin (ZOCOR), lovastatin (MEVACOR) or atorvastatin (LIPITOR), and you need to take a CYP3A4 inhibitor for a week or two, it may be prudent to stop the statin while you are taking the CYP3A4 inhibitor but first check with your prescriber about this. If the CYP3A4 inhibitor is to be given for a longer term, your prescriber may decide to lower the dose of your statin or give you pravastatin instead.

No matter what statin you are taking and regardless of any interacting drugs, you should notify your prescriber immediately if you develop muscle pain, weakness or a darkening of your urine.

Table. CYP3A4 and CYP2C9 inhibitors

CYP3A4 Inhibitors
ketoconazole (NIZORAL)
itraconazole (SPORANOX)*
ritonavir (KALETRA, NORVIR)
amiodarone (CORDARONE, PACERONE)***
amprenavir (AGENERASE)
aprepitant (EMEND)
atazanavir (REYATAZ)
clarithromycin (BIAXIN)**
cyclosporine (NEORAL, SANDIMMUNE)
darunavir (PREZISTA)
delavirdine (RESCRIPTOR)
diltiazem (CARDIZEM, CARDIZEM CD, DILACOR XR, TIAZAC)**
erythromycin (E-MYCIN, EES, ERYTHROCIN)

fluconazole (DIFLUCAN)
fluvoxamine (LUVOX)**
imatinib (GLEEVEC)
indinavir (CRIXIVAN)
posaconazole (NOXAFIL)
quinupristin (SYNERCID)
saquinavir (FORTOVASE, INVIRASE)
tamoxifen (NOLVADEX)**
telithromycin (KETEK)*
verapamil (CALAN, CALAN SR, COVERA-HS, ISOPTIN, ISOPTIN SR, VERELAN)
voriconazole (VFEND)

CYP2C9 inhibitors
amiodarone (CORDARONE, PACERONE)***

capecitabine (XELODA)
clopidogrel (PLAVIX)**
trimethoprim and sulfamethoxazole (BACTRIM, COTRIM, SEPTRA)
delavirdine (RESCRIPTOR)
disulfiram (ANTABUSE)
efavirenz (SUSTIVA)
fluconazole (DIFLUCAN)
fluorouracil (5-FU, CARAC, EFUDEX,FLUOROPLEX)
imatinib (GLEEVEC)
metronidazole (FLAGYL)**
miconazole (MONISTAT 1, MONISTAT 3, MONISTAT 7, MONISTAT-DERM)
valproic acid (DEPAKENE)
voriconazole (VFEND

* Do Not Use in Worst Pills, Best Pills
** Limited Use in Worst Pills, Best Pills
*** Last Choice Drug in Worst Pills, Best Pills