



AVOIDING DRUG INTERACTIONS WITH YOUR TKI

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TKIs



Part 2

Any medication has the potential of interacting with other substances, such as foods, beverages, other prescription drugs, supplements and over-the-counter medicines. One reason is that these substances need to be broken down by specialized enzymes in the liver and intestine, and various substances can have different effects on these enzymes.

In Part 1, we looked at how fruit juices can interfere with how your body metabolizes your TKI (tyrosine kinase inhibitor) medication, which may have an impact on the effectiveness of treatment or the frequency of side effects (see **The grapefruit effect: what you need to know**, CML-IQ, July 17, 2014).

Now let's look at some of the drug interactions that can occur with TKIs (Gleevec, Tasigna, Sprycel).

As mentioned in Part 1, most medications are metabolized by a family of enzymes called the cytochrome P450 system. When you take a medication such as a TKI, certain cytochrome enzymes (called CYP3A4) bind to the TKI and eliminate it from the body. However, if another medication is in your body during this process, the other medication can either inhibit 3A4 enzyme action (e.g. by occupying the enzyme so it isn't available to metabolize the TKI), or it can induce the enzyme (i.e. stimulate it so it is more active).

So an inhibitor, by blocking 3A4, prevents the breakdown of the TKI. This means that the amount of drug in your bloodstream increases, which can result in toxicities or side effects. Common inhibitors include anti-fungal drugs such as ketoconazole (Nizoral) and itraconazole (Sporanox); as well as some antibiotics, such as erythromycin (Erythrocin), clarithromycin (Biaxin) and telithromycin (Ketek). These drugs should generally be avoided if you're taking a TKI.

Inducers, which promote 3A4 enzyme activity, speed up the breakdown of TKIs. This means that blood levels of your TKI will be lower than usual and your CML treatment may be less effective. Drugs to avoid include certain epilepsy medications such as phenytoin (Dilantin) and carbamazepine (Tegretol), as well as St. John's wort, an over-the-counter alternative medicine used to treat depression.

TKIs themselves can also affect the metabolism of other drugs, so certain combinations can create problems. For example, medications that have an effect on heart rhythm should generally be avoided. The list of drugs is quite extensive and includes some antibiotics, such as cefazolin (Ancef), levofloxacin (Levaquin), ciprofloxacin (Cipro) and moxifloxacin (Avelox) (as well as those previously mentioned); antidepressants such as fluoxetine (Prozac), venlafaxine (Effexor), amitriptyline (Elavil), imipramine (Tofranil) and citalopram (Celexa); beta-2 agonists used for asthma such as salmeterol (Serevent) and formoterol (Foradil, Symbicort); and medications used to treat heart rhythm problems.

Gleevec may interact with Tylenol, so exercise caution with this combination. Caution is also needed if you are taking a statin to reduce cholesterol, such as atorvastatin (Lipitor), simvastatin (Zocor), or lovastatin (Mevacor). TKIs can increase the blood levels of these drugs so a lower dose of the statin may be better.

As with many other oral medications, stomach acid is needed to break down TKIs. So medications that make the stomach less acidic can create problems in some cases. Acid suppressing medications, such as omeprazole (Losec, Prilosec), pantoprazole (Pantoloc), lansoprazole (Prevacid) and esomeprazole (Nexium), should be avoided if you're taking Sprycel. H2 blockers, such as ranitidine (Zantac) and famotidine (Pepcid), are also not advised. A better option is antacids (e.g. Maalox, Mylanta) taken two hours before or two hours after taking Sprycel.

Acid suppressing medications have less of an effect on Tassigna and Gleevec so they can generally be taken. H2 blockers should be taken either 10 hours before or two hours after taking Tassigna. Antacids should be taken two hours before or two hours after taking Tassigna.

This list of possible drug interactions is not all-inclusive. So it's important to talk to your doctor or pharmacist about any medication – prescription, non-prescription or alternative – before you take it with your TKI.

