# How PK Enhancers Work

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### *OVERVIEW*

HIV attacks cells within the body's immune system. To spread, the virus needs to enter these cells and make copies of itself. The copies are then released from these cells and infect other cells. Treatment with pharmacokinetic enhancers is one way to help stop the virus from replicating and control HIV infection. Pharmacokinetic enhancers are also PK enhancers.

PK enhancers are used to boost the effectiveness of another drug. When the two drugs are given together, the pharmacokinetic enhancer interferes with the breakdown of the other drug, which allows the drug to remain in the body longer at a higher concentration. Pharmacokinetic enhancers are included in some HIV treatment regimens. It's important to note that PK enhancers do not directly treat HIV. Instead, they function to increase the effectiveness of other drugs, typically drugs that belong to the integrase inhibitor or protease inhibitor classes.

PK enhancers are one of 6 classes of antiretroviral drugs (ARVs) used to treat HIV as part of antiretroviral therapy (ART).

### *AVAILABLE PK ENHANCERS*

Currently, there are 2 PK enhancers that the Food and Drug Administration (FDA) has approved for HIV treatment:

- ritonavir (Norvir)
- cobicistat (Tybost)

PK enhancers are also available in several combination medications. Combination HIV medicines contain 2 or more HIV medicines from 1 or more drug classes.

### *PK ENHANCER MECHANISM OF ACTION*

As mentioned, PK enhancers don't directly target and treat HIV. Instead, they inhibit an enzyme in the human body called cytochrome P450 3A4, also called CYP3A4. Normally, CYP3A4 helps break down drugs and other molecules in the body so that they can be eliminated. Drugs that get broken down, or metabolized, by this enzyme are prevented from staying in the body for too long. However, when CYP3A4 is inhibited by a PK enhancer, it allows for the normal drug targets of this enzyme to continue to exist and work in the body beyond what's normal. By preventing the breakdown enzyme from doing its job, the concentration and efficacy of other drugs may be increased.

Not all drugs are broken down by this enzyme. There are many different enzymes involved in the breakdown and excretion of drugs and other molecules in the body. However, some HIV drugs, including certain integrase inhibitors and protease inhibitors are broken down by CYP3A4. Medications like the integrase inhibitor elvitegravir, and the protease inhibitors atazanavir and darunavir can be used with a PK enhancer and potentially have their efficacy improved. PK enhancers used in HIV treatment are also called CYP3A4 inhibitors.

### *SIDE EFFECTS AND DRUG INTERACTIONS*

PK enhancers may cause side effects such as yellowing of the skin or whites of the eyes. Because PK enhancers impact the way some drugs are broken down, they may have significant drug interactions and should not be taken alongside certain medications. Your healthcare provider will provide you with information on what issues you may be at risk for based on what PK enhancer you are taking and what other medications you should avoid. Some individuals may develop kidney issues or a worsening in previous kidney problems when a PK enhancer is taken with specific medications.

PK enhancers may also impact the way other things like vitamins, supplements, and herbal products are broken down. It is important to tell your healthcare provider if you currently use, or are planning to use, any of these products before starting a PK enhancer.

### *THE BOTTOM LINE*

Pharmacokinetic enhancers (PK enhancers) are medications that have made HIV management possible. It is important that the appropriate antiretroviral drug (ARV) regimen for HIV treatment is carefully selected, depending on your medical history, other illnesses, prior HIV treatment, stage of infection, and individual preferences.

If your healthcare provider has prescribed PK enhancers it's important to stick to your treatment plan to manage HIV. If you have side effects from antiretroviral therapy (ART), there are some tips you can try to manage them. More importantly, talk to your healthcare provider for suggestions and recommendations. Your healthcare provider may also change your treatment plan to help relieve side effects.

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