

# 10 Deadliest Drugs

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## Approved by the FDA—but are your meds safe?

*By Maia Szalavitz for MSN Health & Fitness*

When the AIDS activist group ACT UP staged a protest in 1988 in which it “seized control of the FDA,” it responded to widespread frustration with the agency. The FDA was seen as slow, bureaucratic and unresponsive to the plight of patients who needed better drugs—immediately.

Shortly afterwards, the drug approval process was streamlined and dying patients without alternatives were given early access to promising medications. For drugs given “priority review,” approval times dropped from just under three years in 1986 to as little as six months in 1995.

Now, however, many wonder if the FDA went too far in speeding up the approval process of drugs. Critics claim tragic failures like the approval of the painkiller Vioxx, which may have caused up to 100,000 heart attack and stroke deaths, are a direct result of prioritizing speed over safety reviews.

### **How AIDS changed drug approvals**

The AIDS drugs story illustrates the complex challenges facing the FDA.

In 1988, there was only one AIDS drug—AZT. Activists pushed the FDA to rapidly approve the next drug, DDI; they didn’t want to wait for studies long enough to show that it saved lives, because long-term studies could last longer than the survival prognosis for many patients.

Instead, activists urged study of a “surrogate marker” of the drug’s effect on disease progression. Researchers examined whether the medication could increase the number of disease-fighting CD4-cells.

DDI was approved under this testing regime—but the next drug, DDC, turned out to increase CD4-cells without improving survival. “We lost faith in the marker,” says Mark Harrington, whose work in ACT UP on the FDA and other treatment-related issues led to his current position as Executive Director of the Treatment Action Group (TAG) and to serving on advisory panels to the FDA related to AIDS drugs.

When the FDA prepared to approve the first of a new class of drugs based on it, TAG urged caution. “Most of the people in the community didn’t agree and we were very unpopular for a while,” says Harrington.

Drugs in that new class—protease inhibitors—soon proved effective, and by the mid-90s the “AIDS cocktail,” which combines several drugs, had turned the condition from a death sentence to a severe chronic illness.

Between 1995 and 1997, deaths from AIDS dropped by nearly two thirds.

### **Weaker standards**

Loosening drug approval protocols may have dramatically increased the speed at which effective AIDS drugs became available, but now drug companies seeking approval for medications for much less serious conditions can utilize the weaker standards.

Vioxx was approved under these less stringent standards in 1999—and only after millions of people had taken it was research released showing that high doses quintupled the risk of heart attack compared to a similar painkiller, naproxen (Aleve).

“The arguments used for AIDS—which is a horrible killer—were extrapolated to other drugs. Some were appropriate, like cancer drugs—others [like Vioxx and similar drugs] were not. The abuse happened when drug companies made false analogies and were never forced by the FDA to do follow up research,” says Harrington. The notion of surrogate markers and whether they really predict how well drugs work is an ongoing quandary.

“It’s fair to say that [at first] we didn’t have a complete understanding of the strengths of the FDA and the reasons why its practices were put in place,” says Harrington.

Consumer advocates and experts agree that the FDA needs to do a better job at evaluating drug risks and benefits before approval—and should require additional study afterwards.

### **Taking medications with minimal risk**

So what can you do in the meantime to minimize risk from medications? The first thing is to be an informed consumer and be sure that the drugs you take are necessary and have not been flagged as potentially problematic. For example, the mild opioid drugs Darvon and Darvocet have been found to be no more effective than aspirin—and they can cause heart damage.

“Be careful with new drugs, particularly if other options are available,” says Curt Furberg, Professor of Public Health Science at Wake Forest University.

Some consumer groups advocate waiting seven years after approval of a new drug before taking it; by that time, any problems should have become apparent. But Allen Vaida, PharmD, Executive Vice President of the Institute for Safe Medication Practices, disagrees, noting that if everyone followed this advice, it would be

worthless.

## **The 10 deadliest drugs**

Four of the top 10 deadliest drugs are strong opioid painkillers like oxycodone, according to a 2007 study by Furberg and colleagues, which looked at adverse events reported to the FDA.

Furberg's study did not distinguish between medical use and abuse of opioid painkillers, and other research has found that the overwhelming majority of deaths occur in drug addicts, not patients. In addition, most deaths related to opioid painkillers involve taking a combination of four of five other drugs, which makes them seem more deadly than they are. (See also *The Truth About Painkillers*). Nonetheless, only take these medications exactly as prescribed.

The fifth deadliest drug is another painkiller, this one over-the-counter: acetaminophen (Tylenol). It can cause irreversible and sometimes fatal liver damage in doses that are not much higher than the effective dose. Many prescription painkillers (anything with "cet" in the name, for example) also contain acetaminophen. Extreme care must be taken not to exceed prescribed dosage.

Rounding out the top 10 are two antipsychotic medications, clozapine and risperidone (Risperdal); interferon-beta, a drug that helps regulate the immune system; and two immune-affecting drugs, Infliximab and Etanercept. The antipsychotics should only be taken if there are no other alternatives, as this class of medication can increase mortality risk overall. The immune drugs have highly variable effects, so need to be used cautiously.

### **Rank - Drug - Type - Deaths 1998-2005**

- 1 - Oxycodone - Prescription opioid painkiller\* - 5548
- 2 - Fentanyl - Prescription opioid painkiller\* - 3545
- 3 - Clozapine - Antipsychotic - 3277
- 4 - Morphine - Prescription opioid painkiller\* - 1616
- 5 - Acetaminophen - Over-the-counter painkiller - 1393
- 6 - Methadone - Prescription opioid painkiller\*/addiction medication - 1258
- 7 - Infliximab - Immune-system modulating drug - 1228
- 8 - Interferon beta - Immune-system modulating drug - 1178
- 9 - Risperidone - Antipsychotic - 1093
- 10- Etanercept - Immune-system modulating drug - 1034

**Source: Moore TJ et al., *Serious Adverse Drug Events Reported to the Food and Drug Administration, 1998-2005, Archives of Internal Medicine, Sept. 10., 2007; 167 (16): 1752-1759***

### **Drug interactions**

It's certainly crucial to improve the FDA's approval process and to reduce the risks of unsafe medications being marketed, but once drugs hit the shelves only informed consumers and physicians can ensure they are used appropriately.

Making sure that all your doctors know about everything that you are taking is critical. Vaida notes that many patients are seeing several doctors and can forget to inform them all.

To avoid interactions between medications, use the FDA's medicine record chart—or "brown bag" medications and bring them to each doctor's office for review.

<http://www.wxii12.com/health/15719531/detail.html>