A Tale Of Two – No, Three – Drugs

Wednesday, December 28, 2011

It was the best of times, it was … no, check that, it *was* the best of times. In the recent decision, Wendell v. Johnson & Johnson, 2011 WL 6291792 (N.D. Cal. Dec. 15, 2011), the moving defendants all received summary judgment, so it was just the best of times.

Wendell itself is something of a three ringed circus, insofar as the facts involve three drugs – mercaptopurine (also known, for reasons unknown to us, as "6-MP," which has the advantage of being shorter), Remicaid, and Humira – and the interaction between their respective warnings. The only simple thing about the facts is there is only one prescribing physician.

Here goes.

In 1998, the plaintiff's decedent was diagnosed with inflammatory bowl disease ("IBD"), a nasty autoimmune condition. Prescriber, who didn't ordinarily review drug labeling – but did just enough to preclude summary judgment on that basis – began drug treatment. Initially, the treatment featured Prednisone. Unfortunately Prednisone is well-know among those who prescribe and use it (such as Bexis' daughter, for a while) for causing adverse reactions approximately 100% of the time.

The decedent didn't like the reactions, and Prednisone isn't a very good long-term treatment for a chronic condition anyway. Thus, by 1999, the prescriber went with 6-MP to try to get the decedent off Prednisone. 6-MP isn't without its own risks, either. "At the time [the prescriber] prescribed 6–MP he was aware of a paper reporting the occurrence of lymphoma [that's a kind of cancer] in adults taking the drug." The prescriber warned the decedent about this, although he might have said "malignancy" rather than the precise type.

Apparently, the attempted substitution didn't work all that well, because almost three years later the poor man is still taking both Prednisone and 6-MP. All this (and a lot of what follows) is from the "Background" section of Wendell, 2011 WL 6291792, at *1-5, by the way.

Still trying to get the decedent off Prednisone, the prescriber, now in mid-2002, discusses adding Remicade to the mix. Remicade is an "anti-tumor necrosis factor" drug – an "TNF inhibitor." The tumor necrosis factor in the body causes inflammation, and inflammation is a major problem in a whole host of autoimmune conditions, including IBD. Unfortunately, "tumor

necrosis" means exactly what it sounds like – tumor death. Tumor necrosis factor also kills tumors. Inhibit TNF, as this type of drug does, and one of the body's defenses against cancer goes away.

Thus, Remicade (and probably all TNF inhibitors) is also associated with increased risks of malignancies. It's a trade-off: almost a certainty of less inflammation for an increased risk of possible cancer.

The prescriber knew this, too. And "virtually always" informed his patients of an increased risk of tumors and malignancies.

In 2005 and 2006, more information became available about a possible synergistic effect between 6-MP and Remicade, involving a particularly dangerous form of lymphoma. This development culminated in 2006 with an FDA black box warning about using these drugs in combination.

The prescriber was contemporaneously aware of all of this. Fortunately, the stuff also worked. By mid 2006, the decedent's IBD was in remission. He was taken off Remicade.

One problem with autoimmune conditions is that once they're beat, they don't always stay beat. Half a year later, in November, the decedent had a relapse. Instead of Remicade and 6-MP, the prescriber prescribed Humira and 6-MP. When asked why he had switched from one TNF inhibitor to another, the prescriber stated:

> "So in November '06, we had been aware for some time of complication of hepatosplenic T-cell lymphoma, so that would have been part of my discussion with the family. Ease of therapy is always a discussion with Humira versus Remicade."

Wendell, 2011 WL 6291792, at *4.

However, it was also true that, at that time Remicade bore the aforementioned black box warning about cancer risk, while Humira did not. The prescriber said, essentially, that the black box didn't make much difference to him, since he already was aware of the risk and discussed it with his patients. In addition to being easier to administer, Humir, also had (the prescriber said, we have no independent idea) a "superior" safety profile for other reasons, primarily being 100% human (as opposed to being produced from genetically modified mice) in its origin.

Wendell is a product liability suit, so necessarily the worst happened. After using this second TNF inhibiter for seven months, the decedent got the nasty lymphoma warned about in the Remicade black box and died.

On this record the makers of Humira and 6-MP moved for summary judgment under the learned intermediary rule. The maker of Remicade did not (also for reasons unknown to us).

The court granted the motions.

Here's why.

The prescriber knew full well about the risks involved when he prescribed those drugs. It didn't matter that the black box warning was only on Remicade, because he saw it on that drug before prescribing the other one.

California law is quite good, going back even before Motus v. Pfizer, Inc., 358 F.3d 659 (9th Cir. 2004), on there being no duty – or no causation – where plaintiffs demand that physicians be warned about things they already know:

"[The prescriber] knew of the risk of malignancies associated with 6–MP and Humira, but still prescribed the medication. Thus, there is insufficient evidence to create a material dispute of fact as to whether the warnings that Plaintiffs contend should have been given would have changed [the decedent's] treatment."

Wendell, 2011 WL 6291792, at *6. Indeed, the prescriber had known about the risk of 6-MP since day one – and probably warned the plaintiff about it way back then. Id.

Then it gets really interesting. Plaintiffs love to claim than any post-injury change in prescribing habits means that the same change could have been induced earlier had only there been adequate warnings. But rarely is there any real proof of this. In Wendell the court required some supporting evidence, and when none was forthcoming, pitched the claim:

"Nor is there evidence that a warning specific to pediatric patients or specific to treatments combining 6-MP with TNF-blockers would have led [the prescriber] to stop prescribing 6-MP alone or in combination. . . . Contrary to [plaintiffs'] contention, **evidence that [he] ceased prescribing TNF-blockers in combination with 6–MP after [the decedent's injury] does not prove that he would have changed his prescription practices based on the warning they suggest**. A warning about rare occurrences . . . associated with

therapy combining 6-MP and Remicade is **bound to have less persuasive power** than an instance of the disease affecting a doctor's own patient follow[ing] that therapy."

Id. at *7 (emphasis added). In the end, the issue (at least as to 6-MP) boiled down to prescription despite prior knowledge, "[T]he undisputed fact is that [the prescriber] was already aware of the risk of lymphomas associated with 6-MP, but still chose to prescribe the drug." Id.

Touché.

As to Humira, given the timing of the first prescription, the causation fight was won for these reasons:

- As with 6-MP, a mere subsequent change in prescribing habits, with no additional affirmative evidence, did not mean that it would have happened earlier had there been different warnings. Id.
- The "better safety profile" wasn't linked to black box warnings, or to cancer risk at all, but to a 100% human origin product having fewer allergenic risks – a major concern with an autoimmune patient. Id. at *8.
- With the prescriber already knowing about the risk, there's no evidence that the different state of warnings (black box versus no black box) played any part in the prescription decisions. Id.
- Since the prescriber had prescribed other drugs with cancer risks, whether or not the prescriber believed that Humira had that risk was not by itself causal. Id.
- The plaintiff parents' self-serving statements that they would never have allowed the treatment had they been warned, was immaterial, since the decedent was an adult and made his own treatment decisions. Id.

In states like California, where the basic law concerning learned intermediary causation is well established, collecting analogous fact patterns where causation is defeated as a matter of law is the name of the game. Wendell has some good ones.