

## What do we need to be telling our patients about opioids together with acetaminophen?

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Opioids together with acetaminophen are by far the most commonly prescribed prescription products. Hydrocodone combined with acetaminophen is the number one dispensed medication in the United States market (Table 1).<sup>1</sup> When the recommended dosage guideline is followed the combination of an opioid and acetaminophen is safe and highly effective.<sup>2</sup> The problem, several surveys consistently indicate, is that a quarter of our patients (or 12 million Americans) take more than the recommended dose of pain relievers. Most of us know that acetaminophen can cause liver damage, but a lot of our patients do not realize that there is a narrow therapeutic index.<sup>3</sup> A large number just do not realize that it takes just a little more than the recommended amount to put them in the danger zone. By reducing the acetaminophen content in combination pain relievers to 325 mg, this recommendation by the Food and Drug Administration (FDA) will serve two purposes. One, it will obviously take more to reach the maximum which for most people is 4 g (4,000 mg) of acetaminophen per day, and second, this change will help get the word out that taking just a little more than the recommended amount may get you into serious trouble.

Titrate to effect, right? That is what most of our patients with pain know works with opioids. So how serious of a problem is acetaminophen-induced liver damage and death? More than 150 people in the United States die on average every year from accidentally taking too much of the drug. Seventy-eight thousand land in the emergency room and more than 33,000 are hospitalized from either intentional or unintentional overdose of the drug.<sup>4-6</sup> These data are from the American Association of Poison Control Centers and are likely to be an under estimation. So what is the acetaminophen margin between a safe dose and a potentially harmful dose? The caveat is that there is some

variability among individuals. After the maximum daily amount of 4,000 mg has been reached, a harmful amount for some individuals can be as little as six additional extra strength Tylenol. This amount can put an individual in the danger zone for liver damage. In most toxicity cases, it has been 2-2.5 times the maximum daily recommended dose. As a comparison, ibuprofen, Advil, can cause stomach and gastrointestinal problems at the recommended dose. Aspirin is the same. However, it takes a whole lot more ibuprofen or aspirin to cause death. In one case, 20 times over the maximum daily recommended ibuprofen dose. You have to take six to eight times the maximum recommended dose of aspirin for it to become toxic to your system in an acute ingestion.

The best advice for our patients is to let them know that the FDA has asked prescription drug manufacturers to standardize and lower acetaminophen levels in combination drugs to no more than 325 mg of acetaminophen in a tablet or capsule.<sup>7</sup> They can further reduce their risk of taking too much acetaminophen by reading and following the label. Let them know that prescription labels may list abbreviations for acetaminophen such as APAP. If in doubt, ask a pharmacist. Our patients should be advised to both keep track of the total daily amounts of acetaminophen and to not take more than one product that contains acetaminophen at any given time. If it is necessary to take two or more products containing acetaminophen, use a log to keep track of how much and how often you take the medications.

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**Table 1. Top products by prescriptions**

	Dispensed prescriptions MN	2010	2009	2008	2007	2006
	Total US market	3,995.2	3,949.2	3,866.3	3,825.1	3,706.4
1	Hydrocodone/acetaminophen	131.2	128.2	124.1	119.2	112.4
2	Simvastatin	94.1	83.8	67.5	47.9	14.4
3	Lisinopril	87.4	82.8	76.8	71.1	65.2
4	Levothyroxine sodium	70.5	66.0	61.2	54.6	49.8
5	Amlodipine besylate	57.2	51.3	44.6	27.9	–
6	Omeprazole (RX)	53.4	45.4	35.1	26.6	18.0
7	Azithromycin	52.6	53.8	51.0	46.3	36.5
8	Amoxicillin	52.3	52.4	50.9	53.2	54.7
9	Metformin HCL	48.3	44.3	42.3	40.2	38.4
10	Hydrochlorothiazide	47.8	47.9	48.5	48.5	48.0
11	Alprazolam	46.3	43.9	41.7	39.8	37.6
12	Lipitor®	45.3	51.7	58.5	65.8	74.0
13	Furosemide	43.4	43.5	44.1	44.2	44.3
14	Metoprolol tartrate	38.9	41.1	32.6	31.6	29.2
15	Zolpidem tartrate	38.0	35.1	29.9	16.0	–
16	Atenolol	36.3	39.3	41.8	44.7	46.1
17	Sertraline HCL	35.7	34.2	32.7	31.6	10.8
18	Metoprolol succinate	33.0	26.9	41.5	21.0	0.6
19	Citalopram HBR	32.1	27.1	22.4	17.8	14.0
20	Warfarin sodium	32.0	31.6	30.2	28.8	26.7
21	Oxycodone/acetaminophen	31.9	30.2	28.4	25.9	22.8
22	Ibuprofen (RX)	31.1	30.3	28.5	27.7	26.8
23	Plavix®	29.5	29.9	28.9	25.1	18.4
24	Gabapentin	29.3	25.4	22.2	20.0	18.5
25	Singulair®	28.7	28.6	29.0	31.0	28.1

Source: IMS Health, National Prescription Audit, December 2010.

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