Editorial

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Ask Your Doctor if Direct-to-Consumer Drug Ads Are Right for You

It is the 19th of May in the year of our Lord, 1983, and a pharmaceutical ad—the first of its kind—appears on your low-definition, convex screen TV.[1] A man in a suit and tie and a British accent stands in front of a chalkboard to explain to you that the only difference between Motrin and his company's drug Rufen is the cost: they are both forms of the generic drug ibuprofen.

By today's standards, the Rufen ad is like watching shadows on the wall of Plato's cave, but it spurred the US Food and Drug Administration (FDA) to ask for a moratorium on further ads until they had time to think about the idea. Two years later, in 1985, the FDA approved the use of what would become better known as direct-to-consumer advertising (DTCA), mandating that the ads follow a rigid set of rules that included disclosure of side effects.

It took a while, but by the mid-90s, pharmaceutical companies were beginning to push the proverbial envelope with more elaborate "Ask-your-doctor-if-Vaguetril-could-be-right-for-you" ads. In 1997, the FDA loosened things up a bit, allowing TV drug ads to refer viewers to print ads or other sites for more detailed prescribing information.

The move made ads more consumer friendly; and with that, a multibillion-dollar industry was born. If you think pharmaceutical ads are sponsoring large swaths of television programming, it isn't just your imagination (although if it were your imagination, and you think your memory isn't what it used to be, ask your doctor if Memeron [*memorcorzene*] could be right for you). According to Kantar Media, DTCA for pharmaceuticals increased by over 60% from 2012 to 2016, from $3.9 billion to $6.4 billion, and the vast majority of that new spending went into television commercials.[2]

Digital media production has become so sophisticated that it's sometimes hard to know what is real; the only limit to what can be portrayed on the modern screen is our imagination. Thankfully, the FDA Office of Prescription Drug Promotion (OPDP) still has some power to prevent consumers from being mildly misled *or* spectacularly misinformed.

The OPDP recognizes three basic kinds of drug ads, the simplest being "help-seeking advertisements."[3] These are not regulated by the FDA because by definition they don't include a specific product (although drug companies can include their name in the ad). This type of ad simply describes a disease or a condition—osteoporosis for example—and then encourages the viewer to talk with their doctor or call 1-800-VERT-0-PLASTY or go to *thoseblastedosteoblasts.com* for more information.

So-called "reminder advertisements" are allowed only for drugs that don't carry serious side effects. The OPDP also mandates that these ads "cannot suggest, in either words or pictures, anything about the drug's benefits or risks," which would include, as an example, displaying a picture of lungs in an asthma drug ad.[4] The OPDP website's example of an acceptable reminder ad shows someone sliding a few white pills out of a pill jar and into their hand, over the words "Ask your doctor about Arbitraer."[5] Many doctors would respond by asking a pharmaceutical marketing expert to remind them why one would ever want to spend money on a reminder ad.

The third type of commercial—product claim ads—dominate what we see on TV: a prescription drug (the "product") is identified both by brand and generic name for the treatment of at least one FDA-approved indication (the "claim"). The benefits and

risks of the drug must be presented in consumer-friendly language and in what the FDA calls "a balanced fashion."

For a TV product claim ad, the drug's most important risks must appear in the audio portion of the ad, as should instructions for how viewers can access the rest of the risks found in the drug's prescribing information. Typically, this is via a website, phone number, or a print ad—each of which is obligated to provide the nitty gritty that the TV ad did not.[6]

The obvious practical question is "How does the FDA enforce these laws?", and the best answer is probably "loosely."

Although many companies voluntarily seek advice from the OPDP, there is no mandated preapproval process for these ads. So as the OPDP confesses, "We see many ads at about the same time the public sees them."[7] And you don't have to be an English major or a lawyer to see how difficult it might be to objectively define the terms "consumer-friendly," "balanced," and "most important."

With no preapproval process, the system works on a "better to ask for forgiveness than permission" basis. If reviewers at the OPDP find problems with a particular ad, they will send a letter to the drug company indicating specifically how the ad violated the law and ask that it be either corrected or pulled. Given the timeframe for OPDP review, an ad campaign can run unfettered, or even to its planned conclusion, before consumers are ever notified that it included false or misleading information.

These letters are a rare event; the OPDP sent 9 letters in 2015, 11 in 2016, and 5 in 2017.[8] Either that's because the pharmaceutical industry is a well-behaved bunch, or because the FDA/OPDP is woefully understaffed, or some combination of the two.

Looking past the OPDP's tepid "after-sight" powers, one has to admit that pharmaceutical ads are a fascinating mix of media glitz, psychological savvy, and yes, even science. It is no surprise that these commercials aim to maximize the perception of benefit and minimize the perception of risk, within the limits set by the OPDP on one side, and the threat of consumer litigation on the other.

To that end, the next time you see a direct-to-consumer pharmaceutical ad on TV, compare the "most important risks" being recited by the voiceover (mandated) with the visual images presented at the same time (not mandated). There is a disconnect.

In one ad, a middle-aged woman with a deep vein thrombosis (DVT) switches from warfarin to Eliquis.[9] As she herself recites the risks of taking Eliquis, we see her working in her recently opened children's clothing store. She makes paint choices with her husband; her son flips over the "Open" sign on the front door; customers arrive to "Create a T-shirt"; she hands a customer her bag of purchases. We do not see a visual that illustrates the stated risk of "a sudden sign of bleeding." We do not see her dropping to the ground because of an intracerebral hemorrhage.

In a Xarelto ad, as the risks are recited, an Olympic medalist swimmer with a history of pulmonary embolism challenges a friend to a "race" on a stationary bike at the local gym.[10] We are not presented with a digital rendering of what her potential bleeding stomach ulcer might look like. Afterward, the two enjoy a salad. Ah yes, the recurring subliminal message in novel oral anticoagulant ads: freed from warfarin, you can get back to salads!

Sometimes the contrast is just bizarre. An ad for the lung cancer drug Opdivo shows a grandfather fishing with his son and his Opie-looking grandson, dangling their legs off the end of a dock on a blue mountain lake.[11] And as the viewer absorbs this visual Hallmark moment, the narrator drones through a litany of possible side effects: "cough, chest pain, shortness of breath, diarrhea, severe stomach pain or tenderness, severe nausea or vomiting, extreme fatigue, constipation, excessive thirst or urine, swollen ankles, loss of appetite, rash, itching, headache, confusion, hallucinations, muscle or joint pain, flushing, fever, or weakness."

In the quest for market share, pharmaceutical ads are not above a little semantic slight-of-hand. A 2007 study from the School of Journalism and Media Studies at San Diego State University noted how ads often use qualifying language to diminish drug-related side effects.[12] A sentence they attribute to a Flonase ad read (italics mine) "*If* side effects occur, they are generally *mild* and *may* include. . ." The vague language comes on the benefit side too. Our shop owner with a DVT reminds us that Eliquis had "significantly less" bleeding than the standard treatment, whatever that means.

As the Xarelto ad with a NASCAR driver and an Olympic swimmer demonstrated, when you finally do get some hard numbers, something "sciency," those too can be spun. As large blue crystals representing various blood clotting factors are shown floating over an anatomically skewed graphic of the heart and some blood vessels, viewers are informed that "warfarin interferes with at least six blood clotting factors. Xarelto is selective, targeting just one critical factor, interacting with less of your body's natural blood-clotting function."

Warfarin *interferes*, willy-nilly. Xarelto *interacts*, selectively. I might take the Xarelto, but only after I ask my

doctor if Xarelto—and direct-to-consumer drug ads—are right for me.

Someone has already decided they're right for *us*—and also for New Zealand, the only other country in the world that allows these kinds of commercials. It wasn't a new idea, but in 2015, the American Medical Association called for a ban on DTCAs for prescriptions drugs and medical devices.[13] As anticipated, Big Pharma and Congress have shown high resistance patterns to the suggestion and it seems unlikely that anything will change. Am I a fatalist or a realist, and is there a drug for either of those conditions? Never mind the side effects—will my insurance cover it?

REFERENCES

1. Scott D. The untold story of TV's first prescription drug ad. *STAT*. Available at: https://www.statnews.com/2015/12/11/untold-story-tvs-first-prescription-drug-ad/. Accessed April 19, 2018.
2. Celia F. Pharma ups the ante on DTC advertising. *Pharmaceutical Commerce*. Available at: http://pharmaceuticalcommerce.com/brand-marketing-communications/pharma-ups-ante-dtc-advertising/. Accessed April 19, 2018.
3. U.S. Food and Drug Administration. Prescription drug advertising: correct help-seeking ad. U.S. Food and Drug Administration. Available at: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm082288.htm. Accessed April 19, 2018.
4. U.S. Food and Drug Administration. Prescription drug advertising: basics of drug ads: reminder advertisements. Available at: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072077.htm#reminder. Accessed April 19, 2018.
5. U.S. Food and Drug Administration. Prescription drug advertising: reminder ad. Available at: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm083573.htm. Accessed April 19, 2018.
6. U.S. Food and Drug Administration. Prescription drug advertising: basics of drug ads: product claim ad. Available at: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072077.htm#product_claim. Accessed April 19, 2018.
7. U.S. Food and Drug Administration. Prescription drug advertising: prescription drug advertising: questions and answers. Available at: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm076768.htm. Accessed April 19, 2018.
8. U.S. Food and Drug Administration. Warning letters and notice of violation letters to pharmaceutical companies—warning letters 2017. Available at: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm538552.htm. Accessed April 19, 2018.
9. ELIQUIS. ELIQUIS TV commercial, "A lot on my mind." iSpot.tv. available at: http://www.ispot.tv/ad/wHBB/eliquis-a-lot-on-my-mind. Accessed April 19, 2018.
10. Xarelto. Xarelto TV commercial, "Most challenging opponent" Ft. Katie Hoff, Brian Vickers. iSpot.tv. Available at: http://www.ispot.tv/ad/A9Zd/xarelto-most-challenging-opponent-ft-katie-hoff-brian-vickers. Accessed April 19, 2018.
11. Opdivo. Opdivo TV commercial, "A chance to live longer." iSpot.tv. Available at: http://www.ispot.tv/ad/wIsF/opdivo-a-chance-to-live-longer. Accessed April 19, 2018.
12. Davis J. The effect of qualifying language on perceptions of drug appeal, drug experience, and estimates of side-effect incidence in DTC advertising. *J Health Commun*. 2007;12:607–622.
13. American Medical Association. AMA calls for ban on DTC ads of prescription drugs and medical devices. Available at: https://www.ama-assn.org/content/ama-calls-ban-direct-consumer-advertising-prescription-drugs-and-medical-devices. Accessed April 19, 2018.