Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/focus-on-pharmacy/fda-taking-action-against-marketing-unapproved-drugs/3530/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

FDA: Taking Action Against Marketing Unapproved Drugs

FDA'S ACTIONS AGAINST MARKETING UNAPPROVED DRUGS

You are listening to ReachMD, The Channel for Medical Professionals. Welcome to the FDA Voice, a program discussing the US Food and Drug Administration and its role in protecting and promoting your health. Your host is Dr. Charles Turck, clinical instructor at the Massachusetts College of Pharmacy and Health Sciences.

What specific action is the FDA taking against marketing unapproved drugs and how can healthcare professionals play a role in tackling this public health issue? Welcome to the FDA Voice. With me is Dr. Charles Lee. Dr. Lee is a medical officer at the Division of New Drugs and Labeling Compliance in the Center for Drug Evaluation and Research of the FDA. We are talking about the FDA's actions against marketing unapproved drugs.

DR. CHARLES TURCK:

Dr. Lee, when we talk about enforcement actions toward unapproved medications, what are the top priorities for the FDA?

DR. CHARLES LEE:

Well, in June 2006, we issued a guidance that is entitled "Marketed Unapproved Drugs." We called the compliance policy guide. It is designed to make sure that all drugs marketed in the United States have been shown to be safe and effective and that's for both prescription and over-the-counter drugs. The guidance outlined policies that are aimed at efficiently and rationally bringing all unapproved drugs into the approval process, but it is also aimed at avoiding undue burdens on consumers, who are unnecessarily disrupting the market. For all the unapproved drugs, FDA has 7 highest enforcement priorities. One is drugs with potential safety risks. Removing potentially unsafe drugs from the market protects the public from both direct and indirect health threats.

Secondly, drugs that lack evidence of effectiveness. Removing ineffective drugs protects the public from using these products in lieu of effective treatments, and actually depending upon the indication, some ineffective products would, of course, pose safety risks as well. For instance, somebody, who might be taking an unapproved antihypertensive where there are approved products that we know are effective on the market.

Another enforcement priority includes health fraud drugs. These are drugs that are marketed deceptively and are represented as being

effective in treating, diagnosing, preventing, curing, or mitigating disease, but they have not been proven to be safe or effective. Removing these drugs also protects the public from using these products in lieu of an effective treatment.

Next, drugs that present direct challenges to the new drug approval and OTC monograph systems. We believe by targeting drugs that challenge the drug approval or OTC drug monograph system reinforces the integrity of the systems and makes them more likely the firms to comply with the new drug approval and monograph requirements.

Another priority is unapproved new drugs that also violate the Food, Drug, and Cosmetic Act in other ways. For instance, good manufacturing practices or adverse event report violations. The agency also intends to continue its policy of enforcing the pre-approval requirements of the Act against the drug or firm that also violates another provision of the Act even if they are unapproved versions of the drug being made by other firms in the market. This policy efficiently preserves scarce agency resources by allowing the agency to pursue all applicable charges against the drug or firm and avoids a duplication of effort.

Finally, drugs that are reformulated to evade an FDA enforcement action. There had been instances for companies with anticipated FDA enforcement action against a specific type of unapproved product that made changes to the product to evade that action.

DR. CHARLES TURCK:

I was just wondering if you could give some examples of ways in which a manufacturer might commit a violation of good manufacturing practices or adverse drug event reporting?

DR. CHARLES LEE:

One example might be circumstances where perhaps the product is made under unsanitary conditions, type of environment that is not appropriate for that type of product. For instance, a room that perhaps is not appropriate for preparing a sterile solution, for example, that would be an example of good manufacturing practice violation. Failure to report any adverse events that were reported to the company or that the company would be aware of would be an example of adverse event reporting violation.

DR. CHARLES TURCK:

So a company is required then to submit any reports of adverse drug events reported to it?

DR. CHARLES LEE:

If they have got information about their product and adverse events, they are required to submit that information to the FDA.

DR. CHARLES TURCK:

Do you know how many drugs have been taken off the market since the FDA issued its guidelines on unapproved marketed drugs?

DR. CHARLES LEE:

Yes, actually since the publication of the CPG in June 2006, we have taken action against approximately 400 products and that is among 7 different drug classes. To give you some examples, we took an action against products that contained carbinoxamine in June 2006. We at the agency receive reports of adverse events, which included 21 deaths associated with the use of products containing this ingredient in children under 2 years of age. Another example is quinine sulfate drug products. We took an action in December 2006. Quinine sulfate is approved; its one product approved for treatment of malaria, however, it has been used off label for treatment of leg cramps and restless legs syndrome. There is no evidence that this product or this drug is effective for these conditions. The agency actually had received 665 reports of adverse events including 93 deaths.

DR. CHARLES TURCK:

You had spoken about carbinoxamine. What was that product for?

DR. CHARLES LEE:

Carbinoxamine is an antihistamine. It was included in a number of cold and cough products formulated for use in children. There is two approved carbinoxamine products that are currently marketed, but these were formulations that were specifically designed for use in children under the age of 2 and some of the products were actually labeled for use down as young as one month of age.

DR. CHARLES TURCK:

And what are some other examples of products that have been taken off the market?

DR. CHARLES LEE:

One example is guaifenesin. It's an expectorant, probably people quite familiar with. Timed-release guaifenesin products were removed from the market in May 2007. The reason that this action was taken was that there was a timed release or extended release guaifenesin product that actually went through the approval process previously to that and all of these unapproved products were really challenging the integrity of the system.

Perhaps another good example is injectable colchicine. People are quite familiar with colchicine as being an anti-gout agent, but there is a very low margin of safety of small therapeutic index for injectable colchicine. The agency received 50 reports of adverse events including 23 deaths associated with the injectable forms of this product and that was the reason we took action against that in February 2008. Again, there are available approved oral colchicine products.

DR. CHARLES TURCK:

So many of the examples that you mentioned are active ingredients that actually are approved in the US, but what you are saying is that they are unapproved in certain dosage forms or from some manufacturers?

DR. CHARLES LEE:

That's correct, and that's our concern, in particular, that when companies go through the approval process, there is a fairly stringent standard that is required, in particular, as far as good manufacturing practices, chemistry requirements, and that type of thing. These unapproved products do not have to meet those standards.

DR. CHARLES TURCK:

I am Dr. Charles Turck and I am speaking with Dr. Charles Lee, medical officer at the Division of New Drugs and Labeling Compliance in the Center for Drug Evaluation and Research of the FDA. We are talking about the FDA's actions against marketing unapproved drugs.

Dr. Lee, what role do practitioners have in regards to marketed unapproved medications?

DR. CHARLES LEE:

Well, practitioners play a critical role when it comes to marketed unapproved drugs. Practitioner should be aware that unapproved drugs are marketed, not every drug that's detailed in the office is an approved product. Practitioners should also be aware whether a drug is FDA approved or not, may affect reimbursement, that is, Medicare, Medicaid may not reimburse a product that is unapproved. It is important for practitioners to determine if the drug is unapproved and probably the best way to do this is for practitioners to go to drugs at FDA on the Internet. You can type in the active ingredient or the name of the drug and all the names of the approved companies for the drug will be listed. Practitioners should work with patients to determine if there is appropriate alternative treatment available in the circumstance that a patient is being treated with an unapproved drug. Practitioner should carefully consider the medical condition that is being treated, what the patient's response to that drug has been, and whether or not there are available approved alternatives. As you had mentioned earlier, a lot of times there are approved alternative medications that may be used, and then finally it's important for practitioners to submit adverse event reports. If adverse events are noted, practitioner can complete the voluntary form online. There will be a link to it from the FDA Internet site, it's called the FDA form 3500 or you can just pick up the phone and dial 1800-FDA-1088 and you can report that by telephone as well.

DR. CHARLES TURCK:

I just wanted to ask a followup question or two about determining if a drug is unapproved. You talked about a nice tool at the FDA web site, you know, that lists the approved medications or at least that has a comprehensive listing of approved medications, but I have to imagine there is at least one physician or there is a pharmacist out there saying I can't possibly look up every single drug that each patient of mine is taking. Do you have any recommendations about when the website would be the most useful for the practicing healthcare professional?

DR. CHARLES LEE:

I think a good number of the unapproved products are cough and cold preparations, so that might be one clue. One clue for sure is if there is a prescription nonnarcotic containing cough or cold product, it is probably unapproved. Some of the other products that are unapproved tend to be narcotic products as well, so this might be two kinds of drug classes that one might be a little bit more wary about.

DR. CHARLES TURCK:

Are there any alternative strategies you can recommend when it comes to drugs, that are healthcare professional does not necessarily have the time to look up and append?

DR. CHARLES LEE:

I think in circumstances where we see that somebody has or notices a particularly adverse event in a patient, one might use that as an opportunity to check. I mean, certainly we know that some of these adverse event reports, particularly, is an example of the injectable colchicine that was associated with a chemistry manufacturing issue that ended up in the product being a higher concentration than it should have been. So I think in a circumstance where particularly if unexpected adverse events or higher number of adverse events might be seen among a number of patients, one might consider that.

DR. CHARLES TURCK:

You had also mentioned submitting adverse event reports as a potential way of combating unapproved medications that are around the US market. I was wondering if you could draw the connection between the submitting of adverse event reports and sort of tamping down on the marketing of unapproved meds for our listeners?

DR. CHARLES LEE:

Right, it's an important way for us to get feedback. Again, I can think of two examples of circumstances where we became aware of a problem because of adverse event reports, one is with injectable colchicine, which does have that narrow therapeutic margin where we had a number of adverse events and deaths that turned out to be due to a manufacturing issue.

DR. CHARLES TURCK:

Dr. Charles Lee has been our guest on the FDA Voice. I am Dr. Charles Turck and we have been discussing the FDA's actions against marketing unapproved drugs.

Dr. Lee, thank you so much for your time.

DR. CHARLES LEE:

Thank you, Dr. Turck.

You have been listening to the FDA Voice, a program featuring the US Food and Drug Administration. For more details on this week's show or to download this segment, visit us at reachmd.com and tour the FDA Center for Drug Evaluation and Research website at fda.gov/cder. Thank you for listening.