

NEWS, VIEWS, & REVIEWS

Importing Injectables

The sub-headline of Dr. Kenneth Beer's article in the March 2013 issue of *The Dermatologist* reads: "There are numerous ways to decrease the cost of toxins and fillers, including importing materials from another country and using less expensive materials, but the results achieved with such products may be less than optimal."¹ There is nothing incorrect about this statement; but the possibly harmful repercussions to both patients and practitioners may be significantly greater than outlined in that article. Karen Rothschild, a Regulatory Counsel with the Food and Drug Administration (FDA) in the Center for Drug Evaluation and Research (CDER), has partnered with Dr. Beer to elucidate the scope of the issues such practices raise.

FDA's Office of Drug Security, Integrity, and Recalls

To help protect patients from the potential harm caused by impure, counterfeit, or otherwise illegally sourced drugs, the FDA has established an office within CDER's Office of Compliance that is dedicated to promoting the quality, integrity, and security of human drugs for US patients. Due to the global sourcing of drugs and easy availability of products distributed through dubious supply chains, there was a need to establish such an office. The increasingly complex global drug supply chain has increased the risk of patient exposure to substandard drugs and has necessitated that the FDA dedicate more resources to protecting patients from counterfeit, diverted, or intentionally adulterated drugs.

Drugs purchased through the legitimate, regulated supply chain in the US continue to be safe and effective. The US has one of the most secure regulated supply chains in the world. However, when there is an opportunity to increase profit, unscrupulous suppliers, doctors, other practitioners, and corporations may seek to exploit it. And patients may seek out less expensive "alternative" drugs, without considering or understanding the risks that arise from obtaining drugs from unregulated sources. The combination of a global recession, increasing drug prices, and improving manufacturing and printing technologies create sophisticated counterfeiting opportunities that are cheaper and easier for criminals.

Over the past 2 years, FDA has sent informational letters to well over a thousand doctors, to provide information about suppliers working outside of the legitimate pharmaceutical supply chain. Despite these warnings, some doctors have elected to continue purchasing less expensive products through questionable suppliers. Some of these doctors may know that they are buying unregulated products, but many do not. Amongst the recipients of letters have been many cosmetic doctors, medi spas, and medical practices that were known to have purchased or received drugs from unlicensed, foreign, and unsavory suppliers, which FDA has confirmed have sold substandard or

counterfeit products. When a product is unapproved or comes from a source outside of the regulated supply chain, no one monitors the quality of manufacture, storage, or the purity of the ingredients. Quite simply, no one is looking.

Possible Harm to Patients

Patients may be harmed by drugs that have not been approved by FDA, as the products have not been determined to be safe or effective, and the companies (or individuals) making the drugs have not had their manufacturing practices or handling procedures inspected by FDA. This means that there is no guarantee, or even a reasonable expectation, that the drugs are of suitable quality and there is no reason to believe that they been proven to be safe and effective pursuant to FDA standards. Drugs imported from foreign or unlicensed suppliers may be from unknown sources, may have unknown ingredients, may be counterfeit, or may not have been manufactured, transported, or stored under proper conditions as required by US law, regulations, and standards. Drugs that have not been reviewed for safety, efficacy, and good manufacturing may be subpotent, superpotent, or have no active ingredient whatsoever. These products may not be even remotely close in composition to what the drug is being advertised as by those trying to sell them. They could lead to poor results, adverse reactions, or worse.

With respect to botulinum toxins in general, and Botox[®] in particular, the potential for harm to patients is not new. In November 2004, four patients became paralyzed after being injected with potent, unapproved botulinum toxin that a doctor used instead of FDA-approved Botox[®] Cosmetic. By July 2008, 29 people had been convicted of purposely using an unapproved, cheaper version instead of FDA-approved Botox[®] Cosmetic. These people injected about 1,000 unknowing patients. Unfortunately, despite publication of their names in several local and national newspapers, many of these practitioners remain in practice. Particularly with a toxin, doctors have long known about the precision required for optimal results and for patient safety. However, because patients trust their medical provider to obtain safe and effective injections, patients should be suspicious about any "deals" or discounts. Patients should also be aware that when doctors start to compete based solely on price, the pressure to dilute the products injected may increase substantially. Dilution of Botox[®] is the most common reason for patient complaints to doctors that the injections "don't last" or that "Botox just doesn't work".

How Patients are Scammed

Botulinum toxins are now undergoing a new phase of counterfeit that is extremely dangerous. In contrast with the events of 2004 where the doctors knowingly used an unapproved product instead of Botox[®] on unsuspecting patients, the new danger is primarily driven by patients who demand ever less expensive injections. They come to their doctor offices armed with internet

ads, coupons, and other enticements to get treated with “Botox” at far lower prices than are available for the approved product.

How do you patients find these often-fraudulent offers? The answer is that the offers frequently find them! The ads are ubiquitous; appearing in web advertisements, coupon offerings, magazine ads, even bus kiosks. They are so common, that patients assume they are legitimate. Additionally, there are still unscrupulous practitioners who misrepresent fake products to patients, leading them to believe that they are receiving real Botox[®] Cosmetic. Charlatans may place advertisements, and may display false certificates indicating that they received training from the Botox[®] manufacturer, from the American Academy of Dermatology or The American Society of Plastic Surgery when they have not. These scammers not only violate the objective of the Hippocratic Oath and intentionally put their patients in harms way, but they have sullied the reputation of legitimate, honest, and well-trained cosmetic practitioners.

How Doctors are Scammed

An increasingly alarming trend has been identified as suppliers of false cosmetic injectables scam doctors who look to Canada or Europe for cheaper alternatives; however, there is no easy way to verify that the products are originating from the advertised country. These cosmetic practitioners may be injecting patients with fraudulent products. Sometimes these cosmetic practitioners may feel compelled to look for lower-cost products due to the insistence on discounts by patients. Unscrupulous suppliers are well aware of this pricing pressure and have responded with cheap, fraudulent material. They provide assurances that their “Botox” product or other drugs are US-equivalents, or are products approved in other countries. What they don’t want you to know is that even if they were using the actual products described, simply importing or causing the importation of unapproved drugs when there is an FDA-approved drug available is illegal in addition to being dangerous. Furthermore, even if a product is approved in another country, the fact that it is being sold by a supplier that is outside of the regulated drug supply chain means that there are no assurances that the product was stored or handled under proper conditions on its way to the US. Just because an unlicensed and/or foreign supplier says what the product is, there is no way to know for sure. In the US legitimate supply chain, to be authorized to store, handle and distribute prescription drugs, wholesale drug distributors must be licensed in each state in which they do business.

FDA alerted healthcare practitioners and the public in April and July of 2013 that fraudulent versions of Botox[®] are being sold to medical practices by unlicensed suppliers who are not part of the legitimate U.S. supply chain. FDA sent doctors, clinics, medical practices and spas letters alerting them to the dangers of buying unapproved or counterfeit products, and specifically alerting them about the fraudulent versions of “Botox”. Under federal law, no form of botulinum toxin may be commercially distributed for use on humans in the US unless it has been approved by FDA. At this time, Botox[®] and Botox[®] Cosmetic (made by Allergan Inc), Xeomin[®] (made by Merz) and Dysport[®] (made by Ipsen Biopharm) are the only Type A botulinum toxins approved by FDA.

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Counterfeiters have become good at making fake copies of packaging and product, and it may be difficult to tell the fake from the legitimate just by looking. An example of the subtle difference between the FDA-approved Botox[®] for injection (100 units/vial), manufactured by Allergan, and a known illegal version, is that Allergan’s Botox[®] is labeled as “OnabotulinumtoxinA”, while the illegal version is labeled as “Botulinum Toxin Type A”. While a fraudulent version of a drug may purport to have the same active ingredient as the FDA-approved product, one cannot be sure what it actually contains. The fraudulent version is not legally marketed and has not been established by FDA to be therapeutically equivalent to or interchangeable with any US approved product. It is important to remember that if it has not been approved by FDA, and is not bought within the legitimate supply chain, there is no telling what you or your patients might be getting.

How to Protect Yourself and Your Patients

There are several ways in which you can protect yourself, your patients, and your practice. First, always know whom you are buying your medications from. Assure that you either purchase medications directly from the manufacturer of the FDA-approved drug, from an authorized distributor for the manufacturer, or from a wholesale drug distributor properly licensed in the United States. You can check to see if the distributor holds a current license before placing an order. Most states have this information online on their website.⁸ Be wary if the price of a medication sounds too good to be true. Deep discounts may be offered because the product is stolen, expired, counterfeit, unapproved, or otherwise substandard. Also, carefully inspect all product and packaging. The following signs may indicate that the product is not FDA-approved or otherwise does not meet US regulatory requirements:

- The medication has a different brand name than what was ordered.
- The packaging or label looks different from the product you usually receive.
- Portions, or all, of the labeling are not in English – when you have previously seen the labels in English only.
- Shipping addresses, postmarks, or other materials indicate that the package came from outside of the US.
- The labeling does not state “Rx only” even though the product is restricted to prescription use in the US.
- The dosing recommendations are unfamiliar.
- The dosage form or route of administration is different than what you usually receive (eg, ampule instead of pre-filled syringe).

- The product does not display a National Drug Code (NDC) number.^b
- The lot numbers and expiration dates on the carton do not match those on labels of the containers included in the carton.
- The medication was not shipped under conditions that satisfy labeled storage requirements. For example, if the medication is labeled to require refrigeration, it was not shipped with cold packs or other measures to ensure temperature control.

Footnotes

^aFDA has compiled website links or contact information to state agencies responsible for licensing of wholesale prescription drug distributors on their website at: <http://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/ucm281446.htm> .

^b Inclusion of an NDC number on the label is not required, nor does it denote FDA approval of the product. However, the absence of an NDC on the label may suggest that the product was not originally manufactured for the US market, and that in turn may suggest that it may not comply with US requirements.

Additionally, if you suspect that product that you have purchased and/or used may not be legitimate, either through appearance or by unexpected adverse events, it is critical that FDA is notified.

Health care professionals and patients can report suspect solicitations, and questionable sources and products to FDA through the following methods:

- Call FDA's Office of Criminal Investigations (OCI) at 800-551-3989, or
- Report to OCI at www.accessdata.fda.gov/scripts/email/oc/oci/contact.cfm, or
- Email - DrugSupplyChainIntegrity@fda.hhs.gov

Further, healthcare providers and patients are asked to report adverse events related to the use of suspect medications to the FDA's MedWatch Safety Information and Adverse Event Reporting Program either online, by regular mail, by fax, or by phone by:

- Completing and submitting the report online: www.fda.gov/MedWatch/report.htm or
- Downloading form at: <http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/ucm082725.pdf>, or
- Calling 1-800-332-1088 to request a reporting form, then completing and returning it to the address on the pre-addressed form, or submitting by fax to 1-800-FDA-0178

What to Say to Patients

So when a patient comes to you waving coupons, ads, or otherwise demanding a better price than is reasonable for authentic product, what can you say? First, it is incumbent upon you to explain that one gets what one pays for. If the patient wants the cheapest injection, try to make them understand that this is a mistake and they could be harmed. You can explain clearly and simply that you are a trained and accredited professional, and that you would not inject them with anything but the product that FDA has reviewed and approved as safe and effective for its intended use. Emphasize your training and accreditation. Let your patients know that you are uniquely positioned through your education and training to work with them individually (not a one-injection-fits-all shop), and educate them as to the meaning of using authentic, FDA-approved product. They are most likely unaware that prescription drugs from unlicensed or foreign suppliers may be counterfeit, and/or may be drugs from foreign or unknown sources that are not approved for distribution in the United States. They may not understand that these drugs may have unknown ingredients, and may not have been manufactured, transported or stored under proper conditions as required by US law and regulations. They also may not realize that importing foreign, non-FDA-approved products when there is an FDA-approved drug available is illegal, and could be dangerous to them. You don't want to put your patients in harms way by skirting the regulatory system, which is put in place to protect patients from unsafe, ineffective, and potentially dangerous drugs. Remind your patients that they want be able to put a proud face forward, and not risk the losing face by wearing the results of shoddy procedures, untrained efforts, or fake medicines.

Disclosure

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1. Beer K. Importing Injectables. *The Dermatologist*. 2013; (3):24-25.

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