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# The Akorn Bankruptcy

Six experts on what ophthalmology can expect.

Roundtable hosted by Ruth D. Williams, MD,
with Wiley A. Chambers, MD; Michael Ganio, PharmD; David B. Glasser, MD;
Michael X. Repka, MD, MBA; and George A. Williams, MD.

IN FEBRUARY, AKORN FILED FOR CHAPTER 7 bankruptcy, closing its U.S. operations, including its production facilities. The abrupt closure may lead to—and may have already led to—some drug shortages in two categories: first, medications that ophthalmologists prescribe for patients, and second, diagnostics for ophthalmic offices.

To discuss the situation and what might come next, Ruth D. Williams, MD, chief medical editor of *EyeNet*, hosted a roundtable in early April with participants Wiley A. Chambers, MD, of the Office of New Drugs, Center for Drug Evaluation and Research at the FDA; Michael Ganio, PharmD, at the American Society of Health-System Pharmacists (ASHP), which is a member organization in the End Drug Shortages Alliance; David B. Glasser, MD, Academy secretary for Federal Affairs, who also represents the Academy at the Relative Value Scale Update Committee, or RUC; Michael X. Repka, MD, MBA, Academy medical director for Governmental Affairs; and George A. Williams, MD, Academy senior secretary for Advocacy. *(This discussion took place on April 5. It has been edited for length and clarity.)*

## Diagnostics in the Clinic

***Ruth Williams:*** *Let's talk about diagnostics in the ophthalmic office first. Which drugs will be affected by the Akorn bankruptcy, and which of these are of the greatest concern?*

**Michael Repka:** Akorn was a manufacturer of cyclopentolate, tropicamide, and phenylephrine, all commonly used in the office setting. These are the three diagnostic agents that ophthalmologists would be most concerned about. Akorn was responsible for perhaps one-third of the U.S. production of cyclopentolate and tropicamide and 90% of the U.S. production of phenylephrine.

**Ruth Williams:** George, Akorn also manufactured injectable fluorescein. Will you talk about how that might affect retina practices?

**George Williams:** Akorn had more than 80% of the fluorescein market at the time they stopped production. There was a fair amount of the Akorn product in the supply chain, but now, in April, as that supply is dwindling, there's a worry that distributors will no longer have access to enough fluorescein. This concern has created issues for retinal diagnostics, fluorescein angiography in particular. Many retina practices have been scrambling to find another source. Fortunately, at the moment, it looks like Alcon has been able to step up because they have a product, Fluorescite, that is currently available. I've heard doubts, though, about whether Alcon will be able to maintain that supply chain.

**Ruth Williams:** Have you heard of retina practices that are already having trouble getting injectable fluorescein?

**George Williams:** I have, and some retina practices have started cutting back on the dose per patient. It turns out that even a half dose—which is routine for smaller individuals, children, and those with a sensitivity to fluorescein—is more than adequate, and I think that's a reflection of the improved digital imaging capabilities in most retina practices. Because imaging systems are no longer film-based, I think we can get away with using less fluorescein.

Patrick Faricy

**David Glasser:** George, is there any role for increased use of OCT angiography (OCTA)? Can it substitute for fluorescein angiography for those who have the technology?

**George Williams:** Yes, there are certain disease states, AMD for example, where OCTA is helpful. Where fluorescein shines is in inflammatory disease—for example when you're trying to determine whether there's vasculitis—and certainly for any type of peripheral imaging. Very few centers have widefield OCTA capabilities, and I think most practices don't have enough OCTA capabilities to really meet the need.

**Michael Repka:** One product we haven't mentioned, which has been in shortage for the last decade, is fluorescein strips. Akorn was one of the companies that stepped up to help with increasing production. Now, nobody complains about a scarcity of fluorescein strips anymore. But now I'm concerned that we'll see shortages again. Akorn had a moderate market share.

**George Williams:** Well, that can be an important issue because certainly if you're practicing in a hospital setting, compliance officers are limiting the use of products such as Fluress because the dropper can touch the eye and contaminate the contents. Our hospital just stopped using Fluress and went to fluorescein strips to deal with that concern. A shortage of strips may not be as much of an issue in private practice, however.

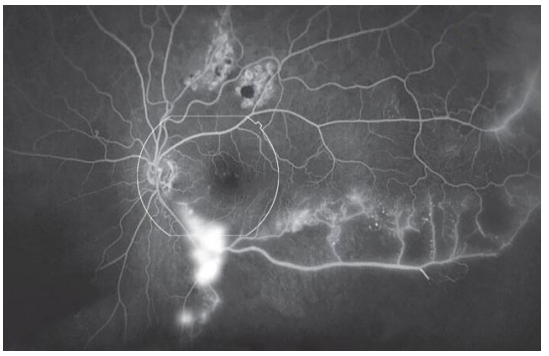
## Abrupt Closure

***Ruth Williams:*** *Drug shortages are certainly not a new issue, but the abrupt closure of Akorn production facilities could create a production capacity issue.*

**Michael Ganio:** Resilience in the supply chain is a challenge. ASHP has been tracking drug shortages for about 20 years, and we find that shortages affect mostly sterile generic injectables and sterile ophthalmics. The sterile products are slightly more difficult to manufacture and require a few more quality checks than other types of drugs. Also, as you noted, capacity can be a problem. The FDA surely is working behind the scenes with other manufacturers to see what it can do to assist in boosting production. This caught a lot of us by surprise.

**Wiley Chambers:** Yes, the FDA has a team that tries to monitor the supply chain, particularly the approved products. When they identify a shortage, they try to see if other manufacturers who are approved for that drug can increase their production to cover for any potential shortages. This has been the case since we were notified that Akorn was shutting down.

**Michael Ganio:** In retrospect, the Akorn closure may not be surprising. Over the last few years, the Akorn facilities had several FDA inspections that were concerning, which is not uncommon with some of these generic plants. What seems to be a robust supply chain because there are multiple manufacturers can break down quickly with the closure of one manufacturer, like Akorn, that supplies 90% of the phenylephrine ophthalmic market.



***FLUORESCEIN.*** *Fluorescein angiography is a key tool in the diagnosis of retinal vasculitis.*

Normally, there's very little transparency into how much of the market a manufacturer supplies. However, in this case, the End Drug Shortages Alliance was able to pull that information out of a private clearinghouse database called IQVIA to supply this information as a resource to practitioners[1] so they have some idea of what other options are available and can see how much the community relied on Akorn.

## Pricing

***Ruth Williams:*** *Do you think that a shortage of diagnostics will affect the cost to ophthalmic practices?*

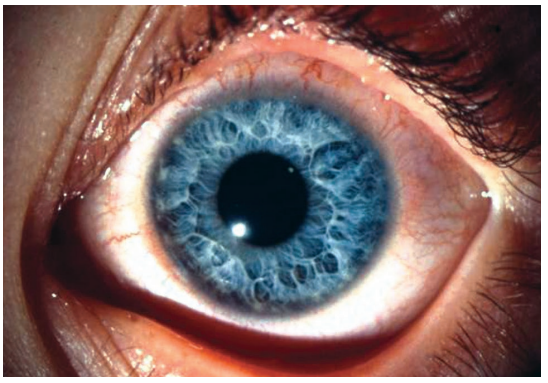
**David Glasser:** Past experience would suggest that with supply issues we will see spikes in prices.

**Michael Repka:** As a historical comparison, the fluorescein injectable price has gone up in the past few years as its supply has fluctuated.

**Michael Ganio:** A 2019 study in *Annals of Internal Medicine*[2] looked at drug prices before and after shortages. According to its findings, you can expect the price to go up. To be honest, a price increase might be a correction in the market. If that's what it takes to support a sustainable generic marketplace, maybe we need to allow it to happen.

**Ruth Williams:** The problem is that increased cost is borne by the ophthalmic practice.

**David Glasser:** There's not a lot of opportunity to get the increased practice expense plugged back into the Medicare allowable. Normally, a CPT code is reviewed and revalued every so many years by the RUC and CMS. We like to avoid revaluations because it usually doesn't end well



***ALLERGIC CONJUNCTIVITIS.*** *Akorn manufactured ketotifen, which is a first-line therapy for patients with allergies.*

for us. When a code comes up, we submit invoices from practices, and that gets plugged into the practice expense piece. Whether a code happens to be reviewed by the RUC at a time when prices are spiking is anyone's guess.

## Repercussions for Patients

***Ruth Williams:*** *Let's shift our conversation to drug shortages that our patients might experience due to the Akorn bankruptcy. Which of the drugs might be affected, and which of those are of most concern?*

**Michael Repka:** The ones that I noticed were topical atropine and ketotifen. The latter is a first-line step therapy drug for allergic conjunctivitis. It probably will be quite messy when this medication is not available.

**Ruth Williams:** And the copay will be high.

**Michael Repka:** Yes, a very high copay.

**David Glasser:** The other classes of drugs on the list are less likely to be problematic. With fluoroquinolone topical antibiotics, there are multiple manufacturers and multiple choices, and, usually, you can substitute one for another. The same is true for some of the glaucoma medications, although we have seen shortages of various glaucoma medications for other reasons in recent years.

**Ruth Williams:** As a glaucoma specialist, I would add that switching patients from a generic to a branded drug can be very expensive, depending on coverage, resulting in patients sometimes not using their medications.

## Equitable Distribution and Usage of Drugs in Short Supply

***Ruth Williams:*** *If we have limited supplies of certain drugs or if there's a supply chain disruption, might there be a diversity, equity, and inclusion issue around distributing the limited supply in an equitable manner? If so, how can we think about it clearly?*

**George Williams:** I would think it's very much an issue because the distributors will always try to keep their best customers whole. I'm part of a very large group; when we recognize that there may be an issue, we contact our distributor—and, fortunately, we're able to maintain supply. But a smaller practice, one that doesn't have that kind of pull with a distributor, absolutely will be disadvantaged. And those tend to be the practices that are also serving underserved populations.

***Ruth Williams:*** *What can we do about it, or how can we think proactively?*

**Michael Ganio:** There is a similar issue in hospitals. The large academic centers and the big teaching hospitals have more resources and might even have drug shortage committees, whereas the smaller hospitals don't have the same resources. Within the hospital setting, there are regional networks that may work out an arrangement to trade product or help provide product to smaller rural hospitals. A network like this is probably much more difficult in private practice than in a health-system setting, but there may be ways that you can work within your region to make sure there's equitable access for these medications.

## What You Can Do in Your Practice

**Mike Repka:** One thing that doctors should be careful about: don't throw away bottles before their expiration date—in spite of inaccurate messages about how long the drops are usable after the bottle is opened. Also, consider using only one drop instead of two. Two drops are used because that way we're sure the drop is getting in the eye, but one drop might be sufficient. Diagnostic drops will last a long time after you open a bottle.

**Ruth Williams:** The 28-day expiration is such an important issue. Wiley, you wrote a beautiful editorial in *Ophthalmology* recently[3] about this issue. Would you explain the 28-day issue and why we can and should keep using our diagnostic bottles?

**Wiley Chambers:** It seems there has been confusion about how long drops are good for. In Europe, many bottles are labeled to be thrown away 28 days after they've been opened. There has been an assumption that this is the standard life for bottle drops throughout the world. But that's not what the FDA expects from a stability perspective for products approved in the United States. Our stability studies are carried out through the expiration date—that's why we put an expiration date on the bottle. The FDA is in the process of changing the label of most ophthalmic drug products so that people understand the bottle is good until the expiration date, regardless of whether the bottle has been opened or not.

## Report Shortages: Why and How

***Ruth Williams:*** *Any other thoughts on the issue?*

**Michael Repka:** One thing to add is that the FDA and the Academy cannot make a manufacturer produce a product safely, efficiently, and inexpensively. The Academy and FDA can talk to manufacturers; we can advocate; but we can't actually tell them to make a decision that's not in their best business interest.

**Wiley Chambers:** I agree with that, and I encourage ophthalmologists and patients to report to the FDA when they notice a drug shortage. The agency can't try to mitigate the problem if it doesn't know about it.

**Michael Ganio:** The critical thing is getting the drug on the FDA shortage list. The manufacturers are supposed to report, but it's not necessarily a priority for them. When practitioners report to the FDA, or to ASHP, it raises the profile of that shortage. Because of reports from individuals, the FDA has added drug shortages even though it doesn't seem like a manufacturer has reported it.

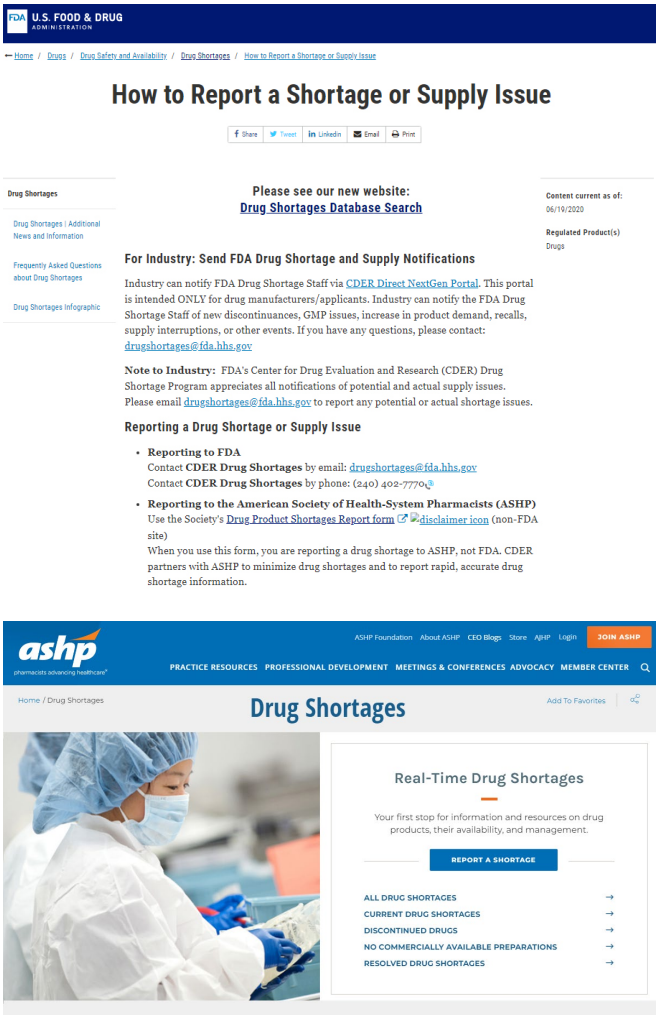
***Ruth Williams:*** *How does one go about reporting a drug shortage to the FDA?*

**Wiley Chambers:** There is information on the FDA drug shortage page at www.fda.gov/drugs/drug-shortages/how-report-shortage-or-supply-issue.

**Michael Ganio:** Yes, and same with ASHP. If you pull up the drug shortage page (www.ashp.org/drug-shortages), there's a blue box that says Report a Shortage.

**Ruth Williams:** Super easy. Takes what? Two minutes to do, correct?

**Wiley Chambers:** Yes.




***REPORT A SHORTAGE.*** *Using the FDA or ASHP websites to report a shortage takes a matter of minutes and increases the likelihood that the FDA will be able to get involved to try to find a solution (see "Report Shortages: Why and How").*

## Role of Compounding Pharmacies

**David Glasser:** That's a great comment about reporting shortages, Wiley, because if a drug goes on the shortage list, compounders can step in to help make up for the shortfall. And that's a critical piece because sometimes the compounders can only intercede when a drug is on the shortage list. Some of the compounders complain that they can't produce products in shortage long enough for it to be financially feasible for them, and that's an issue. But if they don't know, they can't start.

**Wiley Chambers:** They also frequently need some lead time. So again, if the proper parties don't know that there's a shortage, it's difficult to try and mitigate it.

***Ruth Williams:*** *Do we know that compounding pharmacies will fill in the supply chain for some of these Akorn products?*

**Michael Ganio:** It might be too early to say. It is happening for one product, and that's albuterol nebulizers that are used in continuous nebulized solutions, particularly for pediatric patients. The compounders had a little bit of advance notice that this might be coming. There are only two manufacturers of that product, and one of them is actually a compounding facility.

The potential for ophthalmology is certainly there, but, as noted, it takes some time to develop the formulation and to complete stability and sterility testing. And then, as soon as that product is off the shortage list, the compounder has to stop

selling, so any money that it invested in developing that formulation is essentially lost. It's a high-risk proposition.

## A Look Ahead

**Ruth Williams:** *Well, we're coming to the end of our discussion. Does anyone have anything to add?*

**George Williams:** I would say, Ruth, that these problems are likely to continue because we're dealing with a situation where payers are trying to drive costs down, so we will see continued pressure in the pharmaceutical space. We're not talking about new drugs but rather drugs that we've been using for, in some cases, generations. The harsh reality is the market has spoken. There is not enough profitability to incentivize companies to produce these agents, and that's likely to continue to be the case if financial pressures from the payers persist.

**Ruth Williams:** And, Mike Ganio, I'm sure this isn't a problem isolated to ophthalmology.

**Michael Ganio:** It absolutely isn't. George hit the nail on the head. It's an economic decision. Why make a product with a margin that's pennies when you can shift production to a product with higher margins? I do think this will continue to be a problem. We have a payment system in the U.S. that rewards producing drugs as cheaply as possible, unfortunately. Providers generate revenue in the margins between cost and reimbursement, so of course we're going to buy our drugs as cheaply as possible. As a result, there's no incentive for manufacturers to invest in quality. This is what ultimately did Akorn in. It experienced repeated run-ins with quality issues, and it couldn't invest in its manufacturing facilities and its processes to get up to par and out from underneath the scrutiny of inspectors and drug quality issues. Until there's incentive for boosting quality, we will continue to have these problems.

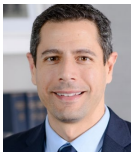
**Michael Repka:** On the other hand, with the tainted eyedrops in the artificial tear market now, it's necessary that the FDA goes in and checks out manufacturing facilities, and this practice probably needs to be even strengthened.

**Ruth Williams:** You know, I get asked about that, oh, at least five or six times a day. I see you nodding which means the rest of you do, too. All right. Well, thank you so much, George, David, Wiley, Mike, and Mike. This was a fascinating conversation, and I appreciate your contribution to our discussion.


1 www.enddrugshortages.com/files/Akorn-Pharmaceuticals-ceases-operations.pdf. Accessed April 11, 2023.
2 Hernandez I et al. *Ann Intern Med.* 2019;170(1):74-76.
3 Chambers WA. *Ophthalmology*. 2021;128(12):1667-1668.


## MEET THE EXPERTS

**Wiley A. Chambers, MD** Director of the Division of Ophthalmology in the Office of New Drugs, Center for Drug Evaluation and Research at the FDA. *Relevant financial disclosures: None.*



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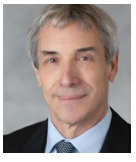

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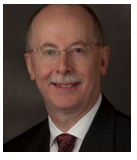

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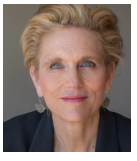

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**See disclosure key,** page 8. **For full disclosures,** see this article at aao.org/eyenet.