



Trends-in-Medicine

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Quick Pulse

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BAUSCH & LOMB PULLS CONTACT LENS SOLUTION FROM U.S. MARKET

On Monday, April 10, 2006, the FDA announced that Bausch & Lomb was voluntarily suspending all U.S. shipments of ReNu MoistureLoc contact lens solution. The action, which B&L officials characterized as “temporary,” comes after a report by the Centers for Disease Control and Prevention (CDC) of 109 cases in less than six weeks of a relatively rare but very serious fungal eye infection, *Fusarium* keratitis, in soft contact lens wearers.

Fusarium keratitis has been reported in Florida, New York, New Jersey, Iowa, Connecticut, and 12 other states. According to the FDA, a *Fusarium* infection can lead to vision loss requiring corneal transplants.

In February 2006, B&L suspended sales of ReNu MoistureLoc in Hong Kong and Singapore after numerous cases of *Fusarium* keratitis appeared in those cities, starting in November 2005. There have not been any reports yet of contact lens-associated *Fusarium* keratitis in Europe. A B&L official said that in a significant number of the cases in Singapore, the patients were non-compliant with lens care guidelines or basic hygiene.

Fusarium keratitis is not spreading from Asia to the rest of the world the way SARS spread or avian flu is spreading. *Fusarium* is a common fungus that lives on plants, most frequently in tropical environments. *Fusarium* keratitis has typically been associated with being poked in the eye by a plant carrying the fungus. *Fusarium* is found in many plants, soil, and tap water. Fungal keratitis also is associated with trauma to the surface of the eye and immunodeficiency. The FDA estimated that the annual risk of contact lens-related microbial keratitis is 4-21 per 10,000 patients.

Fusarium keratitis is a serious problem. An expert explained, “We have some very good medications to treat most bacterial infections, but the medications that are available to treat fungi are much less specific. As a result, your kill is not this kind of instantaneous quick death, and some of the fungi are spore-forming. They have more survival skills than bacteria, less than *Acanthamoeba*, but more than bacteria...Potentially, a patient could go blind. If the patient develops a central ulcer, the cornea could end up needing a graft...So once it has healed, you could graft the patient and have a reasonable expectation of a good outcome as long as the cornea isn't neovascularized. That is better than *Acanthamoeba* where patients sometimes don't do well even after grafting because of the way that bug, which is not a fungus, has its life cycle. So, *Fusarium* keratitis is not as devastating as *Acanthamoeba*. The drug of choice is nystatin.”

The CDC and other health authorities are reviewing the 109 cases of fungal keratitis to determine the precise cause. So far, 30 cases have been fully reviewed,

and 28 involved soft contact lens wearers. Of these 28 patients, 26 said they used ReNu in the month prior to the infection, though five said they also used another solution in addition to ReNu, and nine said they wore their contact lenses overnight, which is a known risk for microbial keratitis. None used another lens solution exclusively.

B&L chairman and CEO Ronald Zarrella said, "The CDC data...are both troubling and perplexing, as there is an apparent disproportionate representation of U.S.-manufactured ReNu with MoistureLoc in the underlying data. The source of these infections has not been determined. Based on our extensive testing, analysis and further internal reviews, and communications with leading experts, the available scientific evidence does not establish any type of ReNu solution as a cause."

Experts are working hard to determine if and how there might be a link between *Fusarium* keratitis and ReNu. A B&L official said, "Epidemiologists, microbiologists, ophthalmologists, researchers of every stripe are looking at every variation, even taking a very careful look at lens cases and the reaction with lens cases, but so far all of this extensive testing has not come up with an answer...Our concern at this point is that the CDC has only really looked at 30 cases." A New England optometrist said, "My guess is that B&L probably has a team working day and night trying to find even a single case of this they can document with a product that is not their own." A Florida optometrist said, "I cannot believe the B&L solution caused the problem. B&L was probably just being a good corporate citizen and pulling ReNu MoistureLoc until we find what is causing this."

One possibility is that the product is contaminated. ReNu MoistureLoc is a relatively new product; it has only been on the market about a year and a half, with 2005 sales (brand and generic) of approximately \$45 million in the U.S. All of the ReNu MoistureLoc worldwide is produced at B&L's Greenville SC manufacturing facility, but a company official denied that there have been any FDA warnings at the plant in the last few months, though FDA officials have been at the plant recently looking for clues to the cause of the *Fusarium* cases.

ReNu MoistureLoc was specially formulated to provide additional moisturizing to contact lenses, to retain moisture in the eye. ReNu MoistureLoc uses a novel preservative, alexidine, which is in the same biguanide-based preservative class as chlorhexidine and polyaminopropyl biguanide (PHMB). An expert suggested there could be a link between the formulation and the fungal infection. He speculated, "My hunch is that this is not a factory contamination issue. My guess is there is something about the product that provides an unfortunate but uniquely supportive environment for the growth of *Fusarium*...It may be something about the formulation that unexpectedly creates a permissive environment for that particular fungus...It appears that it (the *Fusarium* keratitis infection) is primarily associated with this product...We don't know if

there is something unique about this product...For example, let's assume that this product is designed to really hold moisture. So, assume its chemistry is designed to grab moisture and lock it into the solution and hold it there a long time. Now, make the assumption that someone in Asia, someone in New York, someone wherever either doesn't care about hygiene, doesn't listen, or doesn't pay attention and decides – despite the warnings in the packages – that they are, in fact, going to wash the lenses one night in tap water or something other than their solution, and then they put it back in their solution. Whatever they had it in, the moisture that was there – if the solution is working as it should – will be locked into that solution long-term."

One problem for investigators and B&L may be getting patients to admit that they mishandled their contact lenses or didn't clean them properly or as instructed. A source said, "It is possible the product is fine. It could be the way the patients handle the lenses, but the difficulty will be getting patients to admit they ever did anything contrary to instructions...At this point, even if they knew they did something wrong, they aren't telling because they know they have 12 lawyers lined up...The odds are this will cost B&L more than just a drop in the stock price."

What should ReNu MoistureLoc consumers do?

Obviously, they will have to change their contact lens solution since ReNu MoistureLoc will not be available. But they shouldn't panic, doctors cautioned. A Florida optometrist said, "This just shows that contact lenses are a serious business, and people were just not cleaning their lenses well enough. The reality is you have to rub and clean them."

The FDA is advising patients who wear contact lenses to:

- Wash their hands with soap and water and dry them before handling lenses.
- Wear and replace their lenses according to the schedule prescribed by their doctor.
- Follow instructions from their doctor and their solution manufacturer for cleaning and storing lenses.
- Keep their contact lens case clean and replace it every 3-6 months.
- Remove the lenses and consult a doctor immediately if their eyes become red, irritated, or their vision changes.
- Consider performing a "rub and rinse" lens cleaning method, rather than using a no rub method.

The American Optometric Association offered some other tips for consumers:

- Soaking the lenses overnight in enough multi-purpose solution to completely cover the lenses.
- Keep the contact lens case open and dry between cleanings.

- Remember that saline solutions and rewetting drops are not designed to disinfect lenses.
- Only fresh solution should be used to clean and disinfect contact lenses. Never re-use old solution. Contact lens solution must be changed every day, even if the lenses are not used daily.
- Always replace old contacts when you get a new contact prescription.

Will switching to another contact lens solution eliminate the risk of *Fusarium* keratitis?

No cases of *Fusarium* keratitis have been reported in the U.S. in patients exclusively using another brand of contact lens solution. A B&L official said, "There is a concern there will be a false sense of security (with switching)...That's why the most important thing is to meticulously clean and care for your contact lenses...and give them the extra rub if the doctor thinks that is necessary."

What should clinicians do when a patient presents with a case of keratitis?

A B&L official suggested, "Make sure to culture the patient, and make sure that before you begin treatment with an antibiotic, think microbial/fungal infection as well because some of these treatments may be selecting." An optometrist said, "If a patient acknowledges using ReNu and presents with an ulcer that looks fungal – and, in general, fungal ulcers have a particular look that is a little different from (the look of a) viral or bacterial infection – I don't think the average optometrist or general ophthalmologist will culture it. My guess is that if it looks fungal, they will hit it with nystatin (an anti-fungal medication), and if it doesn't respond pretty quickly, the patient will be sent off to the cornea specialist."

Being sure the pharmacy has nystatin in stock also might be useful. A doctor said, "What we've done at our hospital is verify that nystatin was on our formulary because we see a lot of indigent patients. We called the pharmacy the free-care patients have to go to and made sure they brought in a stock of nystatin because we don't want them waiting 24-48 hours for someone to order it...We kind of pre-warned the pharmacy to have at least some modest stock fresh on the shelf in case we need it in a hurry."

Clinicians also should report any cases of *Fusarium* keratitis to the FDA's voluntary reporting program, MedWatch by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178, online at www.fda.gov/medwatch/report.htm, or by mail to:

MedWatch
 FDA
 5600 Fishers Lane
 Rockville, MD 20857-9787

When submitting a report to MedWatch, doctors should include the following information (if available) on the MedWatch reporting form:

- Contact lens solution trade names and lot numbers.
- Contact lens type, trade name, and mode of wear (extended or daily wear).
- Patient non-compliance with contact lens regimen (e.g., overnight wear in daily wear lenses, not cleaning lenses).
- Results of all cultures taken (e.g., corneal, conjunctival, contact lens, care solutions, lens case).
- Special patient characteristics, including whether the patient was immunocompromised (e.g., used topical or systemic corticosteroids or had diabetes), or had any ocular trauma, surgery, or chronic eye problem.
- Topical ocular medications used to treat the patient (including trade names and lot numbers if available).

What does all this mean for B&L?

The bottom line is that this could be a disaster for B&L. An expert said, "My guess is that most patients won't get the nuance part of this – that it is this specific product. I suspect they will probably bail on all ReNu products, at least for the foreseeable future...And the company may have to pick a new brand name to bring it back. But Alcon's Opti-Free has had its troubles as well. They were not as bad as this, but for a while there was a buzz that it was associated with subepithelial infiltrates of the cornea...That is easier to deal with than fungal keratitis, for sure, but none of these products has been perfect."

What does this mean for the contact lens industry in general?

Sources do not believe that this issue will impact contact lens sales, even B&L lenses. An optometrist said, "Most B&L lenses go by a trade name – e.g., PureVision or SofLens 66 – and most people who wear those don't know they are B&L. What they carry away from TV is a product name (ReNu), not B&L. So, I don't think it will wash across the whole B&L product line."

However, if *Fusarium* keratitis starts appearing with other contact lenses, contact lens use might be affected. A source said, "That could make the FDA panic. And people could go to one-day disposable contact lenses – peel off a split pack in the morning, and throw them away at night. No cases and no solutions...But my feeling is that this won't happen. The market drive for these (soft contact) lenses is just too strong...This won't take down contact lenses. My guess is it will take down the ReNu product line and the ReNu product name. B&L will take a hit financially."