# COMPOUNDED MEDICATION AND OCULAR SAFETY

There is an inherent need for compounded medication.

**BY WILLIAM F. WILEY, MD**

Compounded medication is crucial to the safety and well-being of our patients. It is estimated that 3,000 compounding pharmacies fill more than 30 million prescriptions per year in the United States. Many of these medications are distributed for ocular use. Compounded medication can provide access to medications for patients with unique and vision-threatening eye conditions when traditional manufactured medications are not available. Furthermore, compounded medications allow physicians to combine unique aspects of different agents that may provide more benefits than the individual branded medications. During recent shortages of certain key drugs used in eye care, compounded medications have helped fill the gaps.[1]

The innovation cycle for manufacturing medication is an extremely long and expensive process that can restrict patients' access to drugs. Compounding may streamline development and guide the future of commercially manufactured medication. Many of today's agents began their therapeutic use as locally compounded medications.

The increasing expense of certain manufactured drugs has placed their use on an unsustainable course. For example, at $2,000 per injection, Lucentis (ranibizumab; Genentech) has the potential to cripple health care budgets. When using compounded Avastin (bevacizumab; Genentech) instead saves more than $1,900 per injection, it is hard to justify paying for ranibizumab, which provides no measured clinical benefit.[2]

## SAFETY CONCERNS FOR COMPOUNDED MEDICATIONS

The greatest concern regarding the safety of compounded medications is that rigorous FDA studies are not required to prove the safety and efficacy of the drug itself, its concentration, and/or the manufacturing process. Beyond the question of whether the drug is safe and effective, compounding raises the issues of who is making the drug and how. For example, concern over the safety of compounded medicines came to the fore after a recent outbreak of fungal meningitis caused by New England Compounding Center's contaminated methyl prednisone product, which resulted in more than 50 deaths and injured more than 700 individuals.[3] Compounded drugs that fall under state pharmacuetical regulations are subject to different guidelines than those that are manufactured and regulated by the FDA. New England Compounding Center's issues likely resulted from a lack of oversight when the center appeared to change from a loosely regulated compounding pharmacy to large-scale drug manufacturer (which typically requires strict FDA regulation).

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There are other examples of safety breaches that have resulted in severe eye-related morbidity and even mortality. In 2011, 12 patients developed endophthalmitis after receiving intravitreal injections of bevacizumab for treatment of age-related macular degeneration.[4] A similar event occurred in March 2013 when repackaged bevacizumab caused five cases of severe endopthalmitis.[5] Another compounding event that affected ophthalmology was the Brilliant Blue G contamination situation that resulted in multiple cases of endophthalmitis.[6]

## MITIGATION OF SAFETY CONCERNS

Compounding pharmacies have come under increased scrutiny. The Drug Quality and Security Act became law on November 27, 2013, in response to the 2012 meningitis outbreak. The act sets forth guidelines and consequences for compounding pharmacies and providers that use their services. The legislation introduced regulations for large

# WHAT'S THE BUZZ?

IN THE NEWS...

## Fourteen Arrested in Connection With Deadly Meningitis Outbreak

Fourteen people from a Massachusetts compounding pharmacy were arrested in December 2014 in connection with a 2012 national outbreak of fungal meningitis that killed 64 people. The owners of the Framingham-based New England Compounding Center, known as NECC, were among those arrested, according to the US attorney's office in Boston.

The charges are contained in a 131-count indictment. They included 25 predicate acts of second-degree murder as well as counts of racketeering, conspiracy, and mail fraud.

The US Centers for Disease Control and Prevention linked 751 cases of meningitis to the steroid injections in several states. Health officials said the affected individuals came down with fungal meningitis after their spines were injected with a contaminated, preservative-free steroid called *methylprednisolone acetate*.

The high-profile contamination case caused an uproar and prompted new legislation about compounding pharmacies.

sterile compounding pharmacies that require them to use advanced manufacturing standards; the act imposes federal oversight and requires that all pharmacies with an "Outsourcing Facilities" designation comply with Current Good Manufacturing Practices.

Beyond the state and federal laws, compounding pharmacies must self-regulate to preserve their legitimacy in the eyes of the public and medical community. Malpractice can further damage the field, injure patients, and potentially limit access to medications if the negative fallout results in overly strict laws. An example of self-regulation is accreditation with the Pharmacy Compounding Accreditation Board (www.pcab.org).

## CONCLUSION

Overregulation in the field of compounding could stifle growth, access, and affordability. Underregulation could harm the patients involved as well as deny future patients access to needed medication if pharmacies are shut down or overly regulated. Compounded drugs are important, but physicians need to ensure the agents are safe, effective, and worth the potential risk when compared to similar noncompounded medications. Physicians must not be swayed by overly aggressive marketing by big pharma or be influenced by inexpensive options offered by less-than-ideal sources. Instead, they must ensure their patients' compounded medications come from legitimate, appropriately regulated and accredited pharmacies. ■


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