



Published in final edited form as:

Optom Vis Sci. 2021 May 01; 98(5): 456–457. doi:10.1097/OPX.0000000000001696.

Letter to the Editor: The Impact of COVID-19 on the Ophthalmic Pharmaceutical Supply

Arjun Watane, BS, Nicolas A. Yannuzzi, MD, Jayanth Sridhar, MD

Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL

In December 2019, a new lower respiratory syndrome was first detected in Wuhan, China, and reported to the World Health Organization (WHO). The cause was determined to be a novel virus belonging to the coronavirus family, specifically known as COVID-19. Since then, this entity has spread rapidly on a global scale, challenging healthcare systems across six continents. On January 30, 2020, the outbreak was declared a Public Health Emergency of International Concern by the WHO, and finally on March 11, it was declared a worldwide pandemic.

With more than 69 million confirmed cases and 1.5 million deaths worldwide as of December 10, 2020,¹ the COVID-19 pandemic has deeply impacted the global healthcare economy, including the supply chain of the pharmaceutical industry. Several countries, including India, China, and much of Europe, have enforced strict quarantine and international travel restrictions. While these statutes are necessary to curb the pandemic, they impair pharmaceutical manufacturing and transport. Many active ingredients and medications of pharmaceutical companies of the United States are manufactured in overseas and international locations, including India (18%), Europe (26%), and China (13%). Production slow-downs and limitations as a result of travel and shipping restrictions may lead to supply delays and profound socioeconomic effects.² Pharmaceutical supply chain lead times are 4 to 6 months or longer, and their response to demand surges are slower than consumer product supply chains.³ Furthermore, manufacturers rely on highly skilled workers to produce formulations, and this makes the industry especially vulnerable to worker absenteeism. Finally, the American Optometric Association and the American Academy of Ophthalmology have recently reported on ophthalmic supply chain disruptions. Older medications generally incur a lower profit, and as a result of the lack of incentives, manufacturers produce them on a strict supply-demand model.^{4, 5} The backdrop of COVID-19 and the primary efforts to curb virus spread through isolation methods create the perfect environment for supply chain disruptions. This scenario warrants public attention of the potential impact of COVID-19 on the U.S. ophthalmic pharmaceutical industry and elicits a few sequential critical questions.

First, are ophthalmic medications also primarily manufactured internationally? Yes, they are; specifically, the US again relies heavily on India and China for ophthalmic pharmaceutical ingredients and products due to cheaper manufacturing costs. As outlined above, this creates

jsridhar1@med.miami.edu.

the potential for significant ramifications to the ophthalmic drug supply during the COVID-19 pandemic. To illustrate the realities of this evolving situation, the 2017 Medicare Part D Prescriber Public User File was analyzed to identify the 20 most commonly prescribed generic ophthalmic medications, as determined by each medications' total number of reimbursement claims.⁶ Manufacturers for each medication were identified through FDA's Orange Book database.⁷ Each manufacturer's website was searched for its manufacturing locations, and if not found, an exhaustive Google search was employed. If manufacturing locations were not available, then the presence of multiple international offices was assumed to indicate international manufacturing. Each one of the 20 most commonly prescribed generic ophthalmic medications was found to be at least partially manufactured overseas in addition to local sites.

Second, is there already evidence of shortages directly related to COVID-19? As of September 18, 2020, 13 ophthalmic medications are in shortage according to the FDA (Table 1).⁸ Three formulations (Lacrisert, timolol maleate gel, and timolol maleate solution) are in shortage as a result of manufacturing interruptions due to COVID-19, whereas the rest have been in shortage since prior to the pandemic. This is despite timolol maleate having 11 FDA-approved manufacturing sources.⁷

Third, are these shortages clinically significant at this point in time? Potentially, although there is no definite current crisis. Lacrisert is minimally utilized, with only 990 Medicare claims total in 2017, but timolol maleate is a widely prescribed glaucoma medication with 1.8 million Medicare claims in total in 2017. Given COVID-19's effect on in-person visits and intraocular pressure measurements, one could imagine a period of time with medication non-adherence due to the shortage and resultant suboptimal control of intraocular pressure for many glaucoma patients.⁹ Still, alternative glaucoma medications of different classes, such as alpha-agonists, prostaglandins, and carbonic anhydrase inhibitors, are widely available at this point in time, and the subset of patients completely dependent on timolol maleate availability to prevent vision loss is likely quite small. Another example where COVID-19 may potentially have clinical implications should the pandemic force further supply-chain disruptions is for myopia control. Atropine sulfate ointment is used as an off-label treatment for myopia, and patients may experience a myopia rebound if suddenly prevented from receiving this medication.¹⁰ Despite this, one could reasonably conclude that as of December 10, 2020, ophthalmologists, optometrists, and their patients are still in good shape when it comes to the pharmaceutical supply chain.

Still, the full effects of these disruptions may not be fully realized yet. As evidenced by the medications already in shortage due to COVID-19, there will likely be more shortages to come along with delays in meeting the demand for the previously lacking drugs. Additionally, infectious disease experts have suggested threats of a second wave of COVID-19, and a disruption in the supply and reduction in available manufacturers could also impact the pricing of commonly prescribed topical eye drops. Thus, the trickle-down effect of COVID-19 has potential for long-lasting ophthalmic consequences if patient needs are unmet. Through the FDA Safety and Innovation Act, pharmaceutical companies are required to notify the FDA when manufacturing interruptions or production changes may lead to a supply disruption or discontinuation. The FDA actively works with pharmaceutical

companies to assist them when production issues arise or demands change. We urge providers to stay vigilant of fluctuations in drug availability and pricing in the near future and to remain closely in communication with patients who may not report an inability to obtain necessary medication.

The implications of COVID-19 go beyond eye care as its socioeconomic effects affect the entire medical field. Ophthalmologists and optometrists should be mindful of the current pharmaceutical supply deficits, and also prepare for more drug shortages in the near future, a reasonable domino effect of COVID-19. Potential solutions include reducing patients' daily medication usage, switching to similar medications that are more readily available, and careful patient education of COVID-19's impact on pharmaceutical supply. In these unprecedented times, we must constantly re-assess and re-evaluate the state of the pharmaceutical supply chain to best serve our patients.

REFERENCES

1. Dong E, Du H, Gardner L. An Interactive Web-based Dashboard to Track COVID-19 in Real Time. *Lancet Infect Dis* 2020;20:533–4. [PubMed: 32087114]
2. National Public Radio (NPR). Lupkin S. How Coronavirus Is Affecting The U.S. Pharmaceutical Supply; 2020. Available at: <https://www.kpbs.org/news/2020/mar/12/how-coronavirus-is-affecting-the-us/>. Accessed April 20, 2020.
3. Healio Primary Care: COVID-19 Resource Center. Keskinocak P, Ozkaya E. US Pharmaceutical Supply Chain Unprepared for COVID-19; 2020. Available at: <https://www.healio.com/news/primary-care/20200427/us-pharmaceutical-supply-chain-unprepared-for-covid19>. Accessed June 4, 2020.
4. American Optometric Association (AOA). FDA says fluorescein, ophthalmic meds among drug shortages. Available: <https://www.aoa.org/news/clinical-eye-care/public-health/fda-drug-shortage-report?sso=y>. Accessed 12/10/2020.
5. American Academy of Ophthalmology (AOA): Eye on Advocacy. New, Nationwide Ophthalmic Drug Shortages Emerge; 2019. Available at: <https://www.aao.org/eye-on-advocacy-article/new-nationwide-ophthalmic-drug-shortages-emerge>. Accessed December 12, 2020.
6. Center for Medicare and Medicaid Services (CMS). Medicare Provider Utilization and Payment Data: 2017 Part D Prescriber. Available at: <https://data.cms.gov/Medicare-Part-D/Medicare-Provider-Utilization-and-Payment-Data-2017/77gb-8z53>. Accessed April 20, 2020.
7. US Food & Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations; 2020. Available at: <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>. Accessed April 20, 2020.
8. US Food and Drug Administration (FDA). FDA Drug Shortages: Current and Resolved Drug Shortages and Discontinuations Reported to FDA; 2020. Available at: <https://www.accessdata.fda.gov/scripts/drugshortages/default.cfm?panel=15#tabs-3>. Accessed June 4, 2020.
9. Velez-Gomez MC, Vasquez-Trespacios EM. Adherence to topical treatment of glaucoma, risk and protective factors: A review. *Arch Soc Esp Oftalmol* 2018;93:87–92. [PubMed: 29032867]
10. Upadhyay A, Beuerman RW. Biological Mechanisms of Atropine Control of Myopia. *Eye Contact Lens* 2020;46:129–35. [PubMed: 31899695]

Table 1.**Ophthalmic Drugs Currently in Shortage as of December 10, 2020.**

Acetazolamide Injection
Atropine Sulfate Ophthalmic Ointment
Cyclopentolate Ophthalmic Solution
Cysteamine Hydrochloride Ophthalmic Solution
Dexamethasone Sodium Phosphate Injection
Dorzolamide Hydrochloride and Timolol Maleate (Cosopt) Ophthalmic Solution
Dorzolamide Hydrochloride Ophthalmic Solution
Echothiophate Iodide (Phospholine Iodide) Ophthalmic Solution
Erythromycin Ophthalmic Ointment
Fluorescein Injection
Fluorescein Strips
Hydroxypropyl (Lacrisert) Cellulose Ophthalmic Insert
Timolol Maleate Ophthalmic Gel Forming Solution
Timolol Maleate Ophthalmic Solution
Triamcinolone Acetonide (Triesence) Injection, Suspension
Trifluridine Ophthalmic Solution

Bolded medications are those on back order due to manufacturing interruptions due to COVID-19, as reported by the FDA.⁸