OVERCOMING DEVELOPMENT OBSTACLES TO THE DELIVERY OF EFFECTIVE OCULAR THERAPY

Here, Robert Lee, PhD, President of the CDMO Division at Lubrizol Life Science Health, discusses the growth of the ocular drug delivery market, the challenges formulators face in developing novel ocular technologies, and the role contract development and manufacturing organisations have to play in this growing market segment.

The global ocular drug product market was estimated to be worth US$36.7 billion (£26.3 billion) in 2020 and is set to expand at a compound annual growth rate 6.4%. One of the key reasons for this growth is an increasing awareness regarding eye-related diseases among the general public – not just in established markets but in a growing number of emerging economies as well.

From cataracts and age-related macular degeneration to dry eye and conjunctivitis, a wide range of conditions can afflict the eye, causing everything from minor discomfort to serious eyesight issues. The number of patients around the world seeking healthcare support for these conditions is growing rapidly.

This growth in the market is driving demand for advancements in therapies to treat a diverse array of eye conditions. Historically, the ocular therapy space has been focused almost exclusively on the development of topical treatments, such as eye drops and ointments. Such products have the advantage of being non-invasive but are not without their drawbacks. Topical treatments can only treat surface conditions, such as an ophthalmic allergic reaction, limiting the range of health issues they can tackle.

Traditional topical formulations also have disadvantages when it comes to patient experience. Standard eye drops, for example, often leak from the eye and drip down the cheek within moments of being administered. Not only is this messy and unpleasant for the patient, it means the dose can be removed from the eye before the API has been absorbed, undermining its effectiveness as a treatment and often resulting in the need for multiple daily administrations.

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As a result, the industry is moving towards more complex formulations and alternative dosage forms, such as injections and implants, to address the growing number of ophthalmic conditions.

RECENT OPHTHALMIC INNOVATIONS

A significant factor in the growth of the ophthalmic market has been innovations in treatments, including:

- Mucoadhesive topical formulations that have been designed to maximise retention at the target site, thereby extending active duration and allowing more of the API to penetrate.
- Long-acting injectables and ocular implants, which allow for extended drug release over a period of months or years. These enable the development of new treatments for more serious, long-term conditions, such as diabetic retinopathy.
- Drug-eluting contact lenses and intraocular implants that help to avoid leakage and dosing errors associated with topical applications.

With the potential posed by these innovations, it is no surprise that more and more pharma companies are exploring ocular drug products to provide better quality therapies for ocular disorder patients.

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However, many companies face challenges when developing effective ocular drug products, from formulation issues to the choice of dosage form or delivery device, as many of these recent innovations are increasingly complex. This means that it is rare for pharma companies to have the infrastructure and expertise already in-house to develop ophthalmic products successfully on their own. Specialised expertise is needed to develop truly game-changing ocular therapies. To overcome these issues and ensure the successful development of their ocular therapy, drug formulators have several factors to consider.

KEY CONSIDERATIONS IN OCULAR DRUG DEVELOPMENT

Aseptic Processing

It is imperative that any ocular product is sterile to protect patients from infection, as the eye is sensitive and critical for sight. There are strict regulatory requirements in place with respect to sterility for ocular products, as opposed to other administration routes such as oral.

Dosage Form

The form that a drug product will take depends on the specific portion of the eye the API is intended to treat, as well as the desired dosing frequency. Conditions affecting the front of the eye are well-suited for topical formulations, including locally applied solutions, suspensions and emulsions. Retinal issues and conditions affecting the back of the eye are more suited to injections or implants. In these cases, to improve convenience for the patient, it may be preferable to develop long-acting formulations to minimise dosing frequency, and therefore also any discomfort experienced during administration.

API Challenges

The physical characteristics of the API must be factored into the ocular drug development process. The solubility of the API, for example, will affect numerous aspects, including which formulation techniques are used and what excipients are present.

OVERCOMING API SOLUBILITY OBSTACLES

No matter what dosage form is chosen for an ocular drug product, there are often challenges that need to be overcome during development to maximise the therapeutic effect of the finished product.

Across the pharmaceutical industry, more new chemical entities are being registered that exhibit poor solubility. This poor solubility poses challenges not only during the manufacturing process but also causes problems with the bioavailability of the API. Failure to address this issue when formulating the drug will have a negative impact on its effectiveness.

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This challenge is particularly pressing in the ocular drug delivery segment. For example, there are few excipients approved for use in ocular dosage forms to help overcome solubility or bioavailability issues, especially for intravitreal administration. This restricts the avenues available to drug formulators to enhance the solubility of their APIs.

However, there are other formulation approaches available that can help overcome solubility issues. Advanced technologies, such as API physical modification techniques, are particularly effective. One example of this approach is nanomilling, which reduces the API particle size – increasing drug surface area and enhancing content uniformity along with dissolution rate. This can maximise the solubility of APIs that are moderately insoluble and allow for the formulation of highly insoluble APIs. As a result, the drug formulation may offer enhanced bioavailability and be able to achieve therapeutically relevant levels of the API within the target tissue or organ that would not otherwise be possible.

Additionally, nanomilling can create a more uniform colloidal suspension that offers enhanced application benefits – moving more effectively through the device or, in the case of a topical formulation, spreading more effectively across the surface of the eye.

Other techniques include additional physical modification methods, such as micronisation, and API chemical modification methods, such as PEGylation. Regardless of the method, it is important to focus on the drug product's target product profile and let science dictate the rest. Having more than one option or technique at your disposal is very important in the early stages of product development.

THE ROLE OF CDMOs

New technologies offer exciting avenues to both enhance patient convenience and compliance and optimise the effectiveness of drugs by improving the bioavailability of poorly soluble APIs. As more and more people are able to access ocular healthcare across the globe, we can expect patient demand for new and improved ocular products to grow.

To stand out in an increasingly competitive market, drug formulators will need to consider new ways of delivering their products and harnessing the benefits of the new generation of ocular dosage forms. At the same time, they will need to overcome the challenges standing in the way of successful ocular drug development – from bioavailability issues to aseptic processing and other manufacturing obstacles. As a result, contract development and manufacturing organisations (CDMOs) with expertise in this area will continue to play an important role in the development of novel ocular therapies.

ABOUT THE AUTHOR

Robert Lee, PhD, President, Lubrizol Life Science Health, CDMO Division, is responsible for product and business development along with providing the company's strategic direction. Before joining Lubrizol, Dr Lee held senior management positions at Novavax, Lyotropic Therapeutics and Imcor Pharmaceutical Co. He holds BSc degrees in Biology and Chemistry from the University of Washington (Seattle, WA, US) and a PhD in Physical Bioorganic Chemistry from the University of California (Santa Barbara, CA, US). Dr Lee has published more than three dozen articles and five book chapters, as well as holding 11 issued patents and 15 provisional or PCT patent applications. He has over 30 years of experience in pharmaceutical research and development of both therapeutic drugs and diagnostic imaging agents. Dr Lee maintains strong academic ties, including an appointment as Adjunct Associate Professor of Pharmaceutical Chemistry at the University of Kansas (Lawrence, KS, US) in the early 1990s, serving as a reviewer for both the International Journal of Pharmaceutics and Journal of Pharmaceutical Sciences, and serving on the Editorial Board for the journal MOJ Bioequivalence & Bioavailability, The Scientific Pages of Nanotechnology and the Journal of Analytical and Pharmaceutical Research.

ABOUT THE COMPANY

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