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NAVIGATING THE CHALLENGES OF BRINGING INTRANASAL DRUG FORMULATIONS AND DEVICES TO PATIENTS

In this article, Joe Neale, Head of Innovation, Development and Programme Management, and Ross Errington, Head of Drug Product Development, both of Recipharm, explore the obstacles and opportunities facing the intranasal drug delivery market and how manufacturers can overcome them by harnessing innovative platforms like Unidose® Xtra.

The inhalation drug delivery market for both oral and nasal applications is expanding rapidly, offering a promising alternative to traditional routes of drug administration, such as solid-dose oral or injectable methods.

Key to this expansion is the diversification of administration routes for biologic drugs. Traditionally, these types of drugs were limited to parenteral administration – to preserve the API before reaching its target location. These APIs also pose bioavailability challenges to the oral route, as the large molecules within them may have difficulty passing through the membrane of the intestines into the bloodstream, whereas small-molecule APIs can do so with ease.

Advancements in formulation technology now allow for greater exploration of alternative delivery methods, such as inhalation.

A key segment of the inhalation market, intranasal drug delivery, offers additional treatment benefits to patients. Nasal inhalation therapies provide a larger surface area for absorption, as well as direct access to the central nervous system for faster action. These treatments can be administered in various forms, including solutions, suspensions, gels and powders. The selection of the appropriate form depends on the characteristics of the drug, the targeted tissue and the desired rate of absorption.

Drug developers must overcome a range of formulation challenges to ensure efficacy, safe dosage and ease of administration for patients. Manufacturers must also contend with device customisation to optimise spray performance and ensure that they meet the requirements of each treatment.

THE THERAPEUTIC NEED FOR INTRANASAL DRUG PRODUCTS

The global intranasal drug delivery market is projected to reach US$71.3 billion (£59 billion) by 2026.[1] A number of drivers are behind this rapid growth.

The rapid onset of action of intranasal drug delivery products is highly attractive to drug developers. This is possible due to the

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high surface area of accessible blood vessels within the nasal cavity, allowing for fast absorption into the patient's bloodstream. This also results in improved bioavailability for the drug product compared with oral administration, as nasal delivery allows the formulation to bypass the gastrointestinal system and hepatic metabolism.

As a result, intranasal therapies offer more innovative treatment options for a wide variety of conditions. They are particularly attractive for the treatment of chronic and neurological disorders,[2] such as chronic pain, inflammation and headaches. As a non-invasive treatment, this targeted delivery also means that there are typically fewer side effects for patients and a user-friendly, convenient and needle-free experience. This subsequently leads to a higher level of patient acceptance and compliance, as well as easier administration for healthcare professionals (HCPs).

Research has also shown that intranasal delivery of vaccines can result in a more robust immune response compared with delivery of the same vaccine via a traditional injection.[3] Furthermore, this administration method enables user-independent delivery of nasal sprays – an essential, even life-saving, treatment in acute settings, emergencies and critical care situations, such as opioid overdoses or seizures. As a result, the need for intranasal drug delivery is increasing in the medical field as it offers a safe and efficient way to deliver medication to patients.

THE COMMERCIAL NEED FOR INTRANASAL DRUG PRODUCTS

From a commercial perspective, intranasal drug products offer a promising opportunity for drug developers to extend the lifecycle of their biologic products. For example, the patents for many biologics that have been on the market for a long time are set to expire soon, meaning that drug developers are facing the challenge of finding new ways to extend their ownership of their discoveries amid competition from biosimilars.

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By reformulating their biologics as an intranasal product, developers can extend their patent protection and maintain market exclusivity. This is because intranasal drug delivery is considered a novel administration route and can be considered as a new formulation, which can make an existing biologic eligible for new patents.

Other commercial opportunities include:

- **Faster vaccine delivery** – the post-covid-19 drive to deliver vaccines on a mass scale at speed has led to more research into the mucosal delivery of vaccines to shorten administration time.
- **Streamlined regulatory requirements** – as intranasal drugs are considered non-invasive and pose a lower risk of adverse reactions, the regulatory pathway for intranasal drugs is often less rigorous than for parenterally delivered biologics.
- **Demand for self-administration** – the demand for patients to be able to administer their own treatment is increasing, and intranasal drug delivery provides added convenience by enabling patients to take their own medication without visiting an HCP.
- **Greater patient-centricity** – a focus on patient-centricity makes intranasal treatments a more convenient option for individuals who may need to take a vaccine for specific reasons, such as tropical disease vaccinations prior to going abroad.

THE CHALLENGES OF MANUFACTURING INTRANASAL DRUG PRODUCTS

In order to bring the benefits of intranasal drug products to patients, manufacturers must overcome several barriers across both the drug formulation and the design of drug-delivery devices. These barriers include:

- **Compatible delivery device design** – ensuring that the delivery device works well with complex formulations, such as small molecules, peptides, vaccines and biologic formulations, can be difficult when administering intranasally.
- **Optimising spray design** – optimising the effectiveness of nasal sprays requires a high level of understanding of how the formulation and its delivery device interact with one another. The design of the spray nozzle, for example, has an impact on the droplet size and distribution of the formulation, which in turn affects the drug's bioavailability and speed of action.
- **Tailoring to overcome excipient challenges** – the addition of excipients can alter the viscosity and sprayability of the product, further influencing its effectiveness.
- **Engineering the force of actuation** – the force of actuation when administered must also be carefully engineered in accordance with the characteristics of a specific drug formulation. This is because shear forces during administration can damage the API in some large-molecule formulations, risking rendering the treatment ineffective.
- **Ensuring dosage uniformity** – biologic treatments require optimal spray techniques to ensure the correct dosage, with improper techniques resulting in most of the formulation being deposited on the walls of the nose, rather than penetrating further into the nasal cavity, impacting dose uniformity.
- **Aseptic/sterile formulation development** – maintaining sterility during filling in the drug device's primary container is key to launching a successful intranasal drug product.

Manufacturers must ensure compatibility for the drug and its delivery device and consider patient usability for self-administration. Formulators must also find ways to overcome the restricted bioavailability due to the low solubility of some of these drugs. Furthermore, the nasal cavity is a sensitive area, and the use of certain medications can cause irritation or discomfort for some patients, particularly in paediatrics. This can be particularly problematic for medications that need to be administered on a regular basis.

OVERCOMING THE CHALLENGES OF INTRANASAL DRUG DELIVERY

Recent technological advances in the market for both oral and nasal inhalation devices have meant that pharmaceutical companies now have more options available to overcome these issues than ever before. One such example is the proprietary Unidose® Xtra device by Recipharm.

This device was created in collaboration with a pharmaceutical development specialist to establish a "formulation-to device interface specification" for several potential single-dose nasal therapies. This specification informed the device design process, which adopted a platform approach, enabling it to be easily customised to meet the specific formulation and performance needs of the customer with minimal redesign required.

As demand for more convenient and comfortable drug delivery routes increases, devices such as Unidose® Xtra have been developed to accommodate peptides and vaccines, and have the potential to accommodate sensitive biologic molecules – with alternative nozzle technologies available, enabling delivery in a single dose for a variety of formulations. This makes Unidose® Xtra ideal for a wide range of treatments, such as vaccines, opioid overdose, pain relief, seizures and anxiety.

The device can be adjusted to suit formulations with a range of viscosities, and the speed and force of actuation required can be adjusted to ensure that the drug is delivered at the optimal rate for maximum efficacy. This level of customisation is particularly beneficial for users who may have limited strength or dexterity – such as geriatric, disabled or paediatric patients.

ABOUT THE AUTHORS

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Unidose® Xtra is designed to allow patients to easily and safely administer their own medication, without the need for assistance from a healthcare professional, or for rapid use in emergency situations by a caregiver or the patient themselves.

GETTING INTRANASAL INNOVATIONS INTO THE HANDS OF PATIENTS

While intranasal drug delivery and devices offer promising innovations, drug developers looking to harness their potential have several considerations to take into account. Given the complexities of formulating and adapting a drug product to an intranasal drug delivery device, developers must ensure that they have not only the expertise but also the capacity, equipment and regulatory support to successfully bring it to market.

But by collaborating with specialist partners in this area, drug developers can overcome these challenges. The right partner will be equipped with the knowledge, capabilities and state-of-the-art facilities to support the development and manufacture of such innovations, no matter how complex the requirements. For example, by partnering with a company like Recipharm, which has expertise in innovative platforms like Unidose® Xtra alongside formulation development, pharmaceutical and biotech companies can benefit from its experience and resources to develop and manufacture intranasal drug products more efficiently and effectively.

These partnerships can be instrumental in getting intranasal innovations to patients, as they provide the necessary support for the development and manufacture of these products, which can be complex and difficult to produce. This collaboration is key to enabling the expansion and diversification of biopharmaceutical drugs and treatments, resulting in more cost-effective and patient-centric products.

HARNESSING INTRANASAL DRUG DELIVERY TO EXTEND THE DRUG PRODUCT LIFECYCLE

The potential of intranasal drug delivery extends much further than patient and HCP benefits – it also offers the opportunity for developers to extend the lifecycle of their existing products. As patents for injectable and oral biologics expire, drug product owners are looking for innovative solutions to prolong the lifecycle of their products.

With the generics and biologics markets growing increasingly competitive, it is important for drug developers to explore all options for product lifecycle management. Intranasal drug delivery offers a promising solution, enabling companies to streamline the redevelopment process and enhance dosing precision, as well as improve the cost efficiency of the devices themselves. Patient and HCP benefits will also play a role in lifecycle management, with intranasal delivery offering multiple benefits.

Working closely with device experts like Recipharm will give intranasal drug developers access to the tools they require to take advantage of advancements in intranasal delivery technology. Additionally, these partnerships can help to extend the lifecycle of a wide range of drug products well into the future, whilst also offering significant patient convenience and cost-efficiency benefits.

ABOUT THE COMPANY

Recipharm is a leading contract development and manufacturing organisation (CDMO) in the pharmaceutical industry, with almost 9,000 employees. The company offers manufacturing services of pharmaceuticals in various dosage forms, production of clinical trial material and APIs, pharmaceutical product development and development and manufacturing of medical devices. Recipharm manufactures several hundred different products for customers, ranging from big pharma to smaller research and development companies. The company operates development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US, and is headquartered in Stockholm, Sweden.

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