H&T PRESSPART

EMBEDDED CONNECTED METERED DOSE INHALERS MEETING REQUIREMENTS FOR MASS ADOPTION

In this article, Benjamin Jung, PhD, Program Manager, eMDI, and Dana Shears, Sales & Business Development Director, the Americas, both of H&T Presspart, describe the role connected devices can play in the treatment of asthma and COPD, discuss the requirements for mass adoption, and introduce their inhaler, the eMDI, which has connectivity fully embedded.

Non-adherence to medication is a critical problem in healthcare, especially in the area of chronic diseases. The resulting economic burden across all diseases is estimated at US$100-300 billion (£77-230 billion)[1] in the US and at €125 billion (£108 billion) in Europe.[2]

Asthma and COPD are considered as major chronic conditions. Today, more than 300 million people have asthma worldwide and this figure is set to rise by another 100 million by 2025.[3] In addition, globally more than 200 million people suffer from COPD[4] and the number of patients will also increase significantly. Uncontrolled symptoms of asthma and COPD affect quality of life, decrease work and school performance and reduce physical activity.[3] Overall asthma is responsible for 250,000 deaths per year[3] and COPD even for more than three million fatalities.[5]

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The cost burden associated with asthma and COPD is high as well. Healthcare costs, and costs due to lost productivity, have been calculated to be as high as US$92 billion in the US[6,7] and €82 billion in Europe[8] (see Figure 1). Asthma attacks and COPD exacerbations are believed to be the main cost driver. Effective treatment and medications are readily available. In fact, the three main asthma/COPD drugs rank within the top 25 pharmaceutical products by global sales.[9]

Adherence to preventer (controller) medication for asthma and COPD – such as inhaled corticosteroids (ICS) or long-acting beta agonists (LABAs) – is critical to control symptoms.[10] Nevertheless, adherence rates to these medications have been shown to be insufficient and to vary greatly. A meta-study revealed adherence rates of 30-66%, for example, depending on the study population.[11] These rates reflect so-called secondary adherence, which occurs after the first prescription has been filled. Primary adherence, reflecting the share of patients filling the first prescription, is insufficient too.[12] As a result, due to poor adherence, a substantial number of patients do not realise the maximum benefit of their medical

Dr Benjamin Jung
Program Manager, eMDI
T: +44 1254 582 233
E: benjamin.jung@presspart.com

Dana Shears
Sales & Business Development Director, the Americas
T: +44 1254 582 233
E: dana.shears@presspart.com

H&T Presspart
Presspart Manufacturing Ltd
Whitebirk Industrial Estate
Blackburn, Lancashire
BB1 5RF
United Kingdom

www.presspart.com

treatment, often resulting in the overuse of reliever medications, increased exacerbations, frequent hospital admissions, reduced quality of life and even avoidable deaths.[13,14]

CONNECTED DEVICES TO INCREASE ADHERENCE

In general, connected devices are becoming increasingly prevalent in chronic condition management. They track patient adherence, encourage patients to take ownership of their own care, and connect patients better with their providers and other stakeholders in real time. Therefore, they offer a great opportunity to increase adherence and improve the quality of life of patients.

Currently there are a number of approved and marketed connected devices within the healthcare sector. Examples include injector pens, heart rate, blood pressure and blood glucose monitors, and pill packaging and dispensing solutions. In the area of asthma and COPD, connected add-on devices for inhalers (MDIs, DPIs, breath-actuated MDIs and soft-mist inhalers) have been approved by regulatory authorities, are being marketed[15] and used primarily for clinical studies. More recently, embedded device designs have been developed and are being evaluated.

External add-on devices have demonstrated, with proper use, the ability to increase adherence to asthma and COPD medication significantly in clinical studies. The experienced adherence uptake differs to a high degree, as some studies show an improvement above 150% while others show results below 50%. These differences can be attributed to the age and the level of asthma control within the study population and the duration of the study. More importantly, several studies have demonstrated significant improvement in clinical outcomes, including reduced exacerbations, fewer unplanned attendances at the GP or emergency department, decreased hospitalisations and less frequent use of supplemental oral steroids.[16]

In addition to the direct benefits for patients in terms of the clinical outcomes, connected devices for asthma and COPD treatments have potential advantages for a number of other key stakeholders. For physicians, patient monitoring is enhanced, visits can be scheduled more appropriately, patient-physician dialogue is fostered, diagnosis and identification of optimal medication is improved and early warnings due to changing health status can be

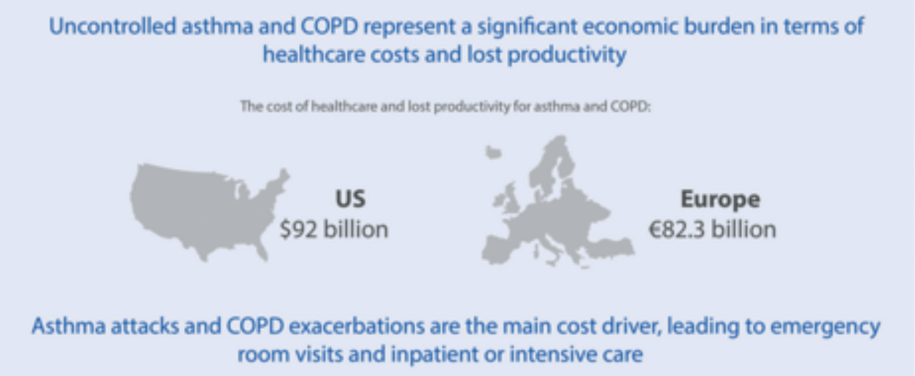

Figure 1: Economic burden of asthma and COPD.

implemented. Payers can potentially realise cost reductions due to improved healthcare utilisation, including fewer hospitalisations. This is especially promising among patients with severe asthma and COPD.[17] Employers may benefit as well, as they will experience fewer missed work days, increased productivity, and potentially a reduction in insurance premiums. Pharmaceutical companies will likely benefit from an increase in refills resulting in greater sales. Additionally, R&D spend could be reduced, as clinical trial outcomes would be more predictable and effective and, post launch, real-life product in-use data can be generated to confirm actual drug therapeutic benefits. Together, adherence and therapeutic benefit demonstrated by real-life data could boost brand image and lead to improved customer loyalty.

REQUIREMENTS FOR MASS ADOPTION

With these potential benefits for various stakeholders possible, why has the adoption of connected devices for asthma and COPD been limited to date? One answer may relate to the fact that, at present, a number of requirements for mass adoption have not been fully satisfied. In an effort to understand why, we have evaluated the situation from four different device-related perspectives: patient, business model, regulatory, and data collection and management.

From a **patient** perspective, broad acceptance is paramount. New devices and products need to be simple and should not present any significant changes to the status quo. The requirement for a patient to add a separate device to their inhaler or perform additional operations, such as recharging or disassembling the device, necessitates the need for further instruction and training. This will lead to a high likelihood of discontinued use. Patient adoption and adherence to the new connected devices for asthma and COPD can be realised through intuitive, discrete and non-reusable designs. These new designs should be based on existing inhaler forms and function similar to conventional "press-and-breathe" MDIs – the most widely used device for administering asthma and COPD medications. Connected devices should also be fully embedded, meaning the electronics are contained totally within the inhaler. This avoids patients receiving an external "add-on" device and an inhaler separately and relying on them to complete the assembly and activation properly.[18]

At the moment, a sound **business model** for connected devices for asthma and COPD is still undefined.

From a pharmaceutical company's perspective, a model based solely on improved sales due to increased adherence is subject to uncertainties, for example regarding the potential increase in primary adherence which is often not covered in studies. The realisation of higher reimbursement by payers is not proven, since validated, accurate data, to-date

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is limited and there are some concerns that healthcare cost reduction may not be achieved in all patient subpopulations. As such, cost sharing between payer and patient has yet to be defined and would certainly effect broad market adoption. In light of this, the features and functionality of connected devices and their associated costs should be carefully considered in order to achieve the necessary economic targets and to promote mass adoption. Therefore, the feature set offering the optimum cost/benefit ratio should be realised.[19]

From a **regulatory** perspective, changes or introductions of new technology can be challenging. In the case of existing formulations, any changes related to the drug delivery performance should be avoided. By design, embedded devices should not disrupt the drug delivery pathway or affect product performance in any way. Re-usable, rechargeable or interchangeable device features will present additional challenges and/or limitations to approval and adoption, since patients will need additional training and more extensive instructions to insure correct use of the device and fulfilment of ongoing maintenance requirements.

Conversely, incorporation of previously approved components for critical features, and replication of current device operation and existing form factors will simplify the regulatory pathway resulting in faster speed-to-market and higher gains in market share.

From a **data collection** and **management** perspective, three aspects are key: data quality, data integrity and data integration. Add-on devices can , because of their design, facilitate the generation of less reliable information as compared with fully embedded devices. In some instances, it may be possible for these connectivity devices to be used without dispensing the medication. It is also possible for the patient to use the connectivity device selectively or interchange the device with multiple inhalers.

Real-time, unadulterated data is key to confirming adherence and therapeutic benefit of prescribed medicines. Data integrity should be governed and secured by a system (connected device and platform) designed for zero data loss, proper encryption and the highest levels of security. Furthermore, data integration between competing systems is critical since there are potentially multiple inhalers, from different pharmaceutical companies used in parallel and applying different systems. Therefore, platforms must be designed to permit full data integration between different systems.

Table 1 summarises the requirements towards connected devices for asthma and COPD from different perspectives as discussed here.

Requirement towards connected devices for asthma and COPD	Underlying Perspective(s)
Intuitive, discrete	Patient
Non-reusable, disposable	Patient, regulatory
Minimal changes to the existing products	Patient, regulatory
Fully embedded design	Patient, business model, data
Based on conventional MDI inhaler designs	Patient, regulatory
Feature set with optimum cost/benefit ratio	Business model
Limited disruption to drug delivery pathway	Regulatory
Integration of approved components for critical features	Regulatory
System designed for zero data loss and proper encryption	Data
Enabling data integration	Data

Table 1: Requirements towards connected devices and underlying perspectives.

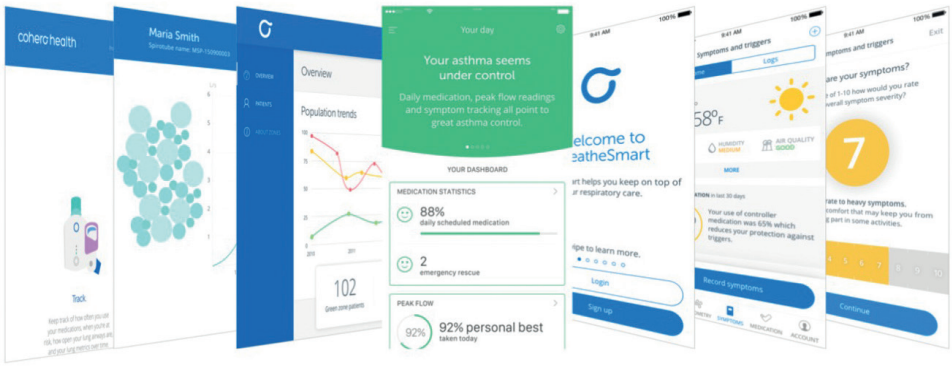

Figure 2: H&T Presspart's eMDI powered by Cohero.

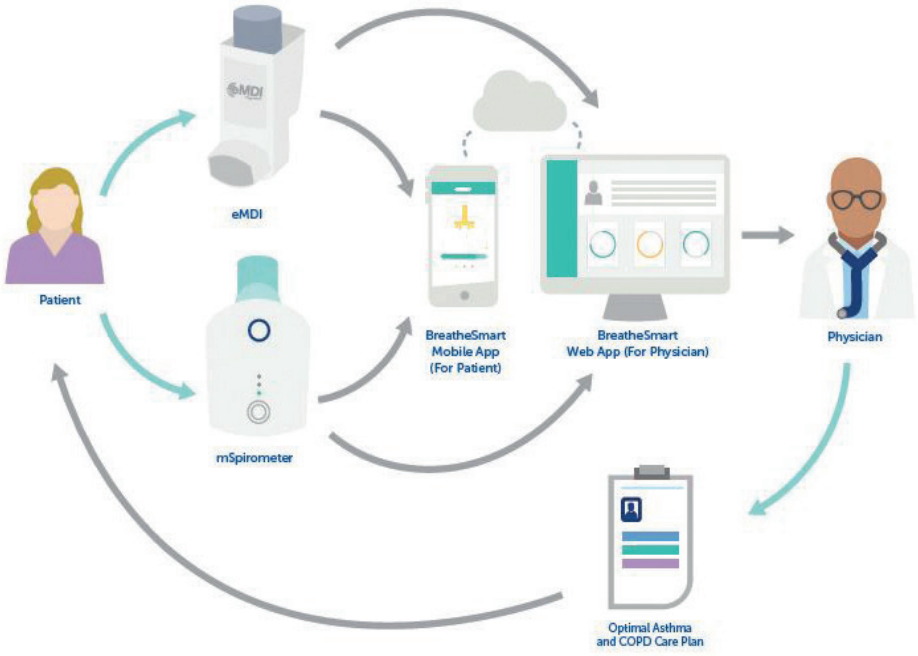

Figure 3: Integration of the eMDI with BreatheSmart from Cohero Health.

> "It is the first fully-embedded, intuitive, connected MDI comprising a feature set with an optimum cost/benefit ratio and allowing fast-track regulatory approval."

H&T PRESSPART'S eMDI POWERED BY COHERO

In an effort to address the ongoing issues of patient adherence in the area of asthma and COPD, H&T Presspart and Cohero Health (New York, NY, US) formed a strategic device development and marketing partnership. The partnership combines H&T Presspart's more than 45-year experience of MDI design and component manufacture with Cohero Health's expertise in digital innovation. As a result of this multi-year collaboration the companies created the first market-ready, fully-embedded, intuitive connected MDI solution: H&T Presspart's eMDI™ powered by Cohero (Figure 2).

H&T Presspart's eMDI powered by Cohero was developed to achieve a broad market adoption by fulfilling the requirements for connected devices – with its pure device design and with its integration with BreatheSmart from Cohero Health.

The eMDI device design represents an evolution of existing inhaler technology. Its connective hardware and software are **fully-embedded** within the actuator design, making it especially **intuitive** for patients to operate, whilst providing increased data quality and greater marketing appeal. The change to existing MDIs' form and function **is limited.** The compact size closely mirrors that of existing MDIs, permitting non-intrusive, **discrete** use by patients.

As a fully **disposable, non-reusable** unit, the eMDI eliminates the need for users to do anything other than press and breathe, as with their **standard MDI**. This eliminates the need for additional training, recharging, assembly or re-assembly. From a risk and reliability perspective, the electronic componentry is **separated from the medication delivery pathway** and the device **incorporates a US FDA-approved mechanical dose counter.**

The eMDI seamlessly integrates with BreatheSmart from Cohero Health (Figure 3), the only comprehensive respiratory disease management platform that enables tracking of both controller and rescue medications, along with clinically accurate lung function measurement via a mobile spirometer. In connection with BreatheSmart, the eMDI enables improved adherence, engagement in self-care and real-time monitoring by caregivers and the healthcare community.

The electronics detect the actuation of the inhaler, adds a date/time stamp, and shares the data wirelessly with a device application, for example on a smart phone, and a cloud. Feedback regarding the patient's actuation technique is also included in the inhaler design. The eMDI powered by Cohero has been designed to capture these key parameters to confirm patient adherence and therapeutic effect without the incorporation of sophisticated, costly sensors and other complicated mechanical parts: Therewith, it offers a **favourable cost/benefit ratio** for global adoption.

From a data perspective, the eMDI in connection with BreatheSmart is **designed for zero data loss, secure encryption** and information storage via a US Health Insurance Portability & Accountability Act (HIPAA)-compliant cloud. The capability for enabling **data integration** with other, even competing systems, has been developed and demonstrated by Cohero Health in a clinical trial in connection with the Koneska Health (New York, NY, US) data platform.[20]

CONCLUSION

With its eMDI powered by Cohero, H&T Presspart has created a versatile product designed to fulfil requirements for mass adoption of connected devices for asthma and COPD. It is the first fully-embedded, intuitive, connected MDI comprising a feature set with an optimum cost/benefit ratio and allowing fast-track regulatory approval. As such, it offers the opportunity to increase adherence and clinical outcomes for patients on a broad scale and to realise the power of real-time, accurate data. In collaboration with pharmaceutical manufacturers, H&T Presspart and Cohero Health are leveraging the potential of the eMDI for asthma and COPD sufferers worldwide. Additionally, they are enabling other stakeholders in overcoming non-device requirements for mass adoption. Together, the burden of insufficient adherence can be eliminated as "drugs don't work in patients who don't take them".[21]

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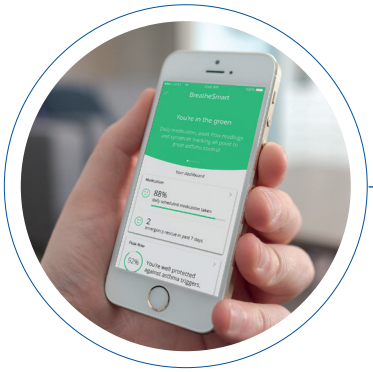
eMDI powered by cohero



Smartphone app connectivity to allow real-time tracking and care management

Mechanical Dose Counter

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H&T Presspart are pleased to introduce the first market-ready, fully-embedded, intuitive and connected metered dose inhaler (eMDI) established to optimize care of patients ensuring from asthma and COPD.

The eMDI integrates seamlessly with BreatheSmart from Cohero Health, the only respiratory disease management platform that enables tracking of both controller and rescue medications, along with clinically accurate lung function measurement, in real-time.