Dose and deliver: How PMDIs are transforming asthma and COPD treatments

Chris Baron, Director of Business Development at Aptar Pharma, explores how pressurised metered-dose inhalers (pMDIs) are continuing to change the landscape of asthma and COPD care

Pharmafile: How do pMDIs aim to treat asthma and chronic obstructive pulmonary disease (COPD)?

Chris Baron: From a pMDI perspective, it's not a new technology; pMDIs have been used now for asthma and COPD for over 60 years. Even though they still look familiar in some aspects, the technologies within the pMDI container closure system and the drug/formulation are very different. It's still using the same delivery methods of trying to treat asthma and COPD. The objective remains to deliver a repeatable and consistent dose to the lungs via aerosolisation of the aerosol, irrespective of the patients' respiratory effort. There are always pros and cons of having a patient wanting or needing to inhale at a specific inspiratory flow rate depending on what type of delivery platform is being used. On a positive note, when you think of a pMDI, if it's a traditional press-and-breathe, the fact that there is a propellant there which is expelling the drug means that even if the patient has very low respiratory efforts, or may be very old or very young, you can still deliver a formulation.

There are other ways – the perfect delivery system, from my perspective, would result in a lower respiratory effort where the patient would use a breath-actuated pMDI. This would help reduce patient coordination errors but would add additional costs.

How do pMDIs compare to traditional treatments for asthma and COPD?

This has been the million-dollar question. When I first came into the business quite a few years ago, we were going through the transition from chlorofluorocarbons (CFC) to hydrofluoroalkane (HFA). In those days, it wasn't global warming or climate change – it was the ozone depletion. People were saying: "Is it the end of the pMDI?" In those days, it was a transition which was mandatory – we had to reduce and then remove all CFC propellants, including those used in medical devices including pMDIs. This resulted in the development of formulations using new HFA propellants. These HFA propellants not only had a zero-ozone impact but they also reduced the actual global warming potential at that time by 300%. It was deemed a win-win for everybody.

At that time, they were thinking, "it's going to be DPIs (Dry Powder Inhalers) that take over". It certainly did not work out like that, and there are reasons for that. The most obvious one is that patients are used to using the pMDI because they are familiar with it. It gives a consistent dose and the patient experience is always the same when you use a pMDI, irrespective of the type of product you're using. Whereas, if you use a dry powder technology platform, it's more likely that you're going to have a very different experience with so many different dry powder inhaler technologies. You have reservoir-type, blister-based, and capsule-based technologies that all offer a different patient experience. This means it's not always easy to switch from one DPI technology to another DPI technology, and probably even more challenging to move from a pMDI to one of the DPIs.

The other thing you must consider if you're taking a rescue medication, like salbutamol, is you could never use a capsule-based DPI. You don't want to be playing with a capsule or putting that capsule into a device when you're having an asthma attack. The other key difference is that the costing aspects of a pMDI per dose are significantly lower than any other technology platform. If you have a 200-dose pMDI, it's much more cost sensitive to the industry versus single dose or multi dose DPIs. It's very difficult to ever replace a pMDI for such rescue medication.

What are the issues with existing treatment options for COPD and asthma?

I think there's an overuse of salbutamol. The challenge we have is that, when patients take medications, including controller medications for asthma & COPD, you may not feel any different for several days, then you begin to feel better, and that's when many patients stop taking their controller medication. With rescue treatments, like salbutamol, delivered by a pMDI, you take the medication and you get an instantaneous hit. The patient

feels like it's doing something, so they continue to take their rescue medication instead of their controller medication. The patient then becomes over-reliant on rescue treatment, as opposed to better managing their symptoms by using an appropriate controller medication. The net result is an over prescription of rescue medication. Perhaps this is maybe more of a communication issue between asthma nurses, physicians, and patients, i.e. not educating the patient enough to ensure that they need to continue with a controller medication. Even when they don't feel that immediate hit or buzz, they need to continuously take the medication in line with the patient instruction leaflet. One could argue that if you are in control of your asthma, then you shouldn't really need to use the rescue medication as frequently.

Another challenge for patients, when we think about the use of pMDIs in particular, some patients historically have co-ordination issues. When you use a conventional press-and-breathe pMDI, you should inhale and press, whilst still inhaling. Some patients may be very old or very young and sometimes patients struggle with coordination issues. To resolve this issue, you could incorporate a breath-actuated inhaler within the pMDI. You inhale through the actuator mouth-piece, which triggers the pMDI and delivers the medication, thus eliminating any coordination issues.

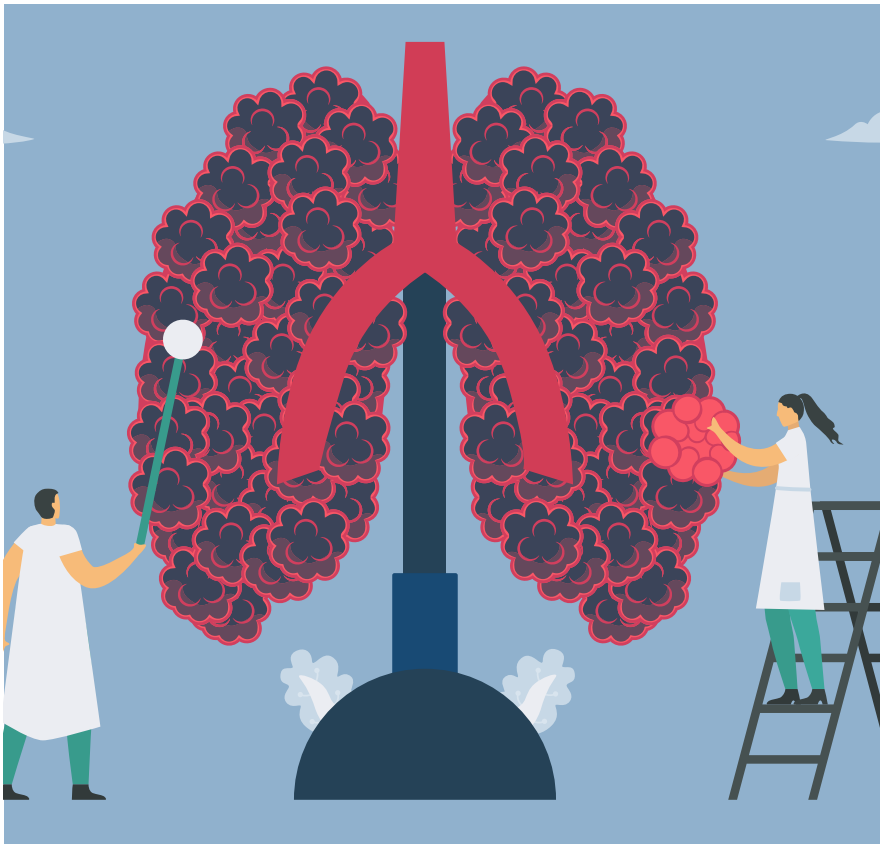
DPIs on the other hand are generally triggered by actually inhaling, which then delivers the dose from the device. This can be considered a pro but there are cons too. Some patients may not have a high enough respiratory effort to trigger the device and deliver the dose to the deep lungs.

The challenge then is cost, because the traditional pMDI is relatively inexpensive versus other technology platforms like DPIs and soft-mist inhalers. These new treatments could be used but it would just mean that the cost is more expensive.

Another key thing to mention is remaining doses. Many pMDIs on the marketplace today still don't incorporate a dose counter. Even though it's mandatory in the US and Australia, it's still not mandatory in Europe, and that's generally due to cost. If the patient knows how many doses are remaining, then they would know when to be in a position to go back to the physician and actually ensure that they've got their next prescription of medication, instead of having lots of pMDIs around the house, some half full, because the patient doesn't know how many doses are left. The final unmet need with pMDIs is that you need to re-prime them if you do not use the pMDI for a period of time (one or two weeks). This means you have waste, and this is a sustainability issue. The other consideration is that most primeless valves are used in conjunction with a BAI (breath-actuated inhaler), which could offer benefits from both a sustainability and a patient compliance perspective. I've just returned from the 2022 Respiratory Drug Delivery Conference, during which there was a significant focus on tackling the sustainability aspects of pMDIs during the Conference. I think the above points are key to meeting those unmet needs.

How can we make them more sustainable?

If you can reduce the number of priming shots, then you're going to have a more sustainable product, and as I mentioned earlier, using dose counters to confirm that the product is nearly empty. Many patients have products that they throw away, which are not empty. The other aspect is the link between digital health and connectivity. You could argue that it will be more expensive, but the patients who are not following their regime, and aren't taking their medication every day, are the ones who end up in the hospital needing emergency care. From a life cycle assessment perspective, this has a significantly higher carbon footprint (more resources in hospitals through emergency equipment) than using a pMDI using existing propellants. If you can have something that is more controlled, and has better compliance and adherence, it will be more sustainable too. It may initially be more expensive for the device, but the final cost to the healthcare system



is more positive, and the burden on the healthcare system is eased. Once a patient requires rescue treatment in a hospital, this becomes very expensive.

From a pMDI perspective there is significant work ongoing to switch pMDIs using the current propellants which have relatively high carbon footprints versus other inhaler device technologies to new low GWP (global warming potential) propellants including P152a & HFO1234ze which have significantly lower carbon footprints.

What are your visions for the future of respiratory treatments?

I've presented at multiple conferences and written various papers looking at improving the sustainability with regards to low GWP propellants. The good news is that low GWP pMDIs are on the horizon, and we can look forward to a much more sustainable future. Several leading Big Pharmacos, including Chiesi, AstraZeneca, and GSK, have all made announcements regarding their new low GWP pMDI programmes.

I think we can have better waste collection centres for used devices and that could include pMDIs, SMIs (soft mist inhalers), and DPIs. We could use more sustainable and reusable resins within the inhaler devices, but this is not going to be a quick thing, because obviously such resins need to be approved to medical grade.

Several major actuator suppliers for pMDIs are looking to utilise such reusable medical grade materials, as and when such materials become available for medical use. It'll just take time for those medical grades to come through and be approved accordingly.

With regards to improving patient experience, then using digital health solutions can make a real difference. Ensuring patient compliance and adherence is crucial, but this needs to be aligned with effective drugs and intuitive delivery devices which the patient will use. As stated previously, I think that, in the UK, there's too much emphasis on rescue salbutamol medication and the overuse of salbutamol, whether that's due to patients being prescribed too many rescue medications, or simply not being in compliance with their medication regimens.

The other thing which I would love to see is the patient coming first. The patient should always be the first thought of the physician, the Pharmaceutical company and the device developer. There are current examples where, after being taught the environment impacts of a product, physicians and Health Care Institutions are provided financial incentives to switch a patient from a pMDI to what they're perceiving is a more sustainable technology. These arbitrary switches may not be what is best in the long-term for the patient or the environment. You are asking a patient to change from a pMDI, which they may be in control of, to another technology without really thinking if this is going to benefit their health. I believe this is a dangerous precedence. A sustainable future is key, but the most sustainable product will be the one which the patient uses correctly and adheres to it. In summary, patient preference should matter as well.

I also think that dose counters should become mandatory in Europe, similar to in the US. Every pMDI should incorporate a dose counter or dose indicator. Why should we be lagging behind other countries purely due to a marginal increase in price? Patients who use products containing dose counters are more likely to be adherent and only replace the pMDI when the product is running out, thus reducing waste and reducing the cost/dose.

Chris Baron is Director of Business Development Pulmonary Category at **Aptar Pharma**. In his role, he is responsible for the global business development activities for Aptar Pharma's inhalation drug delivery devices, as well as their respective services pertaining to the application fields of Asthma and COPD. With an Honors degree in Mechanical Engineering, Chris has gained over 28 years' industry experience in the field of Inhalation Drug Delivery (IDD).

Working daily to improve the health of our patients and our planet

As the market leader in pMDI valve technology for asthma and COPD, Aptar Pharma is committed to improving the environmental impact of our products and ensuring our devices are safe and effective.

That's why we are actively engaged in defining the next generation of pMDIs, finding more sustainable solutions with alternative propellants that align with our sustainability commitments as well as those of our partners and their patients.

To find out more about how Aptar Pharma is advancing pMDI technologies, please visit **www.aptar.com/pharmaceutical/delivery-routes/pulmonary/**

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