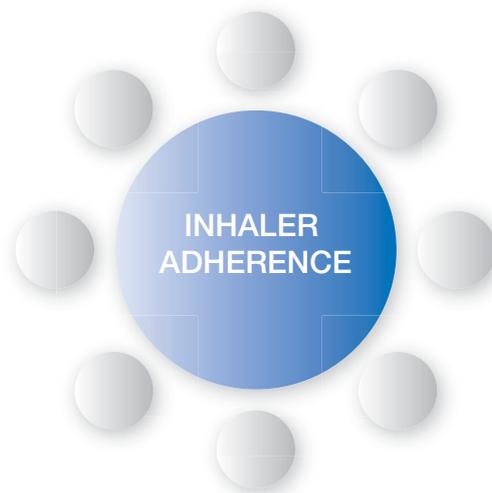


INHALER ADHERENCE
EXPLORING KEY FACTORS



 An expert panel roundtable hosted by Aptar Pharma Prescription Division

■ ■ INTRODUCTION AND OBJECTIVES

Aptar Pharma recently hosted an expert panel roundtable on “Inhaler Adherence*”. This international scientific forum was held in Paris, France on November 29th 2013. The roundtable was organized to explore and exchange views on the issues which may influence inhaler adherence/compliance with a particular focus on asthma and C.O.P.D. therapies and their corresponding inhaler devices (MDIs, DPIs).

Non-adherence, in any class of therapy, is known to be a huge burden on the current healthcare system costs, with an estimated \$100 billion being lost every year in the US alone due to this issue⁽¹⁾. It is estimated that from 16 to 50% of patients with asthma do not comply with their medications^(2,3). It has been reported that one third of the direct costs and three quarters of the total cost of asthma are due to uncontrolled disease⁽⁴⁾ with costs of those with an asthma exacerbation being at least 3.5 times more expensive than those with good control⁽²⁾.

Specifically for MDIs, a number of surveys suggest that they are frequently misused; during the review of 21 published studies the frequency of misuse ranges from 14-90%^(2,3), with an estimated average of 50%. Misuse decreases lung deposition from 20% to 7%⁽²⁾.

The overall objectives of the meeting were to explore the key factors that lead to inhaler device non-adherence/non-compliance, identify some of the unmet needs, and identify potential opportunities for improvements in inhaler adherence.

During this one day meeting the experts shared their knowledge and debated several key themes, structured around the following subject areas:

- Specific user (healthcare professional & patient) issues with inhaler devices and unmet needs.
- Potential avenues for making more adherence-friendly inhalers.
- How healthcare costs, reimbursement and emerging drug therapies may influence adherence.

Invited guests came from a variety of backgrounds ranging from front-line pulmonary clinicians and respiratory nurse practitioners to pharmaceutical company experts as well as members of government committees, e.g. NICE, who are directly involved in setting reimbursement guidelines in the UK.

The summary of some of the discussions held, detailed below, reflects the views of our invited experts and every attempt has been made to reflect the overall consensus of view as accurately as possible.

The roundtable was organized to explore and exchange views on the issues which may influence inhaler adherence/compliance.



* Although the word Adherence is referenced within this article, the term adherence takes into consideration another key factor which is frequently used with the industry i.e. that of patient compliance.

■ ■ CURRENT GUIDANCE WITH REGARD TO THERAPY/INHALER PRESCRIBING

The majority of therapies for the treatment of asthma and C.O.P.D. are administered by portable inhaler devices. International directives for the treatment of asthma⁽⁶⁾ and C.O.P.D.⁽⁷⁾ give guidance on how to approach the selection and prescription of inhaled therapies.

- Asthma – GINA guidance, Global Initiative for Asthma⁽⁶⁾.
- C.O.P.D. – GOLD guidance, Global initiative for chronic obstructive lung disease⁽⁷⁾.

There are three main elements to consider when selecting inhaled therapies.

- The pharmacotherapeutical class: here the prescriber has three main classes to choose from (anticholinergic, B2 agonist (short or long acting) and corticosteroid). Choices are based on the patient's type of disease and its severity and detailed guidance is given in the GINA (asthma) and GOLD (C.O.P.D.) publications.
- The patient's capabilities: here the prescriber must take into consideration several factors related to the specific patient, such as age, coordination skills, inhalation capacity, in addition to factors such as levels of understanding for inhalation techniques and any preferences related to the various inhaler types proposed.
- Inhalation device: here the prescriber has to use a more empirical approach and select from a wide range of inhaler devices from the three pharmacotherapeutical classes available as well as considering the cost of the medication in addition to choices around innovator or generic products etc.

With regard to the literature^(8,9) and practical experience a typical checklist of key criteria for the selection of the inhaler device might include the following:

- In what type of inhaler is the medication available?
- Which type of inhaler is the patient likely to be able to use correctly given their clinical capacity, age, hand/mouth coordination, breathing manoeuvres etc.?
- Is reimbursement available for the chosen inhaler?
- Which is the cheapest inhaler choice?
- Are the selected medicines for either asthma or C.O.P.D. available in the same inhaler type/format?
- Which inhaler is the best suited to the patient considering factors such as their family situation, time to administer, inhaler cleaning, portability etc.?
- What is the use/shelf life of the inhaler prescribed?
- Does the patient have a preference for a certain type of inhaler?

An example of the approach to inhaler selection related to hand-mouth coordination⁽¹⁰⁾ is shown in **Figure 1**, and many other publications or guidances exist on how to select the most suitable inhaler device. Given all the above information and factors, even the selection of the inhaler device is a complicated issue and could take several cycles before the "right" inhaler is found for each patient. All of the above elements can strongly influence eventual inhaler adherence for the prescribed medicine. The participants also noted that the selection of the inhaler device type is likely to be as important as the type of drug therapy prescribed.

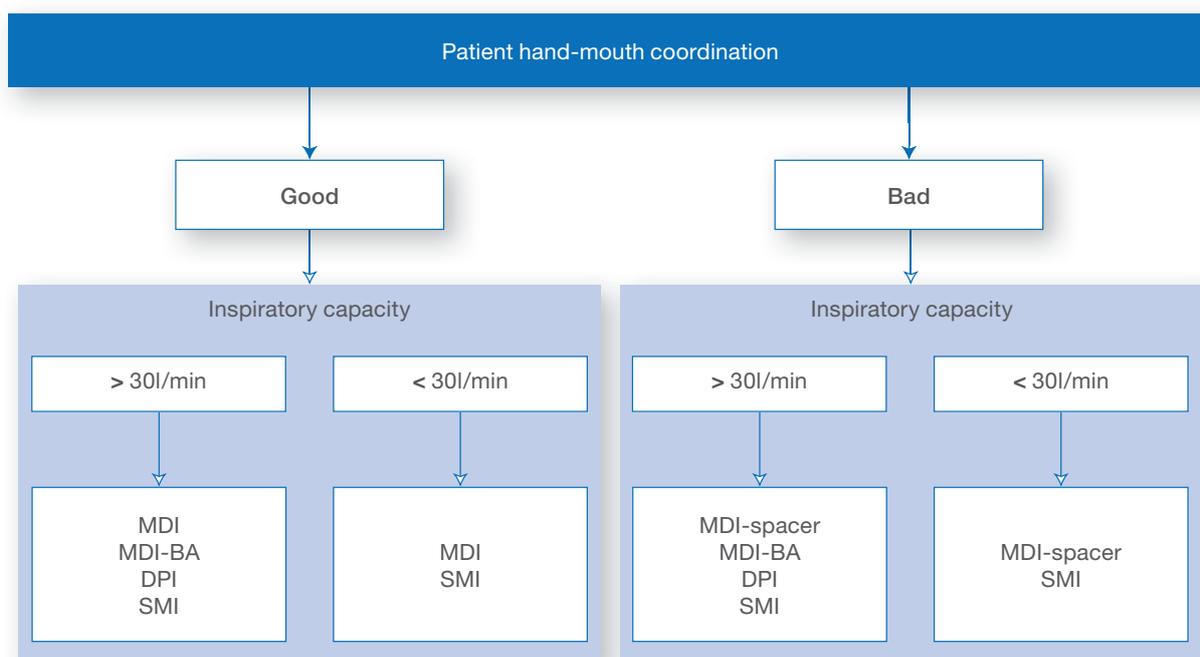


Figure 1: Example of inhaler device selection process⁽¹⁰⁾, MDI=metered dose inhaler, BA=breath activated, DPI=dry powder inhaler, SMI=soft mist inhaler

Inhaler adherence also takes into consideration patient compliance, see **Figure 2**. Adherence is closely related to the patient's behaviour whereas compliance is related more closely to patient inhaler technique.

Patient Compliance and Adherence

Patients fail to properly self-medicate in two ways:

	Term	Description	Example
WHEN	Adherence	Degree of similarity between clinician's recommended dosing frequency and the patient's behaviour.	The ratio of treatments that are taken compared with the number prescribed.
HOW	Compliance	The extent to which a patient follows medical instructions regarding a treatment regimen.	The ratio of treatments that are taken correctly resulting in delivery of a full dose of medication.

Figure 2: Adherence vs Compliance

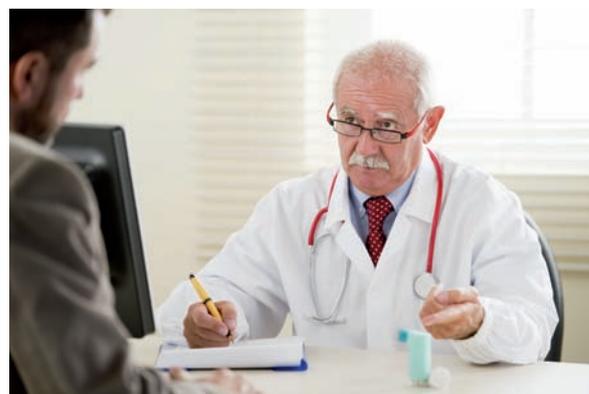
■ ■ SPECIFIC USER (HEALTHCARE PROFESSIONAL & PATIENT) ISSUES WITH INHALER DEVICES AND UNMET NEEDS

On average, physicians in both the UK and France spend around 12 minutes in consultation with their patients to discuss their medical issues. For asthmatic or C.O.P.D. patients this will typically include discussions around test results, explanations, prescription and guidance on how to use the inhaler. Clearly this does not allow much time to provide clear detailed instructions on correct inhaler use. In some instances the patient may meet with a specialized respiratory nurse practitioner allowing more time and confirmation of correct inhaler use; this is perceived as being best practice. Another issue identified as probably contributing to lack of inhaler adherence is the lack of follow-up with the asthmatic or C.O.P.D. patients to ensure ongoing correct use of inhalers over time.

Healthcare professionals and patients also face an issue due to the diversity and number of different inhaler devices available in the marketplace. Very often each one operates in a slightly different way (different steps for use) and many devices are not intuitive for the users, which results in poor techniques.

In contrast it appears that there is also no "one size fits all" option for inhalers as different patient classes have different needs, due to differences in age (youngsters, seniors, etc), cognitive skills, inhalation capacity, lifestyle, etc. It was even noted that poor eyesight or use in the dark could be challenging in terms of identifying the right inhaler to use, reliever vs controller, if the patient had two prescriptions.

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■ ■ POTENTIAL AVENUES FOR MAKING MORE ADHERENCE-FRIENDLY INHALERS

It appears that several recurring themes arise when looking for ways to improve patient adherence with inhalers. These include: simple to use (intuitive), simple to teach (training), feedback following successful dosing, a counting system and some form of reminder (legible, visible and/or audible) to take the medication. In addition systematic and complete instruction and training for correct inhaler technique in conjunction with patient follow-up to ensure ongoing use of the inhaler was identified as potentially being a means to significantly improve inhaler adherence.

A 'reminder' for the patient to use the inhaler is a key issue and suitable 'incentives' for patients to take their medication were seen as a promising avenue to increase adherence. In a recent study in the Isle of Wight, UK ⁽¹¹⁾, with a focus of 'reminders' and 'incentives', it was revealed that expenditure on β -agonists was reduced by 23%, prescription numbers fell by 25% and emergency admissions related to asthma were reduced by 50%.

Looking into the future several ideas seem to hold promise for improving patient adherence with inhalers, including active monitoring and feedback (smart devices, cell phone apps etc.). A new generation of 'e-devices' are becoming available with electronic features such as counting, and the potential to integrate with tele-health systems in the future. In addition the use of biomarkers to monitor disease status as a tool for assuring adherence and optimal therapy use seems to hold much promise.

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■ ■ HEALTHCARE COSTS, REIMBURSEMENT AND EMERGING THERAPIES

In discussions around reimbursement and using NICE (National Institute for Health and Care Excellence) as an example, it appears that more data related to inhalers, particularly around adherence, would be welcome as some of the data being used today to make judgments on reimbursements is somewhat outdated and not very plentiful. It is clear that any new therapies coming to the market place via the regulators' approval process must be carefully judged against the existing therapies in terms of efficacy, cost effectiveness and safety.

There was a perceived lack of incentive for pharmaceutical companies to invest in new advanced technologies which may improve adherence/compliance if there is no guarantee of reimbursement. This suggests that there is a need for health care providers/insurers and pharmaceutical companies to collaborate on this issue. Evidently due to the increasing costs of healthcare around the globe, the cost of the medication in combination with the inhaler device is a major factor in the prescription decisions being made by healthcare professionals today.



■ ■ IN SUMMARY

Inhaler non-adherence is clearly a real and significant issue in the field of asthma and C.O.P.D. therapy and there is evidently a large scope for improvement which would benefit all stakeholders. Relatively good guidances exist in terms of helping the prescribers, including GINA and GOLD, and a multitude of published literature information is also available to help guide inhaler choices. At the point of contact the prescribers need to make some informed and educated decisions in order to find the “right” inhaler meets each patient’s needs.

Several issues were identified as having an impact on patient inhaler adherence, ranging from lack of time to train or instruct the patients all the way to there being too many different types of inhalers already available in the market place. Training and follow-up are obvious avenues for improving inhaler adherence and several add-on features would be welcome on inhaler devices. Looking into the future the role of monitoring and feedback could also play a role in improving adherence. Finally, cost is becoming a major influence on how inhalers are prescribed and ultimately on inhaler adherence, very much tied in with the ever-increasing healthcare cost burden worldwide.



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■ ■ REFERENCES

1. Osterberg L, Blaschke T. "Adherence to medication". N Engl J Med. 2005; 353(5): 487-497
2. Hoskins, G., McCowan, C., Neville, R.G., Thomas, G.E., Smith, B., and Silverman, S. (2000), "Risk factors and costs associated with an asthma attack," Thorax, Vol 55, No 1, pp 19-24
3. Dasgupta, R. and Guest, J.K. (2003), "Factors affecting UK primary-care costs of managing patients with asthma over 5 years," Pharmacoconomics, Vol 21, No 5, pp 357-369
4. Barnes, P.J., Jonsson, B., and Klim, J.B. (1996), "The costs of asthma," Eur Respir J, Vol 9, No 4, pp 636-642
5. V. Giraud, N. Roche, "Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability", Eur Respir J 2002; 19: 246–251
6. GINA, global initiative for asthma, Global strategy for asthma management and prevention, NHLBI/WHO workshop report. Jan 1995, NIH pub 95-3659
7. GOLD, global initiative for chronic obstructive lung disease, 2009, www.goldcopd.com
8. Dolovich MB et al, (2005) "Device selection and outcomes of aerosol therapy; Evidence based guidelines", Chest, Jan; 127(1): 335-371
9. Vincken W et al, (2010) "The ADMIT series; Issues in inhalation therapy; 4) How to choose inhaler devices for the treatment of COPD". Prim. Care Respiratory J. Mar 19(1): 10-20
10. Laube B et al, (2011) "ERS/ISAM task force consensus statement. What the pulmonary specialists should know about the new inhalation therapies", Eur Respir J, Jun37(6), 1308-31
11. NICE study, "Isle of Wight Respiratory Inhaler project", 2010-2011, www.nice.org.uk

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