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Novolizer®

A Multidose Dry Powder Inhaler

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Contents

Abstract

▲ Novolizer® is a multidose breath-actuated dry powder inhaler (DPI) approved for use with salbutamol (albuterol) and budesonide. It has multiple patient feedback mechanisms and an inspiratory flow rate threshold designed to optimise dosage.

▲ In two studies, children aged 4–11 years with asthma correctly used Novolizer® and generated mean peak inspiratory flow rates (PIFRs) through Novolizer® of 76 and 92.7 L/min, well above the Novolizer® threshold of 35–50 L/min.

▲ In healthy volunteers, median lung deposition of budesonide administered via Novolizer® was 19.9–32.1% at mean PIFRs of 54–99 L/min.

▲ In a randomised, double-blind, single-dose study in patients with chronic obstructive pulmonary disease (COPD) and asthma, the 1-hour improvement from baseline in mean maximum forced expiratory volume in 1 second (FEV_1) was 21.3% with inhalation of salbutamol through Novolizer®, and 19.5% through Sultanol® pressurised metered-dose inhaler (MDI).

▲ FEV_1 increased significantly in patients with asthma and COPD treated for 4 weeks in a randomised, open-label comparison of salbutamol through either Novolizer® or Sultanol® MDI.

▲ A randomised open-label study in adults with asthma treated with inhaled budesonide found equivalent improvements in FEV_1 and symptoms with Novolizer® and Turbuhaler®.

▲ Novolizer® was well accepted overall. Most patients preferred it to previously used MDIs or DPIs. Only 4–5% found the taste feedback unacceptable. Physicians observed improved compliance over 4 weeks in 80% of patients with asthma using Novolizer®.

Features and properties of Novolizer®	
Indication	
Delivery of drugs for the treatment of asthma and chronic obstructive pulmonary disease	
Device description	
Multidose dry powder inhaler	
Breath actuated with minimum peak inspiratory flow (PIF) threshold of 35–50 L/min	
Visual, acoustic and taste-based dose feedback mechanisms and dose counter	
Dosage and administration	
Route of drug administration	Inhaled
Dose per actuation (doses per inhaler cartridge)	Salbutamol 100μg (200) Budesonide 200μg (100/200)
Dose delivery (*In vivo* γ-scintigraphy in healthy volunteers)	
Median deposition in lungs	19.9–32.1% at PIF through Novolizer® of 54–99 L/min; 25% at PIF through Novolizer® of 65 L/min
Peripheral : central lung deposition ratio in healthy volunteers	≈1.0 at PIF through Novolizer® of 54–99 L/min
Tolerability	
No increase in adverse events due to inhaler technology	
Patient acceptability	
Positive response based on patient preference, ease of use and convenience	

Inhalation is the preferred method of administration of drugs for asthma[1] and in some cases for chronic obstructive pulmonary disease (COPD).[2,3] The aim is effective delivery of drugs to the lungs, with minimal deposition elsewhere, minimising systemic adverse effects, particularly for corticosteroids.

Compliance with asthma medication is poor, with one large international study finding only 67% compliance, even in patients who had experienced more than ten attacks of asthma in the preceding year.[4] Between 14%[5] and 71%[6] of patients, including those who are willing to comply, have difficulty using pressurised aerosol inhalers. Coordination errors, such as inhaling before or after actuating the inhaler or actuating it twice or more during one inhalation, are common.[5,6] Spacers can improve the outcome from the use of these inhalers and are recommended if pressurised metered-dose inhalers (MDIs) are used with corticosteroids,[1] but many patients are not willing to carry them.[7] Patients who use more than one type of inhaler have an increased likelihood of making errors.[8]

Global Initiative on Asthma guidelines[1] suggest inhalers should be portable, simple to operate, especially for children, not require power, require minimal cooperation and coordination and have minimal maintenance requirements. Dry powder inhalers (DPIs) or breath-actuated MDIs are recommended for children aged >6 years.[1] British Thoracic Society guidelines recommend that patient preference and ability to correctly use the device are considered in deciding which inhaler to use.[7]

Breath-actuated DPIs do not use chlorofluorocarbons and do not require the coordination of actuation and inspiration. The airflow rate through a breath-actuated DPI depends on the patient's inspiratory effort and the intrinsic resistance of the DPI. Higher resistance results in lower flow rates through the inhaler, relative to the patient's inspiratory effort;[9,10] if device resistance is very high, patients may not be able to generate enough inspiratory flow to deliver the drug from the inhaler.

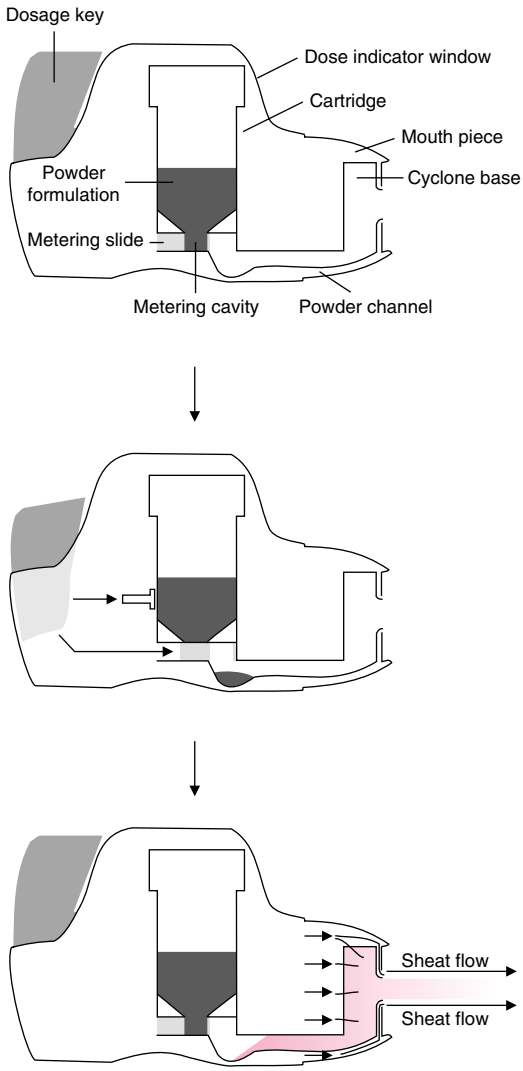
The inspiratory flow rate generated through the inhaler affects the proportion of drug which is delivered from the DPI to the lungs, as opposed to the mouth and upper airways (section 2). However, this is also influenced by other features of the DPI design; inspiratory effort and inhaler resistance on their own do not predict it.[10]

This profile reviews Novolizer®[1], a multidose DPI which has EU approval for use with the corticosteroid budesonide for asthma, and also approval in Germany for delivery of the β_2-agonist salbutamol (albuterol), and budesonide for asthma and COPD. Novolizer® has been compared with Sultanol®, a pressurised MDI, in the administration of salbutamol, and with Turbuhaler® DPI for the administration of budesonide.

1. Inhaler Design

- Novolizer® is a refillable, multidose, dry powder, breath-actuated inhaler which delivers up to 200 metered doses of drug from a replaceable cartridge (figure 1).[11] When the user presses a button on top of the inhaler, a dose is loaded into the powder inhalation channel. A green indicator window confirms the dose is loaded. A correct inhalation manoeuvre is confirmed by a change in the colour of the indicator window.[12,13]
- The Novolizer® design includes moderate airflow resistance which requires the user to generate a peak inspiratory flow (PIF) of at least 35–50 L/min before a drug dose is released from the inhaler.[14] This threshold is designed to support the flow rate necessary to generate a clinically effective fine particle fraction (FPF), and helps protect against the administration of incorrect doses.[12] A cyclone helix in the mouthpiece helps the active drug particles to de-agglomerate from the carrier particles.[14]
- Once the PIF threshold is overcome, the complete dose is released and visual, acoustic and taste-based feedback mechanisms (the change in colour of the indicator window, a click, and the taste of the lactose carrier molecule) confirm that the correct inhalation has been performed.[11] The click also

1 Use of tradenames is for product identification purposes only and does not imply endorsement.



- Cartridge containing up to 200 doses is loaded into inhaler
- Dosage counter tells the patient and physician the number of doses available

- Patient pushes down on dosage button
- Slide at the bottom of dose cartridge moves and a dose is loaded into the powder channel
- Indicator window shows green to confirm that dose is loaded

- Patient actuates Novolizer® by inspiratory flow
- If inspiratory flow is above threshold of 35–50 L/min, sufficient dose is released, trigger threshold is reset, cyclone and shear forces support optimal particle size
- Dose counter changes colour to confirm correct inhalation manoeuvre

Fig. 1. Diagrammatic representation of Novolizer® device

confirms that the dose metering system has been reset by the patient's inspiratory flow.

- There is an additional locking mechanism to prevent accidental multiple-dose administration. Novolizer® also has a dose counter, which changes only after a correct inhalation followed by the next dose loading, which confirms successful drug administration to patients and supervisors. Novolizer® can be used with pure drug, but the salbutamol and budesonide Novolizers® each use a formulation which includes a lactose carrier.[15]

2. Drug Delivery

Influences on drug deposition in the lungs from inhalers include the design of the inhaler,[9] the physical characteristics of the drug particles[16,17] and any carrier molecules,[16] and the inhalation by the patient, including flow rate and hand-breath coordination (for MDIs).[10] Many patient-related

factors, such as loading, carrying and being able to use the inhaler are also influenced by the device design.[10]

The optimum mass medium aerodynamic diameter (MMAD) for bronchial deposition of drug particles is <5μm,[9,10] which is small enough for the particles to remain airborne for a period.[17] The dose of drug with an aerodynamic particle diameter of <5μm released from the inhaler is the fine particle dose. The ratio of fine particle dose to total recovered dose is the FPF. Particles with an MMAD >10μm are usually deposited in the mouth and upper airways[9,12] and when swallowed, increase unwanted systemic effects.

The FPF represents the proportion of small active drug particles which is able to reach the smaller airways in peripheral lung; it is indicative of the clinical response to treatment. FPF was the endpoint in a particle-size study of Novolizer® and two other inhalers[16] and was measured during the validation process in another study.[18] An *in vivo* study directly assessed drug deposition in the lungs of healthy volunteers after inhalation through Novolizer® and Turbuhaler®, using γ-scintigraphy.[18]

As shear forces during inhalation are usually required to separate drug from carrier or to deaggregate drug particles, inspiratory flow, especially at the start of inspiration,[12] affects the FPF. An aerodynamic study assessed the variation in flow rate through Novolizer®,[19] and two studies in children with asthma have assessed the PIF rate (PIFR) achieved through Novolizer®.[20]

Particle Size

- The FPFs of inhaled budesonide at flow rates of about 80 L/min for Novolizer® and 60 L/min for Turbuhaler® (representing flow rates for each inhaler at a pressure drop of 4 kPa) were measured using a multistage liquid impinger, as part of the protocol for a study of lung deposition.[18] Mean FPFs were 35.5% for Novolizer® and 36.2% for Turbuhaler® before radiolabelling and 33.3% and 38.5%, respectively, after labelling.[18]
- A study assessing the effect of batch size variation of budesonide particles on the percentage of drug released as FPF from carrier crystals, at flow rates of 30 and 60 L/min in three different DPIs, concluded that flow rate was also a significant influence on FPF.[16] Drug particle de-agglomeration from carrier molecules was tested in Novolizer®, Inhalator®, Ingelheim® and a special test inhaler, using a multistage impinger to test deposition of different drug fractions.
- The FPF ranged from 20–65%, except with the test inhaler at 60 L/min where FPF was about 90%. FPF increased for all inhalers as flow increased from 30 to 60 L/min.[16] Results also showed that, particularly at lower flow rates, increasing the mean budesonide particle diameter (from 1.08 to 1.56μm) increased the amount of fine drug particles released from carrier crystals (no statistical analysis). At the higher 60 L/min flow rate, which was more efficient in terms of particle de-agglomeration, the budesonide particle size had less impact on the FPF in all three inhalers tested.[16]

In Vivo Lung Deposition

- In a study in healthy volunteers, 19.9–32.1% of radiolabelled budesonide was delivered to the lungs via Novolizer® with a significant difference ($p = 0.002$ for all comparisons) at different inspiratory flow rates.[18,21] Single, radio-labelled budesonide 200μg doses were administered to 14 healthy volunteers on 4 days separated by ≥44 hours, and their distribution between mouthpiece and exhalation filter, oropharynx, and the central, intermediate and peripheral lungs was recorded. Thirteen people completed the study.
- The study was designed to compare, using γ-scintigraphy, the amount of budesonide delivered from Novolizer® at targeted flow rates of 45, 60 or 90 L/min with that from Turbuhaler® at a targeted flow rate of 60 L/min, representing a range of flow rates expected in patients with asthma.[18] The targeted flow rates of 90 L/min through Novolizer® and 60 L/min through Turbuhaler® were estimated to represent maximum inspiratory flow rates, given the difference in the resistance of the two inhalers.[21]

• Budesonide distribution to the whole lung via Novolizer® varied significantly with PIFR. Median lung deposition was 19.9%, 25.0% and 32.1% at respective mean PIFRs of 54, 65 and 99 L/min (p = 0.002 for distribution rates at 54 vs 65 and 99 L/min, and for the rate at 65 vs 99 L/min).[18] Median whole lung distribution was 21.4% with a mean PIFR of 58 L/min through Turbuhaler®, similar to the Novolizer® result at 54 L/min and also significantly lower than drug deposition via Novolizer® at PIFRs of 65 and 99 L/min (p = 0.03 and 0.02, respectively, figure 2).

• In healthy volunteers, the peripheral-to-central lung zone distribution ratio did not differ significantly with varying PIFR or between Novolizer® and Turbuhaler® (all values 0.9 or 1.0). It was suggested that a higher PIFR increases both the likelihood of larger particles impacting in the large central airways and the number of smaller particles which reach peripheral lung, and that the peripheral-to-central ratio may decrease in patients with asthma as airway narrowing occurs.[18]

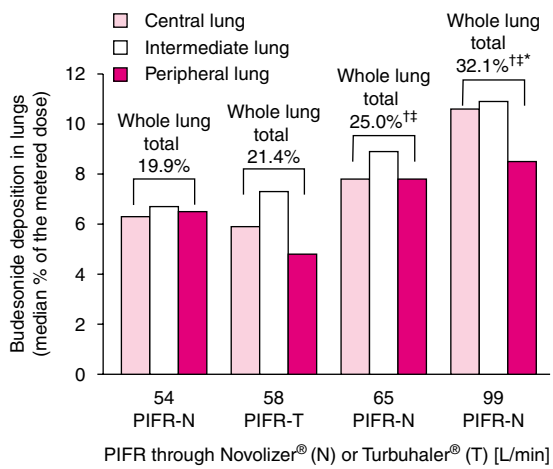


Fig. 2. Drug deposition with Novolizer® and Turbuhaler®. Median lung deposition, by lung region, of single doses of radiolabelled budesonide 200μg administered via Novolizer® or Turbuhaler® at mean peak inspiratory flow rates (PIFRs) of 54–99 L/min in a randomised, crossover study in 14 healthy volunteers.[18] Doses were administered ≥44 hours apart and results recorded via γ-scintigraphy. * p = 0.002 vs PIFR-N 65 L/min; ‡ p = 0.002 vs PIFR-N 54 L/min; † p ≤0.03 vs PIFR-T 58 L/min.

Inspiratory Flow Rates

• A test of 25 Novolizer® inhalers from different manufacturing lots identified a mean inspiratory flow rate of 75 L/min (relative standard deviation [RSD] of 2.3%) at a constant pressure drop, in line with current testing guidelines, of 4 kPa.[19] This confirmed the uniformity and reproducibility of inspiratory flow. A test of six inhalers from different batches at pressure drops corresponding to flow rates of 60–100 L/min resulted in an RSD of <5%, indicating a consistent inspiratory resistance in the samples at these flow rates.[19]

• Two randomised, open-label, multicentre studies assessed the ability of children with asthma (either forced expiratory volume in 1 second [FEV_1] <90% predicted or effective pretreatment with budesonide ≤400 μg/day or equivalent) to generate the PIFR needed to overcome the threshold Novolizer® PIFR of 35–50 L/min.[14] The threshold PIFR must be exceeded if a defined dose is to be released.[14,20] The best of three attempts was recorded. Treatment was not administered in either study.

• In the first study, in 134 patients aged 4–11 years, all but two of the children were able to both use Novolizer® successfully and overcome the threshold PIFR.[20] Over 95% of children had at least two successful inhalations out of three. Two children, a 5-year-old with an FEV_1 of 43% of predicted and one child aged 4 years, with a maximum PIFR through Novolizer® of 33 L/min, used Novolizer® correctly but were unable to overcome the PIFR threshold. Across the whole trial, mean PIFR through the spirometer alone and PIFR through Novolizer® were 147 L/min and 76 L/min, respectively, the 48% difference reflecting the low to medium resistance of the device.[20]

• Results excluding children effectively pretreated with corticosteroids were not significantly different, despite the average baseline FEV_1 changing from 83% for the whole group to 64% if these children were excluded. Based on published graphs, there was a linear relationship between PIFR and age up to 11 years, and between PIFR through Novolizer® and age up to 8 years, after which there were no further increases.[20]

• In a subsequent study designed to compare the PIFR through Novolizer® and Turbuhaler®, children aged 6–11 years who had stable bronchial asthma generated a higher PIFR with Novolizer® than Turbuhaler®, and were all able to generate the PIFR required to overcome the 35–50 L/min Novolizer® PIFR threshold (figure 3).[14] Only two children aged less than 6 years were included, outside protocol.

• The crossover, open-label study design required children to inhale three times through each of Novolizer® and Turbuhaler®.[14] The mean baseline PIFR for the whole patient population (n = 48) through the spirometer alone was 180 L/min compared with 92.7 L/min through Novolizer®. The 48.6% difference is consistent with the previous study and contrasts with a 61.7% difference between baseline spirometer PIFR and mean PIFR of 68.9 L/min through the higher resistance Turbuhaler®. Compared with those in the previous study,[20] children in this study were slightly older (mean 8.3 vs 7.6 years in previous study[20]) and 71% were male, which may account for the higher PIFRs.[14]

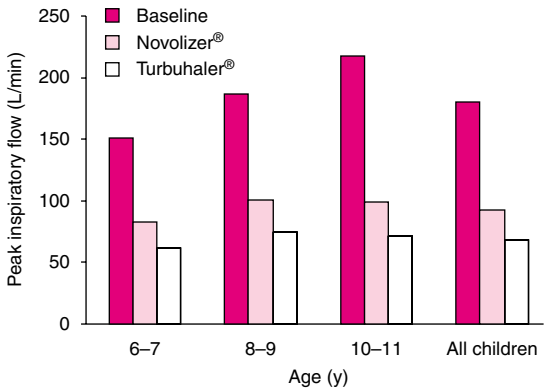


Fig. 3. Peak inspiratory flow rates through Novolizer® and Turbuhaler®. Mean best-of-three peak inspiratory flow rates of 48 children aged 6-11 years (71% male) with asthma defined as forced expiratory volume in 1 second <90% predicted, or effective pretreatment with budesonide 400 μg/day or equivalent.[14] In the randomised, open-label, multicentre, crossover study, children inhaled through spirometer alone, then through Novolizer® and Turbuhaler® in random order. Two children under age 6 years were included, outside protocol. 'All children' includes two subjects younger than 6 years.

3. Therapeutic Trials

Three large (n = 257–314), randomised, multicentre trials compared Novolizer® containing salbutamol[22,23] or budesonide[24] with drug delivery by Sultanol® MDI (salbutamol) or Turbuhaler® (budesonide), respectively, in adult patients with asthma[22-24] and/or COPD.[22] In one trial, reported in an abstract,[23] a single dose of salbutamol 100μg was administered; in the longer trials, treatment was administered for 4–12 weeks and comprised either salbutamol 100μg per actuation, administered via Novolizer® or Sultanol® MDI,[22] or budesonide 200μg twice daily, administered via Novolizer® or Turbuhaler®. The primary endpoint was change in FEV_1.[22-24]

The budesonide study included patients with mild-to-moderate asthma, defined as an FEV_1 60–90% of predicted, with reversibility of >12% after two inhalations of salbutamol 100μg. Some had previously taken corticosteroids (57.4%) and some had previously been treated only with bronchodilators.[24]

A 4-week, postmarketing surveillance study reviewed 3057 children and adults with allergic, nonallergic or mixed bronchial asthma who used Novolizer® with budesonide 200μg at their physicians' discretion (median twice daily); 85% of patients also received bronchodilators. Improvements in lung function (FEV_1 and peak expiratory flow rate [PEFR], the primary endpoint) and cough, wheezing and diurnal, nocturnal and effort-induced dyspnoea were reported.[13] Patients were aged 4–92 years (mean 47 years) with a median duration of mild-to-severe asthma of 5 years; 79% had previously used an inhaler, usually an MDI (54%).

Salbutamol

• Immediate changes in lung function were assessed in a study of 260 adults with asthma, which found the increase in FEV_1 resulting from a single dose of salbutamol 100μg to be similar whether the drug was inhaled through Novolizer® or Sultanol® MDI.[23] In the double-blind, double-dummy, parallel-group study, FEV_1 increased by 21.3% from a

baseline value of 2.07L with Novolizer®, and by 19.5% from a baseline value of 2.15L with Sultanol® MDI (significantly non-inferior result for delivery of salbutamol via Novolizer® compared with Sultanol® MDI; p = 0.002).

- A study in 257 patients with moderate-to-severe COPD and asthma found significant non-inferiority (p = 0.003), indicating therapeutic equivalence, for improvements in FEV_1 1 hour after treatment with salbutamol 100µg administered via Novolizer® or Sultanol®,[22] following a 2-week open-label run-in period with a standard MDI. After 4 weeks' open-label treatment, a significant increase in FEV_1 ($p \leq 0.001$) was evident in both Novolizer® and Sultanol® MDI users (baseline and final measures not reported).

Budesonide

- In an open-label study in 314 patients, the change in mean FEV_1 after 12 weeks of budesonide 200µg twice daily via Novolizer® or Turbuhaler® was therapeutically equivalent ($p < 0.001$ for non-inferiority).[24] Following a 2-week run-in period with salbutamol administered via an MDI, plus corticosteroids where prescribed, participants were randomised to Novolizer® or Turbuhaler®. The lower level of equivalence for FEV_1 was predetermined as −0.3L (i.e. provided there was not more than −0.3L difference in results between the two devices, Novolizer® would be considered equivalent to Turbuhaler®). This was based on a 10% difference in a typical FEV_1 value of 2.7–3.0L for patients with mild-to-moderate asthma. All differences were reported as Novolizer® value minus Turbuhaler® value.

- The mean FEV_1 in the intention-to-treat population at the end of the study was 2.71L for the Novolizer® group and 2.74L for the Turbuhaler® group, a difference of −0.03L, indicating that the efficacy of Novolizer® was at least equal to that of Turbuhaler® (95% CI of −0.19–0.13).[24] Baseline FEV_1 was 2.4L for Novolizer® and 2.45L for Turbuhaler®.[24]

- Absolute mean forced vital capacity changed from baseline by 0.17L to 3.87L in the Novolizer® group and by 0.19L to 3.91L in the Turbuhaler® group (difference in increase −0.02L; 95% CI −0.12–0.09).[24] Mean peak expiratory flow (PEF) improved from baseline by 54 L/min in the Novolizer® group and by 50.4 L/min in the Turbuhaler® group, a 3.6 L/min difference (95% CI −15–22.2 L/min). At study end, mean PEF was 415.2 L/min and 417.6 L/min for patients randomised to Novolizer® and Turbuhaler®, respectively.[24]

- Study-end mean morning and evening PEFR, the number of nocturnal awakenings and the intensity of cough, wheezing and dyspnoea, as recorded in patient diaries using a 4-point scale, twice daily, were similar or identical for both groups. The diurnal changes in PEFR were 16.4 L/min for Novolizer® and 17.0 L/min for Turbuhaler® (95% CI −5.68–4.59 L/min).[24]

- Mean differences between the groups in intensity of morning and evening cough were small at −0.02 and −0.01 (95% CI −0.10–0.06 and −0.08–0.07, respectively). The intensity of wheezing differed by −0.05 and−0.04 (morning and evening) with 95% CIs of −0.14–0.04 and −0.13–0.05, respectively. Morning dyspnoea intensity differed by 0.01 (95% CI −0.08–0.11) and evening dyspnoea intensity and the frequency of nocturnal awakening in the two groups were identical. Salbutamol usage declined similarly in both groups over the trial period (statistical analysis not reported).

- A large, 4-week, postmarketing surveillance study of patients with asthma across 963 medical practices found that administration of budesonide via Novolizer® resulted in a median increase in PEFR (primary endpoint) of 1.1 L/sec (from a median 5 L/sec at baseline to 6.3 L/sec) [n = 2191].[13] Median FEV_1 where measured (n = 875) increased from 2.25 to 2.7L, with a median increase of 0.31L.

- The severity of cough, wheezing and diurnal, nocturnal and effort-induced dyspnoea decreased from a mean total score of 8 (out of a possible maximum of 15) to 2. Patients recorded symptoms on a 0–3 scale, where 0 represented no symptoms and 3 severe symptoms. The percentage of patients experiencing each symptom decreased by between

22.1% (dyspnoea on physical effort) and 50% (wheeze).[13]

4. Tolerability and Acceptability

Three therapeutic studies also assessed the tolerability and patient acceptability of Novolizer® in the administration of either salbutamol or budesonide. Two included an analysis of adverse events and sought patient preference for either Novolizer® or previously experienced MDIs.[22,24] In another, reported as an abstract, 150 adult patients with asthma were asked to complete a questionnaire about the device and its performance relative to previous experience they may have had with a pressurised MDI.[25] Adverse events and patient satisfaction and compliance were also assessed in a postmarketing surveillance study of more than 3000 patients.[13]

- Patient acceptability of Novolizer® is high. In one study, 87% of patients with COPD and asthma using Novolizer® with salbutamol, who had been previously exposed to other multidose DPIs, stated they would use Novolizer® in preference to their previous DPI.[22] In this trial, 92% of patients randomised to Novolizer® had previous experience with an MDI; 78% of these said they would use Novolizer® in future and 59% expressed a preference for it. Overall acceptance of Novolizer® and Sultanol® MDI was similar, with 78% and 69% of the patients, respectively, assessing the efficacy as 'good' or 'very good'.
- In a questionnaire answered by 314 patients with asthma who had used Novolizer® or Turbuhaler® for budesonide 200μg inhalations twice daily for 12 weeks, more than 90% of patients in each group gave the DPI they were assigned the highest rating for all questions.[24] Ninety-eight percent of patients in both device groups rated most questions (ease of use, convenience or transportation, dosage preparation, inhalation effort, cleaning and future use of device) at the highest rating. Almost all (99.4%) said they would use the DPI assigned in the trial in future. Global tolerability assessments performed by the investigator for both Novolizer® and Turbuhaler®, reported separately,[22] were excellent, with 'good' or 'very good' scores for 99% of Novolizer® users and 96% of Turbuhaler® users.
- The specific features of Novolizer® were favourably assessed in a questionnaire provided to 150 patients with asthma following 4 weeks of salbutamol via Novolizer®.[25] The Novolizer® inhalation procedure was regarded as 'easy' by 96%, and 93% found cartridge exchange straightforward. The optical inhalation control was seen as advantageous by 97% of patients, with similar results for the acoustic inhalation control and dose counter (93% and 92%, respectively).
- These results were consistent with those in the postmarketing surveillance study, where 97% and 94% of patients assessed the optical and acoustic controls, respectively, as 'good' (as opposed to poor or not evaluable) and 78% were satisfied with the taste feedback mechanism.[13] The dose counter and overdose prevention mechanism were rated as good by 92% and 81% of patients, respectively, and physicians reported an increase in compliance, related to feedback mechanisms, in 80% of patients. The method of assessment of compliance was not specified.
- The lactose carrier taste feedback mechanism is less universally accepted, with 38% of patients with COPD and asthma reporting no taste in the salbutamol preparation.[22] Four percent of patients in this study and 5% in another[13] found the taste unacceptable or the mechanism unsatisfactory.
- Most adverse events reported in trials were drug-related rather than device-related; for example, coughing and dysphonia occurred with administration of budesonide via both Novolizer® and Turbuhaler®,[24] and candidiasis after budesonide administered via Novolizer®.[13,24] The incidence of bronchospasm in a group of 314 patients with asthma treated with budesonide was similar with Novolizer® and Turbuhaler®.[24]

5. Novolizer®: Current Status

Novolizer® is a multidose breath-actuated DPI approved in Europe for use with budesonide in asthma, and in Germany for use with salbutamol and budesonide in asthma and COPD. Studies in chil-

dren with asthma indicate that those older than 6 years can correctly use Novolizer® and can achieve PIFRs above the inspiratory threshold required for effective drug inhalation. In adults with asthma and/or COPD, Novolizer® with salbutamol was as effective in improving lung function as Sultanol® MDI. In patients with asthma, the improvement in lung function and symptoms using Novolizer® with budesonide was equivalent to that in patients using Turbuhaler® DPI. Many patients preferred Novolizer® to previously used DPIs or MDIs.

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