PRESS RELEASE

Study analysis supports reformulation of Chiesi's triple therapy inhaler with low global warming potential propellant

- Pharmacokinetic analysis of three studies shows similar tolerability and suggests therapeutic equivalence when comparing the low global warming potential (GWP) propellant to the current propellant.[1]
- Data supports reformulation of Chiesi's beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide (BDP/FF/GB) product via pressurised metered dose inhaler (pMDI) using the low GWP propellant.[1]
- Studies represent a positive step forward in Chiesi's development of carbon minimal inhalers to reduce the climate impact of respiratory medicines.[1]

Manchester, UK, 12th June 2024 – Chiesi, the international research-focused biopharmaceutical group, has published results of a pharmacokinetic study analysis of its low global warming potential (GWP) propellant in its pressurised metered dose inhaler (pMDI) for asthma and chronic obstructive pulmonary disease (COPD).[1] The results mark an additional positive step in Chiesi's drive to become Net Zero by 2035.[2] Chiesi has invested significantly in green innovation, including a €350 million investment into reducing the climate impact of its pMDI products while ensuring patients maintain therapy and device choice according to their needs and disease outcomes.[1,3]

Three studies were carried out in healthy volunteers (n=212) to compare Chiesi's fixed triple therapy formulated with a low GWP propellant (HFA-152a) with the current marketed product formulated with HFA-134a.[1] The studies compared the formulations across two primary endpoints: lung availability (as surrogate for efficacy) and total systemic exposure (as surrogate for safety) of the inhaler's active ingredients, beclometasone dipropionate (BDP), beclometasone-17-monopropionate (B17MP; active metabolite of BDP, formoterol fumarate (FF) and glycopyrronium bromide (GB).[1]

Data from across the studies provide evidence of similar lung availability and total systemic exposure across both formulations.[1] This demonstrates comparable tolerability and suggests therapeutic equivalence, supporting the reformulation of the BDP/FF/GB pMDI using the HFA-152a propellant and marking a key step forward in the development of Chiesi's carbon minimal inhaler platform.[1]

"*These study findings represent a vital milestone in our goal to deliver environmentally-conscious solutions for people with asthma and COPD and deliver on our ambitious commitment to become Net Zero by 2035,"* said Ralph Blom, General Manager, Chiesi UK and Ireland. *"We firmly believe patients shouldn't have to choose between their health and the health of the planet, which is why we're striving to maintain choice for patients by delivering carbon minimal alternatives to the therapies they are prescribed*."

Around 1.3 million people are living with COPD in the UK, and around 5.4 million are living with asthma.[4,5] COPD and asthma patients require access to a range of inhaler options depending on their individual needs, including pMDIs, with international treatment guidelines reinforcing the importance of choosing the right medication and appropriate device for the patient to reduce their risk of severe exacerbations.[6,7,8]

This study analysis is in addition to the completion of two short term clinical trials assessing the safety of the propellant, and similar studies conducted with a fixed inhaled corticosteroid (ICS)/long-acting bronchodilator (LABA) combination.[9,10,11] Chiesi's phase

III TRECOS study evaluating the longer-term clinical safety of products containing HFA-152a is also underway, currently with five UK trial sites across Manchester, Portsmouth, Bradford and London.[12]

To find out more about Chiesi, please visit: https://www.chiesi.uk.com.

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About the pharmacokinetics data analysis[1]

The research, 'Evaluating the pharmacokinetics of beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide delivered via pressurised metered-dose inhaler using a low global warming potential propellant', analysed data from three studies of the pharmacokinetics of a triple combination of beclometasone dipropionate (BDP)/formoterol fumarate (FF)/glycopyrronium bromide (GB), formulated in a pressurised metered dose inhaler (pMDI) with a low carbon propellant (HFA-152a), to determine whether it was bioequivalent to one containing an existing propellant (HFA-134a). All three studies involved healthy volunteers and were of similar design: four-way crossover, single-dose, single-centre, randomised, double-blind.

The three studies compared HFA-152a versus HFA-134a in terms of lung availability and total systemic exposure of beclometasone-17-monopropionate (B17MP; active metabolite of BDP), BDP, FF and GB. The European Medicines Agency (EMA) criteria for bioequivalence (meaning the absence of significant clinical difference) provide that the 90% confidence interval (CI) for the ratio of results for the reference and test formulations should be in the range of 80–125%.[13]

In studies one and two, total systemic exposure bioequivalence was demonstrated, except for GB geometric mean maximum plasma concentration (C_{max}) in study two (upper 90% CI limit 125.11%). For lung availability, bioequivalence was demonstrated except for BDP C_{max} and the last quantifiable timepoint (AUC_{0-t}) in study one (CIs 126.96% and 127.34% respectively) and GB in both studies: AUC_{0-t} lower CI was 74.54% in study one, and in study two, upper limits were 135.64% for C_{max} and 129.12% for AUC_{0-t}. In study three, the bioequivalence criteria were met for BDP, B17MP and formoterol with both BDP/FF/GB strengths, and were met for GB AUC_{0-t}, although not for C_{max}. Both formulations were similarly well tolerated in all three studies. While formal bioequivalence cannot be concluded for all analytes, these data suggest therapeutic equivalence of the two propellants.

About Chiesi Group

Chiesi is a research-oriented international biopharmaceutical group that develops and markets innovative therapeutic solutions in respiratory health, rare diseases, and specialty care. The company's mission is to improve people's quality of life and act responsibly towards both the community and the environment.

By changing its legal status to a Benefit Corporation in Italy, the US, and France, Chiesi's commitment to create shared value for society as a whole is legally binding and central to company-wide decision-making. As a certified B Corp since 2019, we're part of a global community of businesses that meet high standards of social and environmental impact. The company aims to reach Net-Zero greenhouse gases (GHG) emissions by 2035.

With over 85 years of experience, Chiesi is headquartered in Parma (Italy), with 31 affiliates worldwide, and counts more than 7,000 employees. The Group's research and development centre in Parma works alongside 6 other important R&D hubs in France, the US, Canada, China, the UK, and Sweden.

For further information please visit www.chiesi.uk.com.

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