

MEDIA UPDATE

Novartis post hoc analysis shows high-dose Enerzair® Breezhaler® reduces asthma exacerbations versus medium-dose, complementing key pivotal IRIDIUM study findings

- *High-dose, once-daily Enerzair® Breezhaler® [IND/GLY/MF] reduced asthma exacerbation rates by 21% (moderate or severe) and 31% (severe) versus medium-dose, over 52 weeks¹*
- *Once-daily Enerzair Breezhaler, which includes an optional digital companion (sensor and app), is the first LABA/LAMA/ICS* fixed-dose combination approved for patients whose asthma is uncontrolled with a LABA/ICS²*
- *Post hoc analysis complements findings from pivotal Phase III IRIDIUM study recently published in *The Lancet Respiratory Medicine*³*

Basel, September 7, 2020 — Novartis today announced that high-dose, once-daily Enerzair® Breezhaler® (indacaterol acetate, glycopyrronium bromide and mometasone furoate [IND/GLY/MF]) significantly reduces both moderate-or-severe and severe asthma exacerbation rates in patients whose asthma is uncontrolled on medium- or high-dose long-acting beta₂-agonist (LABA)/inhaled corticosteroids (ICS), when compared with a once-daily medium-dose of the same treatment. The post hoc analysis from the pivotal Phase III IRIDIUM study—presented virtually at the European Respiratory Society (ERS) International Congress 2020—also showed the safety profile for high-dose Enerzair Breezhaler was in line with previous studies in the Phase III/IIIb PLATINUM clinical development program.

“This post hoc analysis supports the potential of high-dose IND/GLY/MF as an effective step-up treatment option to further reduce asthma exacerbations in patients with uncontrolled asthma,” said Kenneth Chapman, Professor of Medicine, University of Toronto. “These findings also complement the efficacy and safety data from the pivotal IRIDIUM study, which indicated the potential of high-dose IND/GLY/MF to improve lung function and reduce exacerbations compared with salmeterol xinafoate/fluticasone propionate (Sal/Flu), a LABA/ICS* standard-of-care.”

The analysis showed high-dose Enerzair Breezhaler (150/50/160 µg) significantly reduced the annualized rate of moderate-or-severe asthma exacerbations by 21% (p=0.026) and severe exacerbations by 31% (p=0.003) in asthma patients not adequately controlled on current inhaled therapies, compared with medium-dose (150/50/80 µg) over 52 weeks.

High-dose Enerzair Breezhaler also reduced the annualized rate of all exacerbations (mild, moderate and severe) by 14% (p=0.132) compared with medium-dose, but this finding was

not statistically significant. Both doses tested presented with a favorable safety and tolerability profile.

*LABA; long-acting beta₂-agonist, LAMA; long-acting muscarinic antagonist, ICS; inhaled corticosteroid.

About Uncontrolled Asthma

Asthma affects an estimated 358 million people worldwide and can cause a significant personal, health and financial burden when not adequately controlled^{4,5}. Despite current therapy, over 40% of patients with asthma at Global Initiative for Asthma (GINA) Step 3, and over 45% at GINA Steps 4 and 5 remain uncontrolled^{6,7}. Patients with uncontrolled asthma may downplay or underestimate the severity of their disease and are at a higher risk of exacerbation, hospitalization or death⁸⁻¹⁰. Barriers, such as less than optimal adherence, incorrect inhaler technique, treatment mismatch, safety issues with oral corticosteroids and ineligibility for biologics, have created an unmet medical need in asthma¹¹⁻¹⁴.

About Enerzair[®] Breezhaler[®] in the EU

On July 7, 2020, Novartis announced European Commission (EC) approval of Enerzair Breezhaler (QVM149; indacaterol acetate, glycopyrronium bromide and mometasone furoate [IND/GLY/MF]) 150/50/160 µg once-daily as a maintenance treatment of asthma in adult patients not adequately controlled with a maintenance combination of a long-acting beta₂-agonist (LABA) and a high-dose of an inhaled corticosteroid (ICS) who experienced one or more asthma exacerbations in the previous year². This formulation combines the bronchodilation of indacaterol acetate (a LABA) and glycopyrronium bromide (a LAMA) with mometasone furoate (ICS) in a precise once-daily formulation, delivered via the dose-confirming Breezhaler device. Glycopyrronium bromide certain use and formulation intellectual property were exclusively licensed to Novartis in April 2005 by Sosei Heptares and Vectura. Mometasone furoate is exclusively licensed to Novartis from a subsidiary of Merck & Co., Inc, Kenilworth, NJ, USA, for use in IND/GLY/MF (worldwide excluding the US).

IND/GLY/MF will be administered via the dose-confirming Breezhaler device, which enables once-daily inhalation using a single inhaler. IND/GLY/MF is the first asthma treatment in the EU that can be prescribed together with a digital companion; the Propeller Health app and sensor custom-built for the Breezhaler device. The digital companion will provide patients with inhalation confirmation, medication reminders and access to objective data that can be shared with their physician in order to help them make better therapeutic decisions. The sensor for the Breezhaler device was developed by Propeller Health and is a CE marked medical device, designed and licensed to Novartis for use with the Breezhaler inhaler worldwide. The sensor includes a microchip, a microphone, Bluetooth capabilities, an antenna and a battery. The sensor does not alter the drug delivery characteristics of the Breezhaler inhaler itself but produces a recording of each administered dose. Based on the patient's recorded medication usage, personalized content is presented within the app to help the patient better self-manage their asthma.

In keeping with the Novartis commitment to reduce the environmental impact of our asthma combinations, IND/GLY/MF will be available in the hydrofluoroalkane/chlorofluorocarbon (HFA/CFC)-free Breezhaler device. Novartis aims to drive sustainability and has set ambitious targets to minimize its impact on climate, waste and water, including targets to become carbon neutral in company operations by 2025.

About the IRIDIUM Study³

IRIDIUM was a Phase III, multicenter, randomized, double-blind, parallel-group study, designed to compare the efficacy and safety of IND/GLY/MF with IND/MF in patients with asthma.

The purpose of the study was to evaluate the efficacy and safety of two different doses of IND/GLY/MF (high: 150/50/160 µg and medium: 150/50/80 µg), versus two corresponding IND/MF doses (high: 150/320 µg and medium: 150/160 µg) in patients with uncontrolled asthma, as determined by pulmonary function testing and effects on asthma control.

All patients were required to be symptomatic at screening and to have one or more exacerbations in the previous year, despite being on treatment with medium- or high-stable doses of LABA/ICS. Approximately 3,092 male and female adult patients with asthma were randomized 1:1:1:1:1 (approximately 618 patients in each of the treatment groups) to receive one of the following treatments:

- IND/GLY/MF 150/50/80 µg (once-daily)
- IND/GLY/MF 150/50/160 µg (once-daily)
- IND/MF 150/160 µg (once-daily)
- IND/MF 150/320 µg (once-daily)
- Sal/Flu 50/500 µg (twice-daily)

The primary objective of this study was to demonstrate superiority of both high-dose IND/GLY/MF versus high-dose IND/MF and medium-dose IND/GLY/MF versus medium-dose IND/MF, all delivered once-daily, in improving trough FEV₁ (volume of air that can be forced out in the first second of expiration approximately 24 hours post-administration of study drug) after 26 weeks of treatment in patients with asthma.

The key secondary objective was to demonstrate the superiority of both doses of IND/GLY/MF versus respective doses of IND/MF, in improving Asthma Control Questionnaire score after 26 weeks of treatment in patients with asthma.

Other secondary analyses included reduction of exacerbation rate, comparing high-dose IND/GLY/MF with high-dose IND/MF and medium-dose IND/GLY/MF with medium-dose IND/MF. Secondary analyses also included efficacy comparisons for both doses of IND/GLY/MF compared with Sal/Flu (50/500 µg).

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integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this media update as of this date and does not undertake any obligation to update any forward-looking statements contained in this media update as a result of new information, future events or otherwise.

About Novartis

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at <https://www.novartis.com>.

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References

1. Chapman KR, Kostikas K, Kerstjens H, et al. Reduction in asthma exacerbations with indacaterol/glycopyrronium/ mometasone high-dose versus medium-dose: a post hoc analysis from the IRIDIUM study. e-Poster presented at the European Respiratory Society (ERS) Virtual Congress; 2020 Sept 7–9.
2. European Medicines Agency. *Enerzair Breezhaler*. Available from: <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/enerzair-breezhaler> [Last accessed: August 2020].
3. Kerstjens HAM, Maspero J, Chapman KR, et al. Once-daily, single-inhaler mometasone-indacaterol-glycopyrronium-mometasone versus indacaterol-mometasone or twice-daily fluticasone-salmeterol in patients with inadequately controlled asthma (IRIDIUM): a randomised, double-blind, controlled Phase III study. *Lancet Resp Med* 2020. doi: 10.1016/S2213-2600(20)30190-9.
4. GBD Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Resp Med* 2017;5(9):691–706.
5. Asthma and Allergy Foundation of America. *My Life With Asthma Survey Overview*. Available from: <https://www.aafa.org/media/1684/my-life-with-asthma-in-2017-survey-findings-report.pdf> [Last accessed: August 2020].
6. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43(2):343–373.
7. Fang J, Busse WW, Marvel J, et al. Demographic, Clinical Characteristics and Control Status of Pediatric, Adolescent, and Adult Asthma Patients by GINA Step in a US Longitudinal Cohort. *Am J Resp Crit Care Med* 2018;197:A1903.
8. Peters SP, Ferguson G, Deniz Y, Reisner C. Uncontrolled asthma: a review of the prevalence, disease burden and options for treatment. *Respir Med* 2006;100(7):1139–1151.
9. Katsaounou P, Odemyr M, Spranger O, et al. Still Fighting for Breath: a patient survey of the challenges and impact of severe asthma. *ERJ Open Res* 2018;4(4):00076–2018.
10. Price D, Fletcher M, van der Molen T. Asthma control and management in 8,000 European patients: the REcognise Asthma and Link to Symptoms and Experience (REALISE) survey. *NPJ Prim Care Respir Med* 2014;24:14009.
11. Price DB, Trudo F, Voorham J, et al. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. *J Asthma Allergy* 2018;11:193–204.
12. Albers FC, Müllerová H, Gunsoy NB, et al. Biologic treatment eligibility for real-world patients with severe asthma: The IDEAL study. *J Asthma* 2018;55(2):152–160.
13. Bourdin A, Halimi L, Vachier I, et al. Adherence in Severe Asthma. *Clin Exp Allergy* 2012;42(11):1566–1574.
14. Global Initiative for Asthma (GINA). *2020 GINA pocket guide for asthma management and prevention*. Available from: https://ginasthma.org/wp-content/uploads/2020/04/Main-pocket-guide_2020_04_03-final-wms.pdf [Last accessed: August 2020].

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Novartis Media Relations

E-mail: media.relations@novartis.com

Peter Zuest
Novartis External Communications
+41 79 899 9812 (mobile)
peter.zuest@novartis.com

Phil McNamara
Global Head, Respiratory Communications
+41 79 510 8756 (mobile)
phil.mcnamara@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

Novartis Investor Relations

Central investor relations line: +41 61 324 7944

E-mail: investor.relations@novartis.com

Central
Samir Shah +41 61 324 7944
Thomas Hungerbuehler +41 61 324 8425
Isabella Zinck +41 61 324 7188

North America
Sloan Simpson +1 862 778 5052