Published on *Merck Newsroom Home* (https://www.mrknewsroom.com) on 5/22/17 11:30 am EDT

Merck Announces Top-Line Results from the Long Term LABA Safety Study of DULERA (mometasone furoate and formoterol fumarate dihydrate) Inhalation Aerosol

Terms:
Company Statements

Published Date and Time:
5/22/17 11:30 am EDT

KENILWORTH, N.J. – Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced top-line results from the LABA (long-acting beta$_2$-adrenergic agonists) safety trial of DULERA® (mometasone furoate and formoterol fumarate dihydrate) Inhalation Aerosol, which showed that the addition of formoterol (the LABA) to mometasone (the inhaled corticosteroid) maintenance therapy has a similar safety profile to mometasone alone, including a comparable risk of serious asthma-related events, while reducing the risk of asthma exacerbation. These results are being presented at the American Thoracic Society meeting in Washington, D.C. on May 22, 2017.

“We are pleased this study met both its primary safety and key secondary efficacy endpoints,” said Dr. Cindy Weinstein, senior principal scientist, clinical research, respiratory and immunology, Merck Research Laboratories. “These results address an important public health question raised by the FDA about the risk of severe asthma-related events, including death associated with the addition of LABAs to ICS, and reinforce our understanding of the important role that DULERA can have in the management of asthma. Merck is grateful to all of the investigators and patients who participated.”

DULERA is indicated for the treatment of asthma in patients 12 years and older.

DULERA is not indicated for the relief of acute bronchospasm.

This study began in 2011 as a post-marketing requirement from the U.S. Food and Drug Administration (FDA) for Merck and other LABA-manufacturers, who conducted similarly designed studies. In this global, 26-week randomized, double-blind trial, 11,729 adolescent and adult patients (≥ 12 years) with persistent asthma received the fixed-dose combination of mometasone furoate and formoterol (MF/F) or mometasone (MF) alone. Randomized patients had to have a history of one to four asthma exacerbations in the past year, but none during the previous month. Patients with unstable asthma or a history of life-threatening asthma were excluded. The primary safety endpoint was a composite of all serious asthma outcomes (SAOs), defined as adjudicated asthma-related hospitalization (≥ 24 h stay), intubation (endotracheal) and death, assessed by time-to-first event. Non-inferiority of MF/F to MF was defined as a 95% confidence interval (CI) upper limit of the hazard ratio (HR) less than 2.0. The key secondary efficacy endpoint was a composite of asthma exacerbation (hospitalizations ≥ 24 h stay, emergency visits < 24 h requiring systemic corticosteroid (SCS), and SCS for at least 3 consecutive days) assessed by time-to-first event, where superiority of MF/F to MF was defined as a 95% CI upper limit of the HR less than 1.0, achieving statistical significance (one-sided p-value < 0.025).

The results showed that among the 11,729 patients who received at least one dose of MF/F (n=5868) or MF (n=5861), a total of 81 SAOs, all asthma-related hospitalizations, were observed in 71 patients: 45 events from 39 patients in the MF/F group and 36 events from 32 patients in the MF group. No asthma-related intubations or asthma-related deaths were observed. The HR for the first SAO in the MF/F vs. MF group was 1.22 (95% CI: 0.76 to 1.94, p=0.411). At least one asthma exacerbation occurred in 1487 patients; 708 in the MF/F group and 779 in the MF group. The HR for the first asthma exacerbation in the MF/F vs. MF group was 0.89 (95% CI: 0.80 to 0.98, p=0.021).

Merck conducted the study at 431 centers in 35 countries with scientific and operational oversight from an independent joint oversight steering committee.

Selected Safety Information about DULERA®

WARNING: ASTHMA-RELATED DEATH

Long-acting beta$_2$-adrenergic agonists (LABA), such as formoterol, one of the active ingredients in DULERA, increase the risk of asthma-related death. Data from a large placebo-controlled U.S. study that compared the safety of another LABA (salmeterol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of the LABA, including formoterol. Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients.

When treating patients with asthma, prescribe DULERA only for patients whose asthma is not adequately controlled on a long-term asthma controller medication, such as an inhaled corticosteroid or whose disease severity clearly warrants

initiation of treatment with both an inhaled corticosteroid and LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue DULERA) if possible without loss of asthma control, and maintain the patient on a long-term asthma controller medication, such as an inhaled corticosteroid. Do not use DULERA for patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids.

DULERA is contraindicated in the primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required. DULERA is contraindicated in patients with known hypersensitivity to any of the ingredients in DULERA.

DULERA is NOT a rescue medication and does NOT replace fast-acting inhalers to treat acute symptoms. Increasing use of inhaled, short-acting beta$_2$-agonists is a marker for deteriorating asthma. In this situation, the patient requires immediate re-evaluation with reassessment of the treatment regimen.

Patients using DULERA should not use additional formoterol or other long-acting inhaled beta$_2$-agonists for any reason.

Oropharyngeal candidiasis may occur. If candidiasis develops, it should be treated with appropriate antifungal therapy, but at times therapy with DULERA may need to be interrupted. Advise patients to rinse the mouth after inhalation.

DULERA should be used with caution in patients with tuberculosis, fungal, bacterial, viral (including chicken pox or measles), or parasitic infections, or ocular herpes simplex infections because of the potential for worsening of these infections. A more serious or even fatal course of chickenpox or measles can occur in susceptible patients.

Particular care is needed for patients who are transferred from systemically active corticosteroids to DULERA. Deaths due to adrenal insufficiency have occurred in asthmatic patients during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids.

Hypercorticism and adrenal suppression may occur with very high dosages of DULERA or at the regular dosage in susceptible individuals. Patients treated with DULERA should be observed carefully for any evidence of systemic corticosteroid effects. If such changes occur, discontinue DULERA slowly.

Caution should be exercised when considering the coadministration of DULERA with long-term ketoconazole and other known strong CYP3A4 inhibitors, or in patients being treated with MAO inhibitors or tricyclic antidepressants.

There is an elevated risk of arrhythmias in patients receiving concomitant anesthesia with halogenated hydrocarbons.

Discontinue DULERA and institute alternative therapy if paradoxical bronchospasm occurs.

Excessive beta-adrenergic stimulation has been associated with central nervous system and cardiovascular effects. DULERA should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing inhaled corticosteroids, including mometasone furoate, a component of DULERA. Patients with major risk factors for decreased BMD should be monitored and treated with established standards of care.

Inhaled corticosteroids, including DULERA, may cause a reduction in growth velocity when administered in pediatric patients.

Glaucoma, increased intraocular pressure, and cataracts have been reported following the use of long-term inhaled corticosteroids, including mometasone furoate, a component of DULERA.

DULERA, like other medications containing sympathomimetic amines, should be used with caution in patients with convulsive disorders or thyrotoxicosis; and in patients who are unusually responsive to sympathomimetic amines. Doses of the related beta$_2$-agonist albuterol, when administered intravenously, have been reported to aggravate preexisting diabetes mellitus and ketoacidosis.

Be alert to hypokalemia and hyperglycemia as beta$_2$-agonist medications such as DULERA have the potential to produce adverse cardiovascular effects.

The most common treatment-emergent adverse events reported in ≥3 percent of patients and more common than placebo included nasopharyngitis, sinusitis, and headache.

Dysphonia was reported in a longer-term treatment trial at an incidence of 5 percent in patients receiving DULERA 100 mcg/5 mcg and 3.8 percent in patients receiving DULERA 200 mcg/5 mcg.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within

the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2016 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

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Please see Prescribing Information, including the Boxed Warning about asthma-related death, for DULERA (mometasone furoate and formoterol fumarate dihydrate) at
http://www.merck.com/product/usa/pi_circulars/d/dulera/dulera_pi.pdf

and Patient Information for DULERA (mometasone furoate and formoterol fumarate dihydrate) at
http://www.merck.com/product/usa/pi_circulars/d/dulera/dulera_mg.pdf**.**

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