STUDY REPORT SYNOPSIS

Aclidinium Bromide Drug Utilisation Post-Authorisation Safety Studies in the United Kingdom, Denmark, and Germany

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Eklira® Genuair®/Bretaris® Genuair®

ACTIVE INGREDIENT: Aclidinium bromide (ATC code: R03BB05)

Study No: D6560R00005 **NCT:** NCT03333018
TITLE: Aclidinium Bromide Drug Utilisation Post-Authorisation Safety Studies in the United Kingdom, Denmark, and Germany

Developmental Phase: Phase IV

Study Completion Date: Database study (data captured from September 2012 to December 2015)

Date of Report: 18 May 2017

RATIONALE AND BACKGROUND:

Aclidinium bromide was approved in Europe in 2012 as maintenance bronchodilator treatment to relieve symptoms in adults with chronic obstructive pulmonary disease (COPD). As part of the pharmacovigilance plan, a drug utilisation study (DUS) was planned to characterise the use of aclidinium as prescribed in regular clinical practice.

OBJECTIVES:

The objectives of the study for aclidinium monotherapy and non–fixed-dose combination with formoterol (aclidinium+formoterol) were as follows:

- To describe the characteristics of new users of aclidinium bromide and of other COPD medications, regarding sociodemographic characteristics, medical history and prior use of medications.
- To evaluate the potential off-label use of aclidinium bromide in adults, pregnant women, and children.
- To identify and describe users of aclidinium bromide in patient subgroups for which there is missing information in the RMP, including those with renal failure, liver impairment, prostatic hyperplasia, bladder neck obstruction, urinary retention, primary angle-closure glaucoma, arrhythmias, recent myocardial infarction, angina, and heart failure.

- To establish the core of a cohort of new users of aclidinium bromide for the future evaluation of safety concerns described in the RMP.

METHODS:

Study design:

Non-interventional multinational European database cohort study.

Setting:

New users identified in the Clinical Practice Research Datalink (CPRD) in the United Kingdom (UK), September 2012 through June 2015; the National Health Databases in Denmark, September 2012 through December 2015; and the German Pharmacoepidemiological Research Database (GePaRD) in Germany, October 2012 through December 2013. All new users were followed up to 1 year after the date of the first prescription for aclidinium or selected COPD medications.

Subjects and study size, including dropouts:

New users of LAMA medications - aclidinium bromide, tiotropium, other long-acting anticholinergics (Other LAMA), LAMA/long-acting beta2-agonists (LAMA/LABA); new users of LABA; and new users of LABA/inhaled corticosteroid (LABA/ICS). A minimum study size of 1,500 to 2,000 new users of aclidinium in each data source was considered to provide an acceptable level of precision. The final number of users included in each data source was above 2,000 at the time the data were available for extraction.

Variables and data sources:

Main variables were age, sex, smoking, COPD and asthma diagnoses, comorbidity, comedications, COPD severity, indication for aclidinium, and frequency of conditions with missing information in the RMP. Smoking was ascertained through recorded information in the CPRD and the use of smoking-cessation drugs in Denmark and the GePaRD. Medical diagnoses related to smoking were also used in the GePaRD.

RESULTS:

The study included 3,604 new users of aclidinium in the CPRD, 4,613 new users in Denmark, and 13,327 new users in the GePaRD. New users of LAMA medications, including new users of aclidinium, were older (median age, 69 to 71 years) than new users of LABA or LABA/ICS (median age, 55 to 66 years). Smoking was more frequent in users of LAMA medications (19.0% to 37.8% of users) than in users of LABA or LABA/ICS (7.3% to 25.9%).

A diagnosis of COPD was more frequent in users of LAMA medications (44.9% to 95.9%) than in users of LABA or LABA/ICS (25.5% to 67.4%). Asthma only (no COPD) was more frequent in users of LABA or LABA/ICS (12.5% to 59.5%) than in users of LAMA medications (2.3% to 8.9%).

In the CPRD and Denmark, users of aclidinium had more severe or very severe COPD (CPRD, 45.8%; Denmark, 69.9%) than users of the other study medications (CPRD, up to 42.9%; Denmark, up to 65.2%). In the GePaRD, users of aclidinium had more severe COPD (28.3%) than users of other medications except LAMA/LABA (39.0%).

The most frequent comorbidity across the study medications in patients with COPD aged 40 years or older were hypertension (43.6% to 79.5%) and depressive disorders (23.2% to 52.6%). The most frequent comedications in these patients were short-acting beta2-agonists (24.2% to 91.0%), antibiotics (56.8% to 79.3%), and cardiovascular medications (62.2% to 77.3%).

Estimated off-label prescription of aclidinium was 4.2% in the CPRD, 6.7% in Denmark, and 5.0% in the GePaRD. The indication could not be evaluated in 37.7% of users of aclidinium in Denmark.

The most frequent conditions for which information was missing from the RMP were renal failure in the CPRD (21.8%), angina in Denmark (17.9%), and arrhythmias in the GePaRD (20.1%).

Duration of the index episode for aclidinium ranged from 3.9 months in the GePaRD to 5.4 months in Denmark. In all study populations, persistence of use was higher in users of LAMA medications than in users of LABA or LABA/ICS. The highest persistence was among users of LAMA/LABA (32.3% in the CPRD, 36.2% in Denmark, and 38.6% in the GePaRD). The percentage of users of aclidinium bromide who discontinued with switching was 22.4% in Denmark, 11.3% in the CPRD, and 9.5% in the GePaRD.