Qualification Statement

Qualification of Asthma Daytime Symptom Diary and Asthma Nighttime Symptom Diary: Patient-Reported Outcome Instruments for Measurement of Symptoms of Asthma

Date: March 28, 2019

DDT Type: Clinical Outcome Assessment (COA)

DDT Tracking Number: DDTCOA-000006

Referenced COA: Asthma Daytime Symptom Diary (ADSD); Asthma Nighttime Symptom Diary (ANSD)

Type of COA: Patient-Reported Outcome (PRO) Instrument

The Center for Drug Evaluation and Research has determined that the ADSD and ANSD have demonstrated adequate evidence of content validity and cross-sectional measurement properties (i.e., internal consistency reliability, test-retest reliability, convergent validity, and known-groups validity) to measure symptoms of asthma in the context of use described below.

Section I: COA Concept of Interest

The concept of interest is the severity of the core defining symptoms (difficulty breathing, wheezing, shortness of breath, chest tightness, chest pain, and cough) of asthma.

Section II: Context of Use

The appropriateness of the ADSD and ANSD as primary or secondary endpoint measures has not been established. This qualification statement supports the ADSD and ANSD as measures of asthma symptoms in drug development. Further evaluation is needed on the instruments' longitudinal measurement properties (e.g., ability to detect change) and the interpretation of clinically meaningful within-patient change in scores. This information can be obtained in early phase studies in drug development programs.

As further supportive evidence is generated with the ADSD and ANSD, the qualification statement could be expanded to include use of the ADSD and/or ANSD as part of a primary or secondary efficacy endpoint(s) in confirmatory studies. Sponsors seeking to use the ADSD and/or the ANSD as a primary or secondary endpoint measure in confirmatory studies should discuss plans with the appropriate CDER review division. It is recommended to use the ANSD

with the ADSD to better characterize the drug effect and understand the measurement properties of each instrument. Further supportive evidence is required to characterize whether these two instruments (ADSD and ANSD) provide different information related to asthma symptoms.

A. Study population

The recommended target patient population is described as follows:

- Adults and adolescents (aged 12 years and older) diagnosed with asthma
- Clinical diagnosis of mild persistent through severe persistent asthma
- Lung function impairment (i.e., forced expiratory volume in one second [FEV1] of 45%-90% of predicted normal value)
- Demonstrate reversibility consistent with American Thoracic Society (ATS)/European Respiratory Society (ERS) standards for the diagnosis of asthma
- Diagnoses of other respiratory conditions (e.g., chronic obstructive pulmonary disease) or upper airway obstructions are excluded

B. Labeling or promotional claim(s) based on the COA

After the ADSD and ANSD's longitudinal measurement properties, including the ability to detect change, and the interpretation of clinically meaningful within-patient change have been evaluated, the 0 to 10 average ADSD and ANSD scores are intended to support labeling claims related to change in overall symptoms of asthma.

Section III: Interpretation of Change

Information to support thresholds for clinically meaningful within-patient changes on the 0 to 10 average ADSD and ANSD scores are needed. We recommend that these data be gathered and evaluated in early phase development prior to use in confirmatory studies.

Section IV: Contact Information for Access to the Qualified COA

Patient-Reported Outcome Consortium
Critical Path Institute
1730 E. River Road
Tucson, AZ 85718

For more information, please email procadmin@c-path.org; Subject: ADSD/ANSD Inquiry

Instructions for Use in a Regulatory Submission: Please reference DDT COA #000006 in your regulatory application.