P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

File: ■ *Pelargonium sidoides*
■ Umckaloabo®
■ Chronic Obstructive Pulmonary Disease (COPD)

HC 051356-482

Date: October 15, 2013

RE: *Pelargonium* Extract Effective and Safe as Adjunct in Managing Chronic Obstructive Pulmonary Disease (COPD)

Matthys H, Pliskevich DA, Bondarchuk OM, Malek FA, Tribanek M, Kieser M. Randomised, double-blind, placebo-controlled trial of EPs 7630 in adults with COPD. *Respir Med*. 2013;107(5):691-701.

Chronic obstructive pulmonary disease (COPD) is a disease of chronic and usually progressive airflow blockage. It is not fully reversible, and it is associated with an abnormal inflammatory response of the lung to noxious particles or gases. Acute exacerbations can lead to death. EPs 7630 (Umckaloabo®; ISO Arzneimittel; Ettlingen, Germany) is an herbal preparation from *Pelargonium sidoides* roots that has been shown to have anti-infective and immunomodulatory activity in vitro. In addition, a systematic review and meta-analysis revealed that EPs 7630 is more effective than placebo in treating acute bronchitis.[1] The purpose of this multicenter, randomized, placebo-controlled, double-blind study was to evaluate whether EPs 7630, as an add-on therapy, prolongs time to first exacerbation and reduces exacerbation frequency compared to placebo in patients being treated for moderate-to-severe COPD.

The study was conducted in 18 centers in Kiev and Lugansk, Ukraine. The study included patients (n = 200; ≥ 18 years) with a history of chronic bronchitis (characterized by cough and sputum production on most days for ≥ 3 months/year for at least 2 consecutive years), stable disease, ≥ 3 exacerbations in the prior 12 months, and a forced expiratory volume during 1 second (FEV1) < 80% and ≥ 30% of predicted normal value (COPD-II/III). The spirometry for grading and reversibility testing of patients with COPD was performed ≥ 6 hours after the last ipratropium bromide/fenoterol inhalation. Only patients with an improvement of FEV1 ≤ 0.3 liter after 2 puffs of ipratropium bromide/fenoterol were included in the study. Major exclusion criteria were relevant cardiac diseases, pneumonia, active pulmonary tuberculosis, cystic fibrosis, bronchiectasis, lung cancer, asthma, infiltrates or other abnormalities of the lungs; COPD-IV; acute exacerbation within 4 weeks; known concomitant bacterial infection or respiratory tract infections; AIDS; concomitant medication with beta blockers, angiotensin-converting enzyme (ACE) inhibitors, regular inhalative glucocorticoids (except COPD-III) or oral glucocorticosteroids (except during exacerbation),

anticholinergics (except ipratropium bromide), β2-agonists other than salmeterol or fenoterol, analgesics except acetaminophen, mucolytics and antitussives other than dextromethorphan/bromhexine/ammonium chloride, immune modulators (e.g., bacterial vaccines), or coumarin derivatives; known alcohol or drug abuse; tendency to bleed; gastrointestinal disorders; severe heart, renal, or liver diseases; and immunosuppression.

Patients received standard treatment for COPD. Specifically, inhalation baseline treatment for COPD-II included salmeterol regularly and ipratropium bromide/fenoterol as needed, and for COPD-III, salmeterol and budesonide regularly and ipratropium bromide/fenoterol as needed. In the event of exacerbations, additional oral prednisolone and the antibiotics amoxicillin/clavulanic acid or ofloxacin were prescribed. As add-on therapy, patients received 3 × 30 drops/day of placebo or EPs 7630 for 24 weeks. The primary efficacy variable was time to first exacerbation of COPD. Exacerbations were defined as a subjective increase in ≥ 1 chronic symptom over baseline (such as increased sputum production, sputum purulence [yellow pus], and/or dyspnea [shortness of breath]) that required an extra visit to the doctor (moderate exacerbations) or an increased use of ≥ 2-fold mean dose of ipratropium bromide/fenoterol for 5 consecutive days due to increased respiratory symptoms, self-managed by the patient (mild exacerbations). Secondary efficacy variables were number and duration of exacerbations during treatment, health status, patient satisfaction with treatment, and duration of inability to work.

Compliance was nearly 100% in both groups. The median time to first exacerbation occurrence was 57 days in the EPs 7630 group and 43 days in the placebo group ($P = 0.005$). When evaluating mild and moderate exacerbations separately, the time to moderate exacerbation was significantly greater with EPs 7630 than with placebo ($P < 0.0001$); whereas, the time to mild exacerbation was not significantly different between groups. The probability of remaining free of exacerbations was significantly greater for the EPs 7630 group than the placebo group ($P = 0.005$). The median duration of moderate exacerbations was about one day shorter in the EPs 7630 group. Significantly fewer patients in the EPs 7630 group needed antibiotic treatment during exacerbations compared to the patients in the placebo group ($P < 0.0001$, 37.8% and 73.3%, respectively), and antibiotic treatment had a shorter mean duration of treatment ($P = 0.0466$, 8 days and 9.8 days, respectively). After 24 weeks, patient satisfaction with treatment was significantly higher with EPs 7630 compared to placebo ($P < 0.0001$). The EPs 7630 group had a significantly lower average amount of days off work during a mild or moderate exacerbation compared with the placebo group ($P = 0.004$, 1.97 and 4.08 days, respectively). Also, the mean total number of days off work due to exacerbations during the study was significantly less in the EPs 7630 group than placebo ($P < 0.001$, 2.96 vs. 7.17 days, respectively).

A total of 51.5% of patients taking EPs 7630 suffered from adverse events (AEs) compared with 40.0% of patients taking placebo. A causal relationship between AEs and EPs 7630 could not be excluded for 18 patients but was assessed as unlikely. Gastrointestinal disorders were the most frequently reported system organ class for which a causal relationship could not be excluded.

The authors conclude that EPs 7630 add-on therapy was superior to placebo, particularly for moderate exacerbations, less consumption of antibiotics, improved quality of life, and less days of work lost. Health economic studies are needed to determine

whether using EPs 7630 as an add-on therapy provides a benefit in terms of both patient outcomes and financial concerns (i.e., cost of treatment vs. health care utilization vs. loss of productivity vs. mortality rate).

—Heather S. Oliff, PhD

Reference

[1]Oliff HS. *Pelargonium sidoides* use for acute bronchitis. *HerbClip*. September 15, 2008 (No. 050583-360). Austin, TX: American Botanical Council. Review of *Pelargonium sidoides* for acute bronchitis: a systematic review and meta-analysis by Agbabiaka TB, Guo R, Ernst E. *Phytomedicine*. 2008;15(5):378-385.

The American Botanical Council has chosen not to reprint the original article.