ACE inhibitors are recommended for treatment of patients with hypertension, proteinuria due to chronic kidney disease, and heart failure. However, therapy with ACE inhibitors is commonly associated with a dry, hacking cough, which results in discontinuation in 4% to 20% of patients.\(^1,2\)

If the ACE inhibitor cannot be tolerated and the goal of therapy is to block the renin-angiotensin system, substitution with an ARB should be considered. A 2008 systematic review of studies published from 1995 to 2006 compared ACE inhibitors and ARBs in adult patients with hypertension.\(^3\) Studies selected had to have been at least 12 weeks in duration, and had to have compared ACE inhibitors and ARBs head-to-head. A subset of these trials (26 RCTs for hypertension with 10,070 patients) compared rates of cough. Cough was reported in 9.9% of patients taking ACE inhibitors and 3.2% for ARBs (\(P\) value not given).

Another meta-analysis of 22 RCTs (with 1,272 patients) included a comparison of ACE inhibitors with ARBs in patients with proteinuria due to chronic kidney disease.\(^4\) Although differences in study design forced the authors to utilize the more complex statistical measure of ratio of means to compare the pooled groups, no difference was found between reduction of proteinuria in patients treated with ACE inhibitors or ARBs: ratio of means at 1 to 4 months of therapy was 0.99 (95% confidence interval [CI], 0.92–1.05) and at 5 to 12 months was 1.08 (95% CI, 0.96–1.22). Although the incidence of cough was not specifically addressed in these studies, discontinuation rates from all causes for ARBs versus ACE inhibitors was not statistically significant (odds ratio of ARB vs ACE discontinuation=0.78; 95% CI, 0.55–1.11). More recently, the ONTARGET study compared the ARB, telmisartan, and the ACE inhibitor, ramipril, in patients with peripheral or cardiovascular disease, or diabetes with evidence of end-organ damage.\(^5\) A total of 8,542 patients were treated with telmisartan 80 mg and 8,576 patients were treated with ramipril 10 mg. The primary endpoint was death from cardiovascular cause or hospitalization for heart failure. Patients were followed for a median of 56 months, with 99.8% of participants either completing the study or experiencing the primary endpoint.

The relative risk of the primary endpoint occurring for telmisartan compared with ramipril was 0.98 (95% CI, 0.9–1.07). Discontinuation due to cough was 4.2% in the ramipril group and 1.1% in the telmisartan group (\(P<.001\)).\(^2\)

Practice guidelines published by the American College of Chest Physicians in 2006 recommend that if discontinuation of an ACE inhibitor is not an option and the medication cannot be replaced with an ARB, other medications may improve an ACE-inhibitor–induced cough.\(^6\) These medications include inhaled cromolyn, theophylline, the NSAIDs sulindac and indomethacin, the calcium channel blockers amlodipine and nifedipine, and ferrous sulfate. Additionally, a repeat trial of another ACE inhibitor may be attempted.