American College of Cardiology/American Heart Association Guidelines on the Use of Sildenafil in Patients With Cardiovascular Disease

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INTRODUCTION

The American College of Cardiology (ACC) and the American Heart Association (AHA) developed an Expert Consensus Document in 1999 on the use of sildenafil in patients with cardiovascular disease (1). This type of document is intended to inform practitioners, payers, and other interested parties of the opinion of the ACC concerning evolving areas of clinical practice and/or technologies that are widely available or are

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new to the practice community. Topics chosen for coverage by the Expert Consensus document are so designated because the evidence base and experience with the technology or clinical practice are not sufficiently well developed to be evaluated by the formal ACC/AHA Practice Guidelines process. This is an attempt to inform and guide clinical practice in areas in which vigorous evidence is not yet available. Sildenafil, a selective inhibitor of phosphodiesterase-5 (PDE5), became widely available in 1998 for the treatment of erectile dysfunction (ED). In response to inquiries from various parties about the safety of using sildenafil in patients with cardiovascular disease, the ACC leadership decided to develop an Expert Consensus Document on this topic. The writing committee members were selected for specific expertise in clinical cardiology, managed care, vascular reactivity, nitric oxide donors and pharmacology of antihypertensive agents. The AHA was invited to jointly author the document. After the document was developed, 10 external referees reviewed the text. The final document was approved by the ACC Board of Trustees and the AHA Scientific Advisory Committee and published in January 1999 (1).

INFORMATION ON CARDIAC EFFECTS OF SILDENAFIL IN 1998

The information available about the cardiovascular effects of sildenafil at the time of the recommendations indicated it was not present in cardiac myocytes and had no direct inotropic effects on isolated dog trabeculae muscle. Sildenafil is highly selective for PDE5 over human PDE3 (>4000-fold). This is important because cyclic adenosine monophosphate-specific PDE3 inhibitors (milrinone, vesnarinone, and enoximone) have been shown to increase long-term mortality in patients with heart failure (2,3). At the time of the recommendations, however, little information was available about the use of sildenafil in patients with congestive heart failure (CHF).

Sildenafil causes a transient modest reduction in systolic (8–10 mmHg) and diastolic (5–6 mmHg) blood pressure, with a peak effect occurring about 1 h after the dose. The hypotensive effects of sildenafil were neither age dependent nor dose related. No significant effects were observed on heart rate. In normal volunteers, oral sildenafil caused no significant changes in cardiac index. The drug has both arteriodilator and venodilator effects on the peripheral vasculature.

Nitrates were known to markedly amplify the hypotensive effects of sildenafil leading to dangerous drops in blood pressure and