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RESEARCH**

*APPLICATION NUMBER:*

**22-161**

**OFFICE DIRECTOR MEMO**

Date: April 3, 2008  
From: Deputy Office Director  
Subject: Office level memo re: NDSA 22-161 Regadenoson  
To: File

The application under discussion is Regadenoson (Lexiscan), a pharmacologic stress agent to be used with radionuclide imaging. The product is intended to aid in the evaluation of myocardial perfusion in patients unable to undergo stress test based imaging studies. The active ingredient is a modified form of adenosine. A similar agent, Adenoscan, was approved for marketing in 1995 for a similar use.

The drug manufacturer, CV Therapeutics, performed two randomized, double blinded Phase 3 efficacy trials. Patients with various cardiac related symptoms for whom perfusion imaging was indicated first received Adenoscan (the standard of care) and randomized to a second Adenoscan image procedure or to Lexiscan. The intent of these studies was to demonstrate non-inferiority of perfusion defects when comparing pre/post Adenoscan to pre Adenoscan/post Lexiscan. Essentially, image agreement was high, and the size of the safety data base (> 1500 subjects exposed) showed similar safety profile.

In addition to the major efficacy trials, CV Therapeutics performed small studies in subject with Asthma and COPD, respectively. Adenoscan is contra-indicated in these populations because they may experience bronchospasm upon exposure to Adenoscan. In the clinical studies, Lexiscan was tolerated in these subjects. While the data are encouraging, the limited sample size call for observation and caution in administering Lexiscan to these patients; such caution is reflected in labeling. The level of uncertainty is also reflected in a PMC to evaluate the safety in patients with asthma or COPD.

I agree with the review division's recommendations that Lexiscan be approved for use as a pharmacologic stress imaging agent. I also concur with the recommended PMC to evaluate greater numbers of patients who have underlying bronchospastic disease, COPD, and other co-morbid conditions that might predispose them to high rates of adverse events.

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/s/

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Tiffany Brown  
4/7/2008 11:57:43 AM  
CSO

Karen Weiss  
4/8/2008 11:14:02 AM  
MEDICAL OFFICER