

# Brief Summary of the Circulatory System Devices Panel Meeting – March 16, 2016

## The AngelMed Guardian System

### **Introduction:**

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on March 15, 2016, to discuss, make recommendations, and vote on information related to the premarket approval application for the AngelMed Guardian System sponsored by Angel Medical Systems, Inc.

The sponsor has proposed the following Indications for Use:

The Guardian System is indicated to alert patients with prior acute coronary syndrome events to ST segment changes indicating acute coronary occlusion.

Guardian System alerts reduce the overall time-to-door from a detected acute coronary occlusion until presentation at a medical facility independent of patient-recognized symptoms.

### **Panel Deliberations/FDA Questions:**

#### **Question 1: Clinical Trial Issues**

In general, the panel was in agreement that the clinical trial issues highlighted were significantly concerning with respect to their ability to interpret the clinical results from the ALERTS Trial particularly with respect to effectiveness. The early termination of the ALERTS Trial and the multiple look-back windows with a maximum of 90 days were most concerning to the panelists, and particularly for drawing conclusions regarding effectiveness.

#### **Question 2: Effectiveness**

The panel was extremely troubled by the effectiveness results collected in the ALERTS Trial. The results from the trial were: inconclusive between the treatment and control groups; captured very few cardiac/unexplained deaths; had many new Q waves without an alarm; and many alarm events without a new Q wave. Further, when looking at the time-to-door component of the primary endpoint the Panel had a difficult time reconciling how events in the control group caught only in the longest look-back windows could have any connection between the ST deviation detection and the confirmatory testing. Finally, there was concern regarding the interpretability of the positive predictive value (PPV) calculation given the missing data and definition of clinically meaningful events. The false positives and false negatives identified in the study both raised concern.

### **Question 3: Safety**

The panel expressed concerns with the demonstrated safety in the proposed device particularly since the clinical utility of the device has been difficult to determine and device-related complications will only increase after the 6-month endpoint measurement. Several panelists highlighted the well understood chronic risks and implications of a permanently implanted transvenous system, particularly in high risk patients. Some were also concerned about risks of unnecessary intervention due to the device false positive alarms. They noted that without a clear understanding of the benefits of the device all of the risks attendant to the device and its use are difficult to justify.

### **Question 4: Clinical Utility**

The panel expressed most of their thoughts on clinical utility in their answers regarding effectiveness. Most panelists were concerned that the clinical results from the ALERTS Trial were not sufficient to demonstrate the clinical utility of the proposed device because many of the events identified by the device did not appear to be clinically significant and several clinically significant events were not identified by the device.

### **Question 5: Indications for Use and Labeling**

The panel expressed several concerns with the proposed Indications for Use statement's reliance on the secondary endpoint analysis of the time-to-door data. Most notably they highlighted that this type of endpoint was not focused on the clinical utility and impact of the device that the ALERTS Trial initially set out to show. They also noted that the endpoint was not a randomized comparison, showed statistical significance only as a construct of the study and not through real world impact, and is difficult to interpret with the confirmed events in a 90-day look-back window. Furthermore, the panel noted that the indications for this device should be more meaningful to the patient and should more clearly identify the patient population for which the device is appropriate.

### **Question 6: Post-Approval Study**

The panel struggled to provide guidance regarding post-approval study of the device given the lack of pre-market data available from the ALERTS Trial and their concerns regarding the proposed indications for use.

### **Question 7: Benefit & Risk**

Given the concerns with both the safety and effectiveness profiles of the device noted previously the panel expressed considerable concern regarding the benefit risk profile of the device. They noted that particular populations such as women and diabetics that may benefit most from this device would also have higher risks.

**Vote:**

The panel voted on the safety, effectiveness, and benefit-risk profile of the AngelMed Guardian System.

On Question 1, the panel voted 8-0-4 (no-abstain-yes) regarding whether there is reasonable assurance that the AngelMed Guardian System is safe for use in patients who meet the criteria specified in the proposed indication.

On Question 2, the panel voted 12-0-0 regarding whether there is reasonable assurance that the AngelMed Guardian System is effective for use in patients who meet the criteria specified in the proposed indication.

On Question 3, the panel voted 12-0-0 regarding whether the benefits of the AngelMed Guardian System outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

Contact: CDR Dimitrus Culbreath, Designated Federal Officer  
(301) 796- 6872 [Dimitrus.Culbreath@fda.hhs.gov](mailto:Dimitrus.Culbreath@fda.hhs.gov)

Transcripts may be purchased from: (written requests only)

Free State Reporting, Inc. 1378

Cape St. Claire Road Annapolis, MD 21409

410-974-0947 or 800-231-8973 Ext. 103

410-974-0297 fax

Or

Food and Drug Administration

Freedom of Information Staff (FOI)

5600 Fishers Lane, HFI-35

Rockville, MD 20851

(301) 827-6500 (voice), (301) 443-1726