

**24 Hour Summary of the Circulatory System Devices  
Panel Meeting  
Sentinel<sup>®</sup> Cerebral Protection System  
DEN160043  
February 23, 2017**

**Introduction:**

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on February 23, 2017 to discuss and make recommendations on the clinical information related to the De Novo request for Claret Medical Inc.'s Sentinel<sup>®</sup> Cerebral Protection System, a first of a kind embolic protection device to be used with transcatheter aortic valve replacement (TAVR) procedures.

**Device Description:**

The Claret Medical **Sentinel<sup>®</sup> Cerebral Protection System** (Sentinel System) is a percutaneously delivered dual-filter embolic protection device, designed to capture and remove debris dislodged during TAVR procedures. The Sentinel System utilizes an embolic filter delivered to the brachiocephalic artery (Proximal Filter), and a second embolic filter delivered to the left common carotid artery (Distal Filter). At the completion of the procedure, the filters and debris are recaptured into the catheter and removed from the patient.

**The sponsor has proposed the following Indications for Use:**

The Sentinel<sup>®</sup> Cerebral Protection System is indicated for use as a cerebral protection device to capture and remove embolic material while performing transcatheter aortic valve procedures in order to reduce ischemic injury to the brain peri-procedurally. The diameters of the arteries at the site of filter placement should be between 9 – 15 mm for the brachiocephalic and 6.5 mm – 10mm in the left common carotid.

**Panel Deliberations/FDA Questions:**

**Question 1: Safety Results**

*The panel was unanimously in agreement that the device is safe in the context of the TAVR procedure. While the panel expressed some concern regarding the methodology to develop the performance goal and the potentially increased risk associated with the transapical approach, use of the Sentinel system does not raise untoward safety concerns.*

## **Question 2: Effectiveness Endpoints**

*In general, the panel expressed concerns regarding the adequacy and clinical-meaningfulness of the effectiveness endpoint for new lesion volume as evaluated with diffusion-weighted magnetic resonance imaging (DW-MRI). These concerns stemmed from the lack of anatomical evaluation to determine “protected” versus “unprotected” cerebral territories; limitations with processing methodology; and time of imaging relative to the procedure. Overall, the panel unanimously agreed that new lesion volume as evaluated with DW-MRI does not appear to be a good surrogate for clinical stroke; however, it does provide important information in addition to the other clinical measures (e.g., neurocognitive evaluation) and should continue to be collected in future studies. While stroke would be an ideal endpoint, the panel agreed that these studies may be difficult in terms of the required patient numbers for an adjunctive procedure. For future studies, the panel suggested capturing the location of the lesion, vascular anatomy, and additional neurocognitive evaluation with better standardization to potentially enhance future analyses.*

## **Question 3: Effectiveness Results**

*The panel generally indicated that there was no clear correlation between the clinical outcomes of interest (stroke and neurocognitive assessments) and the radiographic findings (DW-MRI assessment of observed new lesion volume reduction in protected territories between test and control patients). Additionally, there was some worry that the small patient number and missing data may lead to an over-estimation of the results. Many also expressed frustration reconciling why the trend in reduced new lesion volume in protected territories was not also seen in the all territories analysis. Most panel members noted that future studies should evaluate all territories as the primary endpoint since truly protected territories cannot be evaluated without capturing patient-specific anatomy.*

## **Question 4: Debris Capture**

*The panel agreed that capturing debris in 99% of patients is meaningful. The panel indicated that it is clinically important to not have debris travel to the brain; however, they were less sure about the clinical consequences of such debris. Most members of the panel noted that the captured debris was most likely due to the TAVR procedure and not due to placement of the Sentinel.*

## **Question 5: Neurocognitive Outcomes**

*The panel agreed that the results of the neurocognitive assessments did not demonstrate a clinically-significant benefit. For future evaluations, the panel suggested improving retention, evaluating floor effects, using a two-tiered cognitive assessment, and adding more longitudinal analyses.*

### **Question 6: Indications for Use**

*The panel recommended removing “in order to reduce ischemic injury to the brain peri-procedurally” from the proposed Indication because the trial did not demonstrate this. Further, they recommended including the limitations of the protection by noting the vessels in which the device is placed or by pointing out the lack of protection in the left vertebral.*

### **Question 7: Labeling**

*Given the difficulty in interpreting the data, the panel suggested that the labeling should include results for both the protected territories and all territories analyses. Partially-protected territories should not be included unless patient-specific anatomy and outcomes are rectified. Additionally, the labeling should include a warning against use in patients with inappropriate anatomy (e.g., when the vessels cannot be successfully cannulated). The labeling should include more explanation on the neurocognitive evaluation. There was disagreement whether the post-hoc analyses of stroke at 72 hours and 90 days should be included.*

### **Question 8: Benefit & Risk**

*In general, the panel felt that the trial failed to demonstrate benefit in terms of a reduction in stroke or improvement in neurocognitive outcomes; however, the panel did indicate that preventing debris from reaching the cerebral circulation is a benefit of the Sentinel device, and that preventing some debris from reaching the cerebral circulation is better than allowing all of the debris to reach the cerebral circulation. In light of the totality of information, this level of benefit and degree of uncertainty is acceptable given that this is an adjunctive procedure with minimal added risks.*

### **Question 9: Post-Market Data**

*The panel agreed that post-market data collection would be valuable to support and better define the probable benefits of the device. The recommendations included collection of additional data to demonstrate the percentage of emboli captured peri-procedurally and to evaluate clinical outcomes and stroke at short- and long-term endpoints. The panel disagreed on the appropriate long-term time point with values ranging from 6 months to 3 years, but the panel did agree that collection of additional imaging long-term may not be valuable. Many agreed that a registry would be useful to capture this information and to update the labeling accordingly.*

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