Brief Summary of the Circulatory System Devices Panel Meeting – January 26, 2011

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on January 26, 2011 to discuss, make recommendations, and vote on information related to the premarket approval application supplement **P040012/S034** for RX Acculink Carotid Stent System, sponsored by Abbott Vascular.

Abbott Vascular is requesting an expansion of the indications for the RX Acculink Carotid Stent System, which was originally approved by FDA on August 30, 2004 (P040012) for use in patients requiring carotid revascularization who are at high risk for adverse events from carotid endarterectomy. The RX Acculink Carotid Stent System is used in conjunction with the Accunet Embolic Protection System (EPS), and the expanded indication is sought for the treatment of patients at standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria pre-specified in the IFU. This request to expand the indications for use is based upon the results of the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST), which was a clinical study conducted under IDE G000080. The new expanded indications are outlined as follows:

High Surgical Risk

The RX Acculink Carotid Stent System, used in conjunction with Abbott Vascular's Accunet or Emboshield family of Embolic Protection Systems (EPS), is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:

1. Patients with neurological symptoms and ≥ 50% stenosis of the common or internal carotid artery by ultrasound or angiogram OR patients without neurological symptoms and ≥ 80% stenosis of the common or internal carotid artery by ultrasound or angiogram, AND
2. Patients must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.

Standard Surgical Risk

The RX Acculink Carotid Stent System, used in conjunction with the Accunet Embolic Protection System (EPS), is indicated for the treatment of patients at standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:

1. Patients with neurological symptoms and ≥ 70% stenosis of the common or internal carotid artery by ultrasound or ≥ 50% stenosis of the common or internal carotid artery by angiogram OR patients without neurological symptoms and ≥ 70% stenosis of the common or internal carotid artery by ultrasound or ≥ 60% stenosis of the common or internal carotid artery by angiogram AND
2. Patients must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.

Panel Deliberations/FDA questions:

The Panel noted that although octogenarians subjects are a higher risk group overall, the data are not complete enough to restrict octogenarians from the indications. The panel also had concerns about the strength of data concerning the use of the stent in symptomatic patients compared to asymptomatic patients. However, they concluded that the data are not strong enough to exclude either group. The panel did note that there were improved outcomes with the device in symptomatic patients over the course of the clinical trial. While the study results indicated non-inferiority for symptomatic patients compared to surgical treatment, the panel felt more comfortable placing conditions on symptomatic patients (i.e. labeling/PAS). The panel agreed that asymptomatic patients may not benefit *enough* from the device due to their stroke risk. The panel did say that asymptomatic patients could be treated if they had a very low stroke risk. These asymptomatic data have been established in historical literature (1%/yr for stroke risk in asymptomatic patients). The panel noted that the data showed a trend towards higher stroke rates with the device, although the myocardial infarction (MI) rate is decreased when the device is used as compared to surgery. They also noted that both physicians and patients must be notified in the labeling that there is a higher incident of strokes with the stent than with surgery.

The panel agreed that the use of the embolic protection device (EPD) should be addressed in a boxed warning, given the risk of stroke if used without the EPD, and that potential patients should be notified of the risk of undergoing this therapy without embolic protection. The incidence of cranial nerve injury was not surprising, but should be taken into consideration when choosing patients and should be included in the patient education packet.

When asked to comment on the clinical significance of the higher death and stroke rate in the stenting arm of the CREST study versus the higher rate of MI in the surgical arm during the peri-procedural period, the panel was ambivalent about the importance of the different stroke and MI rates between the two study arms, noting that they were comparing two different measures. They agreed that MI rates did fall over time and that the MI rates were low. They also noted that the overall risks of both MI and stroke were relatively low. There was no concern regarding the changes to the definition of MI throughout the study.

The panel was also in agreement that the stability of outcomes after one year was representative of what we would see in long-term data.

In terms of the robustness of the conclusions drawn from the CREST study data, the panel felt that the unbalanced number of crossover subjects did not affect the study results enough to be of concern. There was concern about the missing data in general; however, the one year-data were quite good in the per-protocol follow-up. Based on the tipping point analysis, there is a 6.1% chance that including the missing data would result in a different study conclusion. However, the panel was not overly concerned about this.

The Panel commented on the Post Approval Study (PAS) outlined by the Sponsor and agreed that subgroups of symptomatic and asymptomatic patients should both be studied. The PAS should look at the total rate of death and stroke for long-term durability, and death should be included as a key secondary endpoint. Other key points discussed by the Panel were that the PAS should increase the number of patients enrolled and the duration of the PAS should capture data over five years. The Panel generally agreed that the PAS should evaluate the learning curve of physicians, should include an analysis of silent stroke, and stroke adjudication should be objective and involve a neurologist.

Vote:

On Question 1, the panel voted **6-4-1** that the data show that there is reasonable assurance that the RX Acculink Carotid Stent System is safe for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication.

On Question 2, the panel voted **8-2-1** that there is reasonable assurance that the RX Acculink Carotid Stent System is effective for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication.

On Question 3, the panel voted **7-3-1** that the benefits of the RX Acculink Carotid Stent System for use in the prespecified patient population do outweigh the risks of the RX Acculink Carotid Stent System for use in standard surgical risk patients outlined in the proposed indication.

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