



**DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health**

Public Health Service

**Brief Summary of the Orthopaedic and Rehabilitation Devices Panel Meeting –
December 12, 2017**

Introduction:

The Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on December 12, 2017 to make recommendations and vote on information related to the Premarket Approval Application (PMA) for the Barricaid Anular Closer Device by Intrinsic Therapeutics.

The sponsor has proposed the following indications for use:

“The Barricaid is intended to be implanted following a limited discectomy, to prevent reherniation and the recurrence of pain or dysfunction. The Barricaid is indicated for patients with radiculopathy (with or without back pain), a posterior or posterolateral herniation, characterized by radiographic confirmation of neural compression using MRI, and a large annular defect (e.g., between 4-6 mm tall and between 6-12 mm wide) post discectomy, at one level between L4 and S1.”

Panel Deliberations/FDA Questions:

Panel Question 1:

Study Population

1. The sponsor planned to enroll a study population that includes subjects with an increased risk of disc reherniation (i.e. large annular defects defined as between 4-6 mm tall and 6-12 mm wide post-discectomy) that would potentially benefit from a permanent implant to prevent reherniation compared to discectomy alone. After review of the data summarized in Section 3.1 of FDA’s Executive Summary, it appears that patients were enrolled consecutively across multiple sites, and the enrolled study population appeared to differ from prior literature reports regarding the incidence of “at risk” disc herniations types as identified by Caragee (2003). For example, the Barricaid study had a much lower number of “fragment-fissure” type annular defects which are associated with a low rate of recurrent lumbar disc herniation in the enrollment population. Additionally, the majority of study subjects appeared to receive anulotomies (box and cruciate shape) during the discectomy procedure, prior to randomization, which suggests surgical resection of disc annulus may have gone beyond the extent required for performing a limited discectomy as defined by the sponsor. Based on the observations regarding the study population described above and in Section 3.1 of FDA’s Executive Summary, please comment on the following:

- a. Please discuss the patient characteristics, herniation types, and size and types of annular defects that would likely benefit from an annular closure device and if that population was adequately investigated in this study.

The Panel generally believed there were some limitations with respect to the different age groups and other stratifications, but in general, the size of the annular defect was representative of what is seen in the typical patients seen in their practices.

- b. Please comment on the differences noted between the limited discectomy procedures reported in the literature compared to the treatment received by those enrolled in the Barricaid study. Then, please discuss whether the differences had an effect on the clinical outcomes, especially with respect to reherniation rates and subsequent surgical interventions in the control group.

The Panel also generally felt limited to some degree by fact that there is some discrepancy in the written material (i.e., creation of box annulotomy) vs. what was reported in the meeting as an extension of a normal slit annulotomy. Given the uncertainty, and the sponsor's additional explanation during the meeting, it seemed like the study procedure was roughly similar to procedures performed in US practice.

Panel Question 2:

Endplate Lesions

2. The sponsor reported 40% of control patients with an end-plate lesion (EPL), compared to 88% of Barricaid patients. Furthermore, the control patients with EPLs have lesions that are smaller, appear to reach stability sooner, and present features more in line with Schmorl's nodes. In contrast, the EPLs of the Barricaid patients are larger than those of the control, progress in size faster, have radiographically distinct features (e.g., lytic features and a location in proximity to the mesh), and show signs of mesh subsidence into the lesion. However, based on the secondary analyses performed by the sponsor, there does not appear to be a correlation between the presence of EPLs and measured clinical study outcomes. Based on the observations regarding EPLs highlighted in Section 3.2 of FDA's Executive Summary, please address the following:

- a. Please comment on any present and future clinical impact or relevance of the EPLs.

The Panel generally felt that the lesions have some significance. However, they did not show much clinical effect over the course of the follow-up. The Panel still had concerns because it was unclear what the lesions represent. There were also additional concerns with use of this device in an osteopenic population, concerns with long term safety, and concerns that the statistical methodology, through some attrition of data, may not provide a complete picture of long-term outcomes.

- b. Please comment on any additional analyses (e.g., which assessments at what time points), that should be conducted to evaluate the clinical significance of the EPLs.

The Panel generally felt that some initial analysis is important, but were not sure what the best analyses would be. However, some suggestions include MRI with contrast on some sub-groups to track development of lesions histology from biopsy during reoperations or post mortem, and additional correlation of outcomes with posterior ossification. The Panel generally felt that there needed to be longer term follow-up, but there was no consensus on whether 5 year or longer was needed.

Panel Question 3:

Study Endpoints

3. As summarized in Section 3.3 of FDA's Executive Summary, the co-primary endpoints developed a priori included a measure of radiographic reherniation rate designed to capture all disc reherniations (symptomatic and asymptomatic) in order to measure device effectiveness at 24 months. Radiographic endpoints to evaluate device integrity (i.e. migration, disassembly) were also included to evaluate the device function, though positive clinical outcomes occurred regardless of device integrity. In addition, the sponsor reported results from an alternative primary endpoint developed post-hoc that focused on symptomatic reherniations at 24 months. Please discuss the following:

- a. Please discuss all appropriate endpoint(s) (both safety and effectiveness) for an anular closure device, and the control population, the time point(s) at which the endpoint(s) should be evaluated and whether these should be the same.

The Panel generally felt that the appropriate endpoints and metrics of success include avoidance of repeat surgery, and complications of subsequent fusion. They stated that a two year endpoint is not long enough to evaluate success of the device. They generally believed that including all reherniations was important, and additional data in terms of axial MRIs are needed to confirm reherniations. There was additional suggestion of considering functional endpoints such as return to work.

- b. Please provide the specific criteria that should be included in a definition of symptomatic recurrent lumbar disc herniation for the anular closure device and the control.

The Panel generally felt that a number of factors could be utilized in defining symptomatic recurrent herniation, including a symptom free period, correlation of clinical findings to MRI findings, possibly use of MRI with a contrast agent and inclusion VAS leg score.

- c. While both a secondary discectomy and a secondary procedure that results in a supplemental fixation/fusion are typically counted as failures, should they be given equal weight in discussing risks accrued from implanting a device?

The Panel generally felt that both repeat discectomy and other reoperations such as fusion should both be considered failures. To some degree, the weight given to the failures (discectomy vs. fusion) may not be equal depending on the mode of failure (device migration vs. disc herniation).

Panel Vote

The panel voted on the safety, effectiveness, and risk benefit ratio of the Barricaid Anular Closer Device.

1) Is there a reasonable assurance that the Barricaid Anular Closer Device Implant is safe for use in patients who meet the criteria specified in the proposed indications for use described above?

On Question 1, the panel voted 5 (Yes), 0 (Abstain), 9 (No) that the data shows a reasonable assurance that the Barricaid Anular Closer Device is safe for use in patients who meet the criteria specified in the proposed indications for use described above?

2) Is there a reasonable assurance that the Barricaid Anular Closer Device is effective for use in patients who meet the criteria specified in the proposed indications for use described above?

On Question 2, the panel voted 12 (Yes), 1 (Abstain), 1 (No) that there is a reasonable assurance that the Barricaid Anular Closer Device is effective for use in patients who meet the criteria specified in the proposed indications for use described above?

3) Do the benefits of the Barricaid Anular Closer Device outweigh the risks when used in patients who meet the criteria specified in the proposed indications for use described above?

On Question 3, the panel voted 5 (Yes), 1 (Abstain), 8 (No) that the benefits the benefits of the Barricaid Anular Closer Device outweigh the risks when used in patients who meet the criteria specified in the proposed indications for use described above.

Public Speakers

The following Open Public Speaker attended the meeting: Danielle Shapiro, Ph.D., Senior Fellow, National Center for Health Research (NCHR).

Contact: CDR Anderson, Designated Federal Officer,
(301) 796- 7047

Sara.Anderson@fda.hhs.gov

Transcripts may be purchased from:

Free State Court Reporting, Inc.

1378 Cape St. Clair Road

Annapolis, RD 21409

Telephone: 410 974-0947

Or

Food and Drug Administration

Freedom of Information Staff (FOI)

5600 Fishers Lane, HFI-3

Rockville, MD 20857

301-443-1726