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Rejected Again: Advisory Panel Votes Against De Novo Approval For Tennessee Company's Knee Implant

by Brian Bossetta

An FDA advisory committee voted against recommending the agency approve a de novo request from Active Implants for its NUsurface Meniscus Implant. The request is the company's fifth attempt at winning FDA approval.

It's looking more likely that Active Implants will fail again in getting its knee implant on the US market.

The US Food and Drug Administration's Orthopedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee voted 6 to 2 with one abstention against recommending that the agency grant the Memphis-based company's de novo request for its NUsurface Meniscus Implant.

While the vote is not binding, the FDA's decisions are usually consistent with the recommendations from its advisory committees.

The NUsurface is a disc-shaped polycarbonate-urethane implant device for patients after medial meniscectomy, a common knee surgery and is intended as an alternative for total knee replacement.

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Though the NUsurface device, which the FDA granted breakthrough designation in 2019, has been available in Europe for 15 years and in Israel for 12, the six panel members who voted no couldn't get past the device's high rate of failure – as high as 50% in one study comparing NUsurface patients to those receiving non-surgical treatments – and what they deemed insufficient data to support the implant's approval.

In Favor

Christopher Kaeding, an orthopedic surgeon at Ohio State University's School of Medicine who was the first to implant the device in the US, argued in favor of approval because NUsurface "fills a void" between persistent knee pain and knee replacement. "There's a large segment of the population suffering knee pain and we have nothing to offer them as an alternative," Kaeding said.

The advisory committee also heard testimonials from patients, such as 53-year-old Lori Stogner Anderson, who had the device implanted in 2015 and said it has allowed her to resume her active lifestyle with no pain and without medication. "I have a brand-new knee," she said.

John Foerster, 50, and Debra Tongue, 53, had similar praise for their implants; and Lara Wood, 55, who said she has suffered knee pain her entire life but was not a candidate for knee replacement, said that she can now live a "normal, pain free life."

But most on the committee were unmoved.

Voter Responses

Panelist Paul Manner, a professor of orthopaedics and sports medicine at the University of Washington School of Medicine, felt Active Implants "cherry-picked" the surgeons and patients for their trials. "I'm concerned about the highly selected nature of the patients and surgeons chosen," he said. "But even under the most ideal circumstances, the results were not acceptable. There's no doubt these results would be much lower in actual practice in the real world."

Thomas Barber, former associate deputy physician in chief, perioperative services at Memorial Sloan Kettering Cancer Center, agreed, stating that even with the "ideal population" of patients Manner references the failure rate was still too high. "That's not the safety and efficacy I want to see," Barber said.

> *"I believe this device fills a specific niche where there's no good solution." – John Kirkpatrick*

Amy Cizik, a professor at the University of Utah School of Medicine, said the data Active Implants presented showing improvement in pain and function was insufficient. Though most panelist said a change in labeling wouldn't matter, Cizik said it would help. "The wording for the current indication does not work for me.

However, John Kirkpatrick, chief of orthopaedic surgery at the VA in Orlando, voted yes, saying he leaned slightly in favor of approval with a rigorous post market review of the device, such as tracking the number of implants requiring replacement. "But overall, I believe this device fills a specific niche where there's no good solution."

Shelby Reed, director and co-founder, Preference Evaluation Research Group at Duke Clinical Research Institute Duke University Medical Center, was the one abstention. Reed said she considered voting yes because she agreed that the device fit an "unmet need" and that there were few options for patients with knee pain short of replacement. However, she was primarily concerned about the suggested labeling, which she thought was too broad, particularly for those with mild pain and function. "That really gave me pause," she said, adding she was concerned that would result in an overuse of the device.

Not a Surprise

The committee's vote was not surprising in light of the *executive summary* the FDA issued in preparation for the panel, which detailed questions about the device's failure rates and concerns about the need for second surgeries after implantation.

To address these concerns, Active Implants narrowed the proposed indications for the device to patients with "mild to moderate osteoarthritis, mild or greater pain, and cartilage present on the load-bearing articular surface."

The company also attempted to reduce risk of adverse outcomes by limiting patient eligibility to those with a meniscus extrusion greater than 5mm and a tibial spine height no higher than 11mm.

The panel consensus, however, was that these measurements were arbitrary and simply too hard to measure with the degree of specificity and accuracy required.

Ty Subhawong, director of musculoskeletal, department of radiology University of Miami Miller School of Medicine, noted MRIs do not typically measure tibial height and was skeptical orthopedic surgeons implanting the device would measure it as well. Despite these concerns, however, Subhawong joined Kirkpatrick as the second yes vote finding a benefit for the implant in the patient population, even though it was a narrow one.

Regulatory History

The company first attempted to get the NUsurface on the US market in 2008 when it submitted its initial 510(k), which the FDA determined "not substantially equivalent (NSE)" because the plastic material of the NUsurface raised different questions of safety and effectiveness compared to the metals of the devices the company used as predicates.

A second attempt in 2013 also failed because of an NSE from another predicate.

Then, in 2014, the company changed gears and pursued de novo classification, the FDA's pathway for low-risk novel devices. But the FDA denied the request for lack of data.

Still, the company persisted, and after two clinical trials submitted another de novo request in 2020-2021, which the FDA again rejected due to the "large number of device failures and unmitigated risks."

Ryan Belaney, Active Implants vice president of clinical and regulatory affairs, encouraged the FDA to consider that the NUsurface success rate in Europe, where it has been on the market for 15 years, and the culmination of 17 years of work from the device presented to the panel.

Belaney also noted the company has conducted four clinical trials since 2008 totaling more than 400 enrollees, a number he argued was similar to that for most devices granted de novo, including orthopedic ones.

Deryk Jones, the head of the Ochsner Sports Medicine Institute in New Orleans and one of the NUsurface clinical trial investigators, acknowledged the device is not right for every patient, but said it can be a safe and effective alternative for many who suffer from debilitating knee pain. "We want to have in our toolkit," Jones said. "This is something patients and surgeons should have as an option."