

INDUSTRY application

Sample pack boosts Moxatag launch

MiddleBrook Pharmaceuticals, Westlake, TX, was founded in 2000 based on the discovery that changing the daily dosing of an antibiotic changes how bacteria respond to it. To capitalize on the finding, the company developed Pulsys, a proprietary pulsatile delivery method, which it combined with amoxicillin.

The result is Moxatag, a three-component amoxicillin tablet that the FDA approved in January 2008 for the treatment of pharyngitis (strep throat) and/or tonsillitis. MiddleBrook launched the product on March 16, 2009, and it is the first and only once-daily amoxicillin treatment on the market.

"The tablet itself dissolves rapidly in the stomach," said Don Treacy, MiddleBrook's senior vice president of development and manufacturing operations. "It immediately releases the first pulse, and the delayed-release pellets trickle down to the small intestine. Then you get a second release a couple of hours later and a third pulse of amoxicillin a couple hours after that."

The prolonged release of the 775-milligram Moxatag tablet is an improvement over immediate-release amoxicillin, typically a 500-milligram tablet or capsule taken three times a day. That's because the new tablet lowers the treatment dose and re-



Each carton contains five single-tablet physician sample packs that underscore the benefits of Moxatag's once-daily dosing.

duces the dose frequency, improving patient convenience, which improves compliance. Its clinical cure rate is better than 90 percent when the tablet is taken once a day for 10 days. "This is a novel application in the antibiotic field," Treacy said.

Help wanted

As MiddleBrook developed Moxatag, it sought a commercial manufacturer to produce and package it. The search ended in Clonmel, Ireland, where Stada, a German generics firm, manufactures penicillin-type antibiotics. Stada's facility was a good fit, because it is separated from the production of non-penicillin drug products, as the FDA requires. Stada could also take on MiddleBrook's project quickly. "They had most of the equipment we needed for commercial manufacturing," Treacy said. "We bought just a couple pieces of manufacturing equipment to add to their kit." Arrangements were also made for Stada to package the tablets in 30-count bottles for use in US pharmacies.

As those preparations were made, MiddleBrook worked on a 10-tablet blister pack, which it submitted to the FDA with its application. "We had developed the basic blister concept on our own, but at that point it was really for the stability studies. Subsequent to that, we developed the brand and the image and what the pack looks like."

But instead of launching Moxatag in the 10-tablet blister pack, MiddleBrook focused on developing a physician sample pack. The plan was to underscore the simplicity and convenience of once-daily dosing by using a single-tablet blister. With no packaging facilities of its own, the company again sought outside help, and the people at Stada recommended Almac Group, Craigavon, Northern Ireland.

"They had not dealt with Almac directly but had heard of its good reputation, and that was a good starting point," Treacy said. After conducting its due diligence, MiddleBrook arranged a meeting with Almac's busi-

ness and technical personnel. "We had a very favorable impression," Treacy said. "They were interested and very helpful, knowledgeable, and very responsive. Those are the types of things you're looking for out of a contract manufacturer or packager to give you some level of comfort that this is going to work for you."

The two companies reached an agreement and Almac developed a detailed project plan that included more than 400 individual tasks. That plan formed the basis for all project calls between MiddleBrook, Stada, and Almac, defining the lines of communication and each party's responsibilities. It was an approach that Treacy came to appreciate. "[Almac's] project management was very well organized and, honestly, it helped keep us on task. You really can't have too much communication when working on a project like this."

Singular challenges

Moxatag is not MiddleBrook's first product launch. In 2004, it bought Keflex (cephalexin) from Lilly and developed a higher-strength capsule version of it. But Moxatag is the company's first in-house product, and acceptance of it among doctors and patients is fundamental to MiddleBrook's success. It was thus paramount that the sample pack make a good first impression and facilitate treatment of patients.

Physician sample packs were nothing new to Almac, but the tablet's size and the single-tablet blister raised some technical challenges, all of which were overcome on short notice by Almac's engineering group. The group designed and built high-speed feeding equipment to fulfill product demand. It also devised and fabricated tooling to create a stable finished blister that is easy for physicians to retrieve from the carton.

Each blister measures 6.3 by 7 centimeters and the base material is a PVdC-coated PVC. The backing is a 20-micron aluminum foil that came with its own set of challenges. In fact, the seven-step foil artwork process was the most complex Almac's preferred foil manufacturer had attempted.



Pharmacies will dispense Moxatag from 30-count bottles.

Close cooperation between Almac and the manufacturer, coupled with a series of test runs, ensured that the foil met the tight tolerances required for reproducible print runs.

Next came the custom carton, which would contain five sample blisters and required both shelf appeal and ease of use. It thus includes a window to display the sample packs and a perforated tab to allow physicians to easily extract a leaflet with the prescribing information. In addition, the windowed, four-paneled carton was given strength to protect the product and rigidity to withstand handling during transport. The carton also includes tamper-evident features.

Finally, to ensure MiddleBrook met its launch schedule, Almac worked with Stada to coordinate logistics, air-shipping approximately 198 pallets (630,000 cartons) in 12 separate deliveries. Each shipment included temperature loggers, which allowed MiddleBrook to confirm proper handling during transit.

Awaiting results

It's estimated that amoxicillin accounts for about half of the 15 million prescriptions written annually to treat pharyngitis, and the advantages of Moxatag will enable it to replace a

good portion of those prescriptions, Treacy said.

It's difficult to judge the success of a new drug product until after it's been on the market for several months. But 3 weeks after the launch, Treacy expressed optimism about Moxatag's future and the role of the sample packs, which MiddleBrook's 270-member sales team will use to inform doctors about the new tablet.

"It will come down to the number of prescriptions. If that goes well then we're going to be happy. [Physicians] are comfortable writing amoxicillin. We have to explain to them why this is the right choice of formulation and brand of amoxicillin for them. And the sample packs are key to having that conversation. This single tablet in the blister pack works very well, plus the orange and blue have a lot of stopping power. We want to get doctors thinking of Moxatag when they see this color scheme."

Treacy said he and his colleagues are pleased with MiddleBrook's manufacturing and packaging partners. "Honestly, there is nothing I'd do differently. We're happy with how things are going. We may have to put a strain on [Stada's and Almac's] capacity in the future, but that would be good for everybody. Of course, this is a big deal for MiddleBrook. It's the first once-daily FDA-approved amoxicillin, and we're hopeful that it does well for us." T&C

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