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Takeaways From FDA's 1st Waiver Decision

Law360, New York (March 08, 2013, 11:45 AM ET) -- On Feb. 22, 2013, the U.S. Food and Drug Administration approved two generic drugs with a risk evaluation and mitigation strategies (REMS) program that differed from the innovator company's existing REMS program. This decision appears to be the first time that the FDA has waived the requirement for a "single shared system" under Section 505-1 of the federal Food, Drug and Cosmetic Act (FDC Act), which was created by Section 901 of the Food and Drug Administration Amendments Act of 2007 (the FDAAA).

According to the FDA's Internet web page on approved REMS, the FDA has approved only five other shared system REMS, starting in 2010. But all of those shared REMS involve numerous innovator and generic drug sellers using the same shared REMS program.

As background, Section 505-1(a)(1) of the FDC Act gives the FDA the authority to require new drug applications and abbreviated new drug application applicants to submit a REMS when the FDA has determined that a REMS is necessary to ensure that the benefits of a drug outweighs its risks. Under a REMS program, the FDA may require risk management efforts beyond routine professional labeling — including medication guides, communication plans and "elements to assure safe use" (ETASU) — when such efforts are necessary to mitigate the risks associated with a particular prescription drug.

The statute describes that an ETASU may include requirements that health care providers or pharmacists have particular training or experience prior to prescribing or dispensing the drug, that patients using the drug be monitored or be entered into a patient registry or that the drug be dispensed to patients only after documentation of safe use conditions. FDC Act Section 505-1(f)(3).

Along with the REMS requirement imposed on innovator drugs, Congress determined that ANDAs likewise must be subject to the medication guide and ETASU aspects of an existing REMS program. Moreover, in these situations, Congress stated that the innovator and generic drugs "shall use a single, shared system" (SSS). FDC Act Section 505-1(i)(1)(B).

The FDA is statutorily permitted to waive the SSS requirement, however, and "permit the applicant to use a different, comparable aspect of the" ETASU under two circumstances. Id. A waiver may be granted if the FDA determines that the burden of creating an SSS outweighs the benefit, or an aspect of the ETASU is entitled to patent or trade secret protection and when a request for a license under that protection was sought but denied by the patent or trade secret holder. Id.

In this case, the FDA waived the SSS requirement last week when it approved two generic versions of Suboxone (buprenorphine hydrochloride and naloxone hydrochloride) sublingual tablets. The FDA's waiver decision was referenced in its denial of a citizen petition filed by Reckitt Benckiser Pharmaceuticals Inc., also on Feb. 22. See Docket No. FDA-2012-P-1028-0011.

The petition itself (which focused on an alleged risk of accidental pediatric exposure) and the reasons for the FDA's denial of the petition were unrelated to the waiver decision. Still, the FDA covered the SSS REMS issue, stating in the denial letter that the ANDAs must have "the same or comparable ETASU" as the listed drug and that it had approved the generic drugs with a "comparable" one rather than the same REMS program that Reckitt was using. See Denial Letter at pp. 2, 8, 12.

According to the FDA's orange book, which lists drug patents and exclusivity, Suboxone is not subject to any patent or exclusivity terms, so the second statutory waiver justification was not relevant. Consequently, the FDA used the first waiver justification and apparently concluded that the burden of creating an SSS among all of the affected NDA and ANDA applicants outweighed the benefit of an SSS. In the denial letter, the FDA did not specifically describe either the "burden" or the "benefit" but stated merely that the waiver was granted because the statutory criteria were met. Id. at 12.

Nevertheless, one clue to the agency's "burden versus benefit" decision may be found elsewhere in the denial letter, where the FDA noted that there were "efforts to secure its [Reckitt's] participation in a single shared REMS for this product." Id. at 15. Those efforts apparently failed, since Reckitt is not included in the listing of companies posted on the FDA's approved REMS web page that are involved in the shared REMS program, named "Buprenorphine-containing Transmucosal Products for Opioid Dependence (BTOD)."

As a result, there are two separate REMS programs for BTOD products — one administered by the grouping of generic drug suppliers and one administered by Reckitt.

In summary, we note that the FDA has only recently begun to fully implement the statutory REMS provisions, and this SSS REMS waiver decision appears to be the FDA's first. Consequently, the FDA is likely still fleshing out its benefit-versus-burden analysis.

At this point in time, it is unclear what factors the FDA would find persuasive in that analysis, whether considering either the "burden" or the "benefit" aspect. Congress did provide one factor though, telling the FDA that it must "take into consideration the impact" on the varied stakeholders who are affected by pharmaceuticals and specifically listing out health care providers, patients, the generic drug manufacturer and the innovator drug manufacturer. FDC Act Section 505-1(i)(1)(B)(i).

Under the statute, then, the FDA should consider all of these disparate voices and balance the competing objectives. In addition, the FDA's analysis likely will take into account the same variety of factors found in its mission statement, such as assuring the safety, efficacy and security of drugs; speeding innovation for new medical treatments; making medicines more affordable; and helping the public get accurate, science-based information they need to use medicines to improve their health.

Given this mission statement, one could argue that the FDA must balance the potential benefits and burdens in all of the agency's regulatory decision-making.

Going forward, the pharmaceutical industry should look to future FDA waiver decisions to continue to elucidate the burden-versus-benefit analysis that the FDA will undertake under Section 505-1. The BTOD situation may be the only such waiver decision by the FDA for several years.

Or, if others in the innovator drug industry balk at joining a shared system REMS with generic companies, as Reckitt apparently did, similar decisions to that of the FDA waiver may become more common.

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