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Dual Rx/OTC Status In US 'Additional Condition' Switch Proposal: Necessary Or Questionable?

FDA Shift In Requirements For OTC Switch Follow-On Approvals Also Discussed By Experts

by Malcolm Spicer

OTC drug development and marketing consultants discuss FDA allowing simultaneous Rx and OTC sales of same drug formulation with the same indication and about opportunities for follow-on generic equivalents of switches approved as additional condition for nonprescription use OTCs.

A proposed US rule to facilitate OTC switches for chronic conditions would bend two basic rules of drug regulation, one keeping approvals of Rx and nonprescription drugs separate and the other setting approval requirements for follow-on generic equivalents of switched products.

Both pieces of the Food and Drug Administration's "Nonprescription Drug Product with an Additional Condition for Nonprescription Use" *proposed rule* published on 27 June are likely to generate volumes of comments.

In one, the Rx/OTC separation, the FDA's Center for Drug Evaluation and Research is proposing to move counter to a fundamental plank in its platform for approving and regulating pharmaceutical ingredients: drugs are approved either as Rx or OTC, as there isn't a third class, and a formulation of a drug with a certain indication is available in one class or the other, not both.

For generic equivalents' approval requirements, the agency has pivoted from a plain interpretation of its rule requiring follow-on OTCs to match the Drug Facts label as well as the formulation of the innovator switch.

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In the second article from interviews with HBW Insight, OTC drug industry product development and marketing consultants discuss the FDA allowing simultaneous Rx and OTC sales of the same drug formulation with the same indication and about opportunities provided for follow-on generic equivalents of switches approved as additional condition for nonprescription use (ACNU) OTCs.

Additionally, these experts consider whether the FDA will allow actual rather than virtual self-selection testing for access to ACNU switches. While the proposed rule references only digital channels, some sponsors may have in mind testing pharmacy or other retail store staff conduct with customers *(see related story below)*.

Since 2012, No Shortage Of Variety In US OTC Switches While Short Of Chronic Conditions

By Malcolm Spicer

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From intranasal corticosteroids to a lice treatment, and from an addition to the OTC PPI market to the first nonprescription acne drug reaching the market through an NDA, US OTC switches in the past 10 years, since FDA began considering widening switch opportunities, haven't lacked for variety.

Read the full article here

Continued Rx Option A Barrier To Switch?

The CDER frames its proposal to allow a formulation of a drug – same ingredient at the same dose and in the same delivery format – labeled with same indication to remain available Rx after it's switch as an ACNU OTC as providing an option for consumers who won't or can't use digital channels necessary for self-selection and for point-of-sale clearance to buy the product.

Susan Levy, founder and principal of SBL Consulting Group LLC in Cranford, NJ, expects that as well as an option for some consumers, continuing to allow Rx sales of a drug product after it's approved as an ACNU switch will be a barrier to follow-on generic equivalents of the OTC product.

Marketers of Rx drugs approved through abbreviated new drug applications could find it more beneficial to keep their products available prescription-only after the relevant reference listed drug is made available as an ACNU OTC.

Proposed OTC Switch Rule Anticipates Digital World

By Malcolm Spicer

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"One thing that really jumps out at me is that prescription ANDAs will be able to stay Rx. That's going to be a huge disincentive for OTC

sponsors because it will enable a lot of volume to stay Rx. In some cases, the prescription generics may be less expensive than the OTCs with an ACNU because of the additional burden on the sponsors to both develop and monitor the ACNU," Levy said.

Potential ACNU switch sponsors also might be dissuaded. "For the sponsors who are working on Rx-to-OTC switches, it's really a disincentive for innovation when products are allowed to continue to be sold by prescription," she added.

FDA's "Additional Condition for Nonprescription Use" proposal is all about information which won't be printed on DFLs but will be integral to whether some switch proposals' approval. But agency doesn't explicitly exclude switch sponsors from assigning delivery of ACNU information to staff in stores or in online chats.

Read the full article here

A Needed 'Degree of Flexibility'?

For longtime FDA's OTC drug advisory board member Eric Brass, though, allowing simultaneous Rx and OTC sales of the same drug formulation was necessary to facilitate making more drugs available nonprescription, particularly ingredients for chronic conditions,

The FDA's historic and rigid policy of a formulation being either nonprescription or prescription "was absolutely dichotomous," said Brass, professor emeritus of medicine at the UCLA School of Medicine and a principle with ZnCu Consulting LLC in Rancho Palos Verdes, CA.

"This allows a blending where if a drug approved as an ACNU consumers can still access it through the conventional pathway through their healthcare provider. And I think that's one example of an important degree of flexibility that's included in this new proposed rule," he said.

Allowing an option for some consumers to using an ACNU digital process also makes sustaining Rx sales necessary.

Previous Failed Switch Proposals Could Signal Help

The CDER explained in the proposed rule that an applicant can submit information explaining the necessity of the ACNU for appropriate self-selection and use when the agency previously has "signaled that labeling alone is not sufficient to ensure appropriate self-selection or appropriate actual use, or both."

Those signals, Hemwall pointed out, should already be known to the drug industry about statin drugs proposed for OTC switches, proposals he worked on while at Merck & Co. Inc. which the FDA most recently in 2008

"There is an interesting caveat or additional rationale there. The FDA has now explicitly acknowledged that not all consumers may be able to use all additional conditions to access the medication. Therefore, if you're approved with an ACNU, you can also keep the medication on prescription status, so that those other consumers can access the effective medication in the conventional way," Brass said.

"This represents an evolution in thinking that I think is part of the reason to create this separate process, to allow a justification for what is a very rational set of conditions."

Change For Generic Follow-On Approvals ...

The FDA started on its initiative leading to the ACNU proposed rule acknowledging that while it could grant a firm an approval for a drug with certain voluntary restrictions, such as a digital self-selection questionnaire consumers must use before purchasing an OTC, the agency's regulations left sponsors with little incentive to innovate in this way.

Former FDA Commissioner Margaret Hamburg in 2012 characterized regulations at the time by saying "generic competition wouldn't have to" comply with the innovator's voluntary restrictions. "They could just have 'nonprescription drug' in their fact box and that would be it," she said. (Also see "*FDA To Tackle Critical Generics Issue In Switch Paradigm Debate*" - Pink Sheet, 12 Mar, 2012.)

But she also noted the FDA was considering whether it can expand the definition of nonprescription drugs to include requiring "conditions of safe use."

Under such an expanded regulatory scheme, which the FDA has now proposed with ACNU switches, when the agency deems safe use of a drug means any additional conditions of use

didn't approve, adhering to advisory board concerns. (Also see "*Merck's Mevacor not approved*" - HBW Insight, 28 Jan, 2008.)

"They slipped in a little phrase in there about the FDA has previously signaled consumers won't be able to do it without some sort of labeling aide. In the case of statins, it was previously signaled. Anyone working on switching a statin maybe already have that signal," he said.

Some firms already are working on the kind of digital self-selection technologies the FDA now says will be evaluated for ACNU switch approvals after a sponsor convinces the agency that more than a DFL is needed.

"That's the kind of thing you'd want to get clear with an FDA meeting," Hemwall said, "to get some real clarity on what what's really needed."

"Because in the past, it's just been a guessing game waiting for FDA to take a position on how something like this is conducted under the law."

would be needed, it must "be able to require it to be attached to any drug that would be a nonprescription drug like that," the former commissioner predicted.

In the proposed rule, the CDER has imposed that requirement on follow-ons to ACNU switches, but with flexibility needed to prevent innovators from effective blocking competition.

Edwin Hemwall, a switch consultant in Villanova, PA, and previously an OTC products executive in a career spanning multiple firms, noted that the proposal doesn't stipulate systems or technologies to use for ACNU procedures.

"I think that it's noteworthy that … the device on a website or a phone app system can be varied. And that's the key to allowing generics to come in. They don't have to necessarily have the exact same system, but they have to have something that would be similar," Hemwall said.

"To me, that was one of the bigger challenges, that is how to allow generics," he added.

The FDA, he also noted, isn't ignoring that ACNU switch sponsors might attempt to slow competition. The proposed rule asks for comments on, among other questions, whether a sponsor could patent its ACNU system.

"Of course, that's why they give the workaround for generics, if a system is patented," Hemwall said.

… Likely To Be 'Sorted Out'

Comments are likely, Brass suggested, about that question.

What could "be subject to a lot of discussion is related to the requirements of the follow-up product after an innovator, the generic or store brand, and how they can rely on the data from the innovator to support their follow on," he said.

"How do they demonstrate that their technology accomplishes the same objective as the

Proposed Rule Making More OTC Switches Likely In US Makes More Tools Necessary For Sponsors

By Malcolm Spicer

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OTC drug development and marketing consultants spoke with HBW Insight about FDA's "Nonprescription Drug Product with an Additional Condition for Nonprescription Use" proposed rule. In first of two articles, they discuss proposed rule's likely impacts on industry and remaining concerns around incorporating extra-label information in drug labeling.

Read the full article here

innovator? Will the innovator try to put IP protections around their technologies or other tools they develop? They may restrict and create barriers to those follow-ons."

Brass allowed that the proposed rule makes clear that the CDER expects and encourages those types of follow-ons and attempted to "define a relatively reasonable set of conditions for the follow-on products."

"How all of that gets sorted out in this new environment is going to be interesting. … But I think I could imagine there be challenges to interpretation, and great incentives for the innovator to try to put IP barriers around whatever it is they developed in an effort to inhibit those follow-on products."

Flexibility for digital self-selection tools or not, early ACNU switch sponsors will face a steep approval process.

"I think they've built a level of flexibility to allow for different kinds of approaches. I think that's in recognition that the first one or two that go through them are going to be trailblazers. People are going to be watching very closely to see what the standard of proof is, or the burden of proof that FDA requires some of these situations," Hemwall said.

Who Decides Whether DFL Alone Will Work?

A step in a potential ACNU switch process before a sponsor would submit to the CDER its proposed digital self-selection channel also is likely to generate questions.

That's the point at which the center would say whether a sponsor has shown that an Rx ingredient couldn't be made available OTC safely and effectively using information limited to the Drug Facts label.

"I'm concerned about the phrase 'if the applicant demonstrates and FDA determines that labeling alone is insufficient.' What if the applicant believes that they have adequately proven self-selection and proper use by consumers and FDA disagrees? Who really determines whether an ACNU is necessary? How will disagreements be adjudicated?" Levy asked.

"It's really interesting to me that they didn't put an 'or' in there, if the applicant demonstrates it is sufficient and FDA determines that labeling alone is insufficient," she added.

The CDER, Levy suggested, could leverage this step in a switch process to put holds on a sponsor's clinical trials. "Even though sponsors have done their homework and have demonstrated that the label does adequately demonstrate the ability for products to be used safely?"

Rather than a potential stumbling block, Hemwall says, switch sponsors should approach this step as another box they need to check on the way to an ACNU approval.

The CDER states in the proposed rule that a sponsor would need "robust self-selection studies and label comprehension studies that demonstrate that consumers could not appropriately self-select [a potential switch] with labeling alone."