BEHIND-THE-COUNTER DRUGS

New Life for an Old Idea?

by David M. Fox and Abigail E. Brandel

The notion of "behind-the-counter" drugs is not new. According to at least one observer, the idea of restricting some drugs to sale only in pharmacies, by pharmacists, or under the supervision of pharmacists has been the subject of discussion and debate for "over a century."[1] However, recent events have brought BTC drugs back to the forefront at the Food and Drug Administration (FDA).

In 2006, FDA approved BTC availability for the emergency contraceptive drug Plan B (levonorgestrel). The Food and Drug Administration Amendments Act of 2007 (FDAAA), which explicitly authorizes FDA to impose conditions on the dispensing of a drug, was enacted. In October 2007, FDA began publicly exploring the possibility of making some drugs currently available only by prescription eligible to be dispensed without a prescription but "only after intervention by a pharmacist," and is expected to issue a specific proposal on the issue.

In light of these events, this article examines FDA's authority and history of practice regarding BTC drug products, the potential impact of FDAAA, and the future of BTC drugs.

FDA's Authority

The federal Food, Drug, and Cosmetic Act (FDCA) explicitly recognizes two categories of drug dispensing: prescription and nonprescription. FDA may require a prescription for a drug only if, "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, [the drug] is not safe for use except under the supervision of a practitioner licensed by law to administer such drug."[2] When a drug is approved for use by prescription, the drug can be dispensed only by pharmacies and other authorized healthcare providers. All other drugs are presumed to be available for general over-the-counter (OTC) sale and use.[3]

Most drugs marketed under approved new drug applications (NDAs) are initially marketed as prescription-only products. Prescription drugs marketed under approved NDAs may be "switched" to OTC use through an NDA supplement. FDA must approve such a supplement if prescription dispensing is "not necessary for the protection of the public health by reason of the drug's toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use," and "the drug is safe and effective for use in self-medication as directed in proposed labeling."[4]

In view of this dichotomous statutory scheme (and the FDCA's focus on the safety, efficacy and manufacturing of drugs, not their retail sale, the regulation of which has generally been left to the states), FDA has indicated on multiple occasions that it lacks the statutory authority to mandate that a drug be sold BTC. For example:

- 1974: "No controlled studies or other adequate research data have been supplied to support the position that any class of OTC drugs must be dispensed only by pharmacists in order to assure their safe use…. There is at

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this time no public health concern that would justify the creation of a third class of drugs to be dispensed only by a pharmacist or in a pharmacy. The 'third class of drug' issue is at this time solely an economic issue. The Commissioner therefore categorically rejects the establishment of a third class of drugs at this time."[5]

- 1984: FDA stated that its authority to create a "pharmacist-only class of drugs" is "questionable," and that "[u]nder the [FDCA] there is no provision for an intermediate class of drugs between OTC and prescription products. The statutory requirement that a drug either be limited to prescription dispensing or available OTC with adequate directions for use seems to preclude the agency from establishing a class of drugs whose labeling would need to be supplemented by a pharmacist's instructions."[6]
- 2005: FDA noted the "dichotomy between prescription and OTC drugs," and solicited comment on how the agency would, if it were to limit the sale of an OTC product to a particular subpopulation (while the same product remained available only by prescription for the rest of the population), "be able to enforce such a limitation as a matter of law."[7]

FDA Practice

Over the last two decades, however, FDA has developed informal methods of restricting the distribution—including the dispensing—of drug products.[8] The agency takes the position that it approves a drug product based on the "conditions of use" presented by the sponsor. Where the sponsor proposes restrictions on its own product, the restrictions become conditions of use and part of the terms of FDA's approval. FDA characterizes these restrictions as "voluntary" and "agreed-upon" by the sponsor, although some would say they are coerced and effectively dictated by the agency because most sponsors would prefer to agree to conditions than risk non-approval of their products. In either case, such limitations have become standard practice within the approval process.

In at least one instance, agreed-upon distribution restrictions have included BTC access. As part of the approval of Plan B (levonorgestrel), the sponsor agreed that the product will be sold only by prescription to women 17 years of age and younger.[9] It will be sold without a prescription to "consumers" 18 and older[10] with government-issued proof of age. Under the terms of the approval, Plan B has labeling and packaging that are intended to meet both the prescription and OTC drug requirements. The front panel states that the product is "Rx only for age 17 and younger." There is also space for a pharmacist to apply the standard prescription label information before dispensing pursuant to a prescription. The back panel has the "Drug Facts" information and format required for OTC drugs.

According to FDA, because Plan B is labeled with the "Rx only" legend:

State and Federal law . . . require that the packages be dispensed only by pharmacies and other healthcare providers such as physicians and clinics authorized to dispense prescription drugs. The product will not be available through convenience stores and gas stations because they will not be authorized to sell the prescription product.[11]

For these reasons, Plan B must be sold BTC. Any change to these terms "must be discussed with FDA prior to its implementation and is subject to FDA's review."[12]

Impact of FDAAA

Until recently, nothing in the FDCA explicitly authorized FDA to unilaterally restrict the sale or distribution of most drugs.[13] However, FDAAA gives the agency explicit authority to impose restrictions on the dispensing of drug products. It authorizes the agency to impose a Risk Evaluation and Mitigation Strategy (REMS) requiring that a drug be dispensed to patients "only in certain health care settings, such as hospitals[.]"[14] FDAAA also enables FDA to require that a drug "be dispensed to patients [only] with evidence or other documentation of safe-use conditions, such as laboratory test results."[15]

Some have speculated that FDAAA increases FDA's ability to move drug products BTC. However, it seems unlikely that FDA will exercise its authority under FDAAA in this manner because a drug probably cannot meet the criteria for both REMS distribution restrictions and nonprescription availability.

One of the hallmarks of nonprescription drugs is a wide safety margin. That margin presumably could be somewhat narrower for products in a BTC class (than products available OTC) by virtue of pharmacist involvement or oversight. However, the standard for a REMS distribution restriction under FDAAA is that the restriction is necessary "to mitigate a specific serious risk listed in the labeling of [a] drug,"[16] and FDA's practice has been to limit the use of REMS to prescription drugs with serious risks like birth defects and fatal or life-threatening infections. Such products seem unlikely to qualify for BTC

status – even though criteria for BTC status have yet to be articulated. Thus, FDA is more likely to continue to use its longstanding approval authority to elicit "voluntary" sponsor commitments to restrict drug dispensing should the agency deem BTC access appropriate.

The Future of BTC Drugs

FDA officials have made several public statements in the last year indicating that the agency is interested in exploring the creation of a BTC class. On November 14, 2007, FDA held a public meeting to obtain comment on "the public health benefit of certain drugs being available without a prescription but only after intervention by a pharmacist."[17] At least one agency official stated after the meeting that a "specific proposal" from FDA on the topic will be forthcoming.

As the public meeting illustrated, however, there is no consensus about the necessity or advisability of creating a BTC class. Key stakeholders continue to disagree about whether a BTC class would improve access to care, and to debate the impact of a BTC class on costs to patients, patient privacy, the precise role of the pharmacist, and, of course, the criteria that would be used to determine whether a drug would be eligible.

The possibility of a formal BTC class may be relevant or useful to other agency initiatives and approvals. The amount of public pressure on and scrutiny of FDA oversight of drug safety continues to increase. Perhaps the agency views creating a BTC class as one component in a larger effort to improve oversight of OTC drugs. (For example, legislation requiring companies to report serious adverse events associated with nonprescription products took effect on Dec. 22, 2007, and FDA recently publicized the dangers of using OTC cold and cough medicines in young children.)

FDA may wish to use BTC as a means to transition a product between prescription-only and OTC status—a sort of "OTC with training wheels." Cholesterol-lowering agents are frequently cited as good candidates for that approach. FDA also is gathering information on adolescent use of OTC drugs, "including adolescent decision-making skills (compared with adult skills)," and "mechanisms to promote appropriate and optimal use of OTC drugs by adolescents."[18] Perhaps FDA is considering whether a BTC system would be such a mechanism.

Recent events suggest that FDA's interest in creating a BTC class of drugs is on the rise, but the idea remains controversial. Whether its time has come or the century-old debate will rumble on indefinitely remains to be seen.

1 G. Fisher, "Third Class of Drugs – A Current View," 46 *Food Drug Cosm. L.J.* 583 (1991).
2 21 USC 353(b)(1)(B).
3 *See* 21 CFR 330.10(a)(4)(vi).
4 21 CFR 310.200(b).
5 39 Fed. Reg. 19880, 19881 (June 4, 1974).
6 FDA response to citizen petitions filed by the National Association of Retail Druggists and the American College of Apothecaries (Docket No. 84P-0028).
7 79 Fed. Reg. 52050, 52051 (Sept. 1, 2005).
8 Typically, these restrictions have been part of schemes termed risk management plans or Risk Minimization Action Plans (RiskMAPs). For example, only pharmacies that enroll in the RiskMAP for Accutane (isotretinoin), a known teratogen, may dispense the product.
9 S. Galson Mem. to NDA 21-045, S-011 at 4 (Aug. 24, 2006).
10 Presumably, the term "consumers" in the labeling and the approval letter refers to both men and women. Only the prescription version of the product appears to be specifically limited to women.
11 *See* note 9, *supra*.
12 *Id.*
13 One notable exception is products approved under the accelerated approval framework. FDA has explicit authority to restrict the distribution of those products.
14 Pub. L. 110-85; 121 Stat. 823 (2007) (codified at FDCA 505-1(f)(3)).
15 *Id.*
16 *Id.*
17 72 Fed. Reg. 56769 (Oct. 4, 2007).
18 72 Fed. Reg. 62481 (Nov. 5, 2007).