EXECUTIVE SUMMARY

Check your clinic's stock for norgestimate and ethinyl estradiol birth control pills distributed by Glenmark Generics. The company recently issued a voluntary, nationwide, consumer-level recall of seven lots of the Norgestimate and Ethinyl Estradiol Tablets USP (0.18 mg/0.035 mg, 0.215 mg/0.035 mg, 0.25 mg/0.035 mg) pills because a packaging error could leave women without adequate contraception and at risk for unintended pregnancy.

- The packaging defects do not pose any immediate health risks, the company states; however, consumers exposed to affected packaging should begin immediate use of a nonhormonal form of contraception.
- Patients with affected product should be instructed by clinicians to return the product to the pharmacy.

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The tablets were manufactured and packaged by Glenmark Generics of Mumbai, India, and are distributed by the company's U.S. division. The product was distributed to wholesalers and retail pharmacies nationwide between Sept. 21, 2011 and Dec. 30, 2011.

Look for lot numbers

The packaging error occurred when select blisters were rotated 180 degrees within the card, reversing the weekly tablet orientation and making the lot number and expiry date visible only on the outer pouch. Any blister for which the lot number and expiry date is not visible is subject to recall. The packaging error is limited to the following seven lots listed of Norgestimate and Ethinyl

Estradiol Tablets USP, 0.18 mg/0.035 mg, 0.215 mg/0.035 mg, 0.25 mg/0.035 mg (listed by lot number, expiration date): 04110101, 07/31/2013; 04110106, 07/31/2013; 04110107, 07/31/2013; 04110114, 08/31/2013; 04110124, 08/31/2013; 04110129, 08/31/2013; and 04110134, 09/30/2013.

According to the company, the packaging related issue was discovered when a consumer complaint was received regarding a blister pack with pills packaged in reverse order. The correct packaging configuration calls for three pouch packs packaged in a carton, with each pouch pack having one blister containing 28 tablets (seven tablets each of a different strength and inactive tablets) in which the sequence is white to off-white tablets on the top row and inactive light green tablets in the bottom row.

Any adverse events that might be related to the use of the recalled product should be reported to Glenmark Generics at (888) 721-7115 from 8 a.m. to 5 p.m. Monday to Friday. Adverse events also may be reported to the Food and Drug Administration's (FDA) MedWatch Program. Go to www.fda.gov/Safety/MedWatch/default.htm, and click on "Report A Serious Medical Product Problem Online" to access Form FDA 3500. Events may be entered online; the form may be printed and mailed to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787; or it may be faxed to (800) 332-0178.

Are OCs in your stock?

The recall marks the third OC packaging recall since October 2011. *(See the* Contraceptive Technology Update *articles "Pfizer issues recalls for Akrimax OCs," April 2012, p. 42, and "Qualitest pulls suspect OCs, December 2011, p. 137.)* However, there is a reasonably high likelihood that the Glenmark recall has not made an impact in your practice, as the company recently entered the U.S. generic contraceptive market.

The company received its first FDA approval in April 2010 for Heather, the generic equivalent of Nor-QD (Watson Pharmaceuticals), followed by the July 2010 approval of norethindrone 0.35 mg, the generic version of Micronor (Janssen Pharmaceuticals). Since then, it has received approval for Briellyn, the generic version of Ovcon 35 (Warner Chilcott); Alyacen 1/35, the generic version of Ortho-Novum 1/35 (Janssen Pharmaceuticals); Alyacen 7/7/7, the generic version of Ortho-Novum 7/7/7 (Janssen Pharmaceuticals); and Marlissa, the generic version of Nordette (Duramed Pharmaceuticals). The FDA approval for the norgestimate and ethinyl estradiol tablets USP (0.18 mg/0.035 mg, 0.215 mg/0.035 mg, 0.25 mg/0.035 mg) pills, the generic version of Ortho Tri-Cyclen, came in June 2011. ■

Progestin-only pill eyed as OTC OC candidate

With relatively few contraindications to use, progestin-only pills might be a possible candidate for over-the-counter (OTC) use in the United States. But what will it take to move progestin-only pills to the drugstore shelves?

New research underscores the low prevalence of contraindications to progestin-only pills.[1]

Researchers looked at data from two studies, the Self-Screening Study (a sample of reproductive-aged women in the general population in El Paso, TX) and the Prospective Study of OC Users (a sample of current oral contraceptive [OC] users who obtain pills in El Paso clinics or over the counter in Mexican pharmacies). Researchers found just 1.6% of women from the general population and 0.6% of current users in El Paso had at least one contraindication to progestin-only pills. This finding contrasts with the prevalence of contraindications to combined oral contraceptives, which has been reported to be as high as 39%.[2]

If progestin-only pills were available over the counter, they could improve women's access to contraception and better enable women to prevent unwanted pregnancies, says **Kari White**, PhD, assistant professor in the University of Alabama at Birmingham School of Public Health. In addition, this move would provide women with an OTC contraceptive option that is more effective than methods currently available, such as condoms and spermicides, says White, who served as lead author of the current research.

Although there tend to be a perception that progestin-only pills are less effective than combined pills, there are formulations registered in Europe that contain desogestrel that have been found to be quite effective at preventing ovulation and pregnancy and are very popular, says White. With Cerazette, a 75 mcg desogestrel pill marketed internationally by Merck, ovulation inhibition is maintained after 12-hour delays in tablet intake, with return of ovulation taking at least seven days.[3] While the pill is available in several international countries, it is not available in the United States. *(To read more about Cerazette, see the* Contraceptive Technology Update *article, "Progestin-only pills: Where do they fit in?"*

EXECUTIVE SUMMARY

With relatively few contraindications to use, progestin-only pills might be a possible candidate for over-the-counter (OTC) use in the United States. New research now underscores the low prevalence of contraindications to progestin-only pills, which opens the door to further research of a potential pill candidate.

- One-fifth of (20.25%) of Contraceptive Technology Update readers who participated in the 2011 Contraception Survey say they support over-the-counter availability of progestin-only contraceptives.
- About 23% said they support pharmacy access to oral contraceptives when a pharmacist can screen for contraindications.
- About 25% said they did not support OTC access.

January 2006, p. 9.)

One-fifth of (20.25%) of CTU readers who participated in the 2011 Contraception Survey say they support over-the-counter availability of progestin-only contraceptives. About 23% said they support pharmacy access to oral contraceptives when a pharmacist can screen for contraindications. About 25% said they did not support OTC access.

More research needed

What are the next research steps in bringing a potential OTC product to the U.S. market? With support from the Society of Family Planning, the Oral Contraceptives Over-the-Counter Working Group recently completed a nationally representative survey of women of reproductive age on their opinions about OTC access to OCs and their interest in using the pill if it were available OTC, says **Dan Grossman**, MD, a member of the Working Group and senior associate at Ibis Reproductive Health in Oakland, CA. The Working Group is a coalition of reproductive health rights and justice organizations, nonprofit research and advocacy groups, university-based researchers, and clinicians who are advocating for a safe, effective OTC pill. *(*CTU *reported on the Working Group. See "Is it time to bring OCs over the counter?" July 2010, p. 77.)*

"We are completing the analysis of that now, and we hope to submit for publication in the next month," says Grossman. "Other research that will be needed is a label comprehension study and an actual use study of a potential OTC product."

Move past hurdles

Reproductive health advocates have been on the move since the recent December 2011 rejection of full OTC status for the emergency contraceptive Plan B One Step by Health and Human Services Secretary Kathleen Sibelius. How did the rejection impact plans, if any, for possible development of an OTC OC? *(Read more about the move; see "OTC access to EC blocked — What's next?" February 2012, p. 15.)*

"Secretary Sibelius' decision to overrule the recommendation of the Food and Drug Administration (FDA) is certainly outrageous and very disappointing," says Grossman. "Until this has been resolved, it seems unlikely that an OTC application for an OC product would be approved without a similar age restriction."

The New York City-based Center for Reproductive Rights in February 2012 asked the

federal court to reopen the center's 2005 lawsuit against the FDA for imposing unnecessary age restrictions on emergency contraception. The center also requested the addition of Sebelius as a defendant in the reopened case for her role in overruling the FDA's decision to approve Plan B One-Step for over-the-counter status in December 2011.

"We remain hopeful that the evidence-based recommendation of the FDA regarding Plan B One-Step will eventually prevail," says Grossman. "But in the meantime, we are continuing with our efforts."

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Threat up for gonorrhea that is multi-drug resistant

Public health officials are sounding the alarm on the growing threat of multi-drug resistant gonorrhea. What will it take to turn the tide against gonorrhea, the second most commonly reported communicable disease in the United States?

"Though there is no evidence yet of treatment failures in the United States, trends in decreased susceptibility coupled with a history of emerging resistance and reported treatment failures in other countries point to a likelihood of failures on the horizon and a need for urgent action," says **Judith Wasserheit**, MD, MPH, professor and vice chair of the Department of Global Health at the University of Washington in Seattle and co-author of a new analysis of the emerging threat.[1]

Gonorrhea is the second most commonly reported communicable disease in the United States. The Centers for Disease Control and Prevention (CDC) estimates that more than 700,000 persons in the United States get new gonorrheal infections each year.[2] *Neisseria gonorrhoeae*, the bacteria that causes the sexually transmitted infection (STI), is wily in its resistance to antimicrobial agents. It developed resistant to sulfanilamide in the 1940s, penicillins and tetracyclines in the 1980s, and fluoroquinolones by 2007. Third-generation cephalosporins are the first-line treatment options now recommended by the CDC.[3]

EXECUTIVE SUMMARY

Public health officials are sounding the alarm on the growing threat of multi-drug resistant gonorrhea. Though there is no evidence yet of treatment failures in the United States, trends in decreased susceptibility, coupled with a history of emerging resistance and reported treatment failures in other countries, point to a likelihood of failures on the horizon and a need for urgent action.

- Clinicians should treat all cases of gonorrhea with the most effective regimen: a 250-mg intramuscular dose of ceftriaxone.
- One gram of azithromycin also should be given orally to cover other copathogens and to provide another antimicrobial with activity against N. gonorrhoeae at a different molecular target.

Drugs losing ground

The effectiveness of cephalosporins for treating gonorrhea is decreasing rapidly, warns the CDC.[4] *(To read more about the decline, see the September 2011* STI Quarterly *supplement article, "Options running out for gonorrhea treatment, p. 3.)*

Researchers with the CDC's Gonococcal Isolate Surveillance Project have reported a 17-fold increase in elevated minimum inhibitory concentrations, which serve as a measure of drug susceptibility. In the past, national treatment recommendations have been changed to focus on other effective drugs when resistance to drugs has increase; however, there are no other drugs available to successfully treat the infection.

"The bottom line is that gonorrhea is a very complex bacteria, and we've seen it evolve and become resistant to every antibiotic recommended for treatment over the years," says **Gail Bolan**, MD, director of the CDC's Division of STD Prevention. "In the past, CDC has kept pace with this evolving organism, monitoring for trends in susceptibility and changing treatment guidelines as needed because we had alternative antibiotics to use.

However, public health officials are at an impasse, since there are no new drugs in development, and new options are urgently needed, says Bolan, who serves as lead author of the current analysis. "CDC is working with the National Institutes of Health on a randomized controlled trial to see how effective different combinations of existing drugs are at treating gonorrhea," says Bolan. "We hope to have find-