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Smarter science. Safer medicines.

**Richard H. Roberts, M.D., Ph.D.**
President
Chief Executive Officer

September 20, 2010

Mr. Clark G. Sullivan, Esq.
Arnall Golden Gregory LLP
171 17th Street, NW Suite 2100
Atlanta, GA 30363

**Sent Via: Federal Express**

**RE: Hikma's Continued Endorsement of Unapproved and Illegal Colchicine Tablets**

Dear Mr. Sullivan:

I am writing to correct some of the many factually incorrect statements in your September 1, 2010 letter and to once again encourage your clients Hikma Pharmaceuticals PLC ("Hikma") and its subsidiary West-Ward Pharmaceutical Corp. ("West-Ward") to cease the manufacture and distribution of illegal and potentially dangerous unapproved colchicine tablets in the United States.

Contrary to the assertions in your letter, Mutual Pharmaceutical/URL Pharma (collectively, "Mutual") has *proven* that the previously accepted thinking on the proper use of colchicine to treat acute gout, as reflected on the labels and product inserts for your clients' unapproved colchicine, is outdated and dangerous. As a result of the clinical studies performed by Mutual during the FDA approval process for COLCRYS®, several important discoveries were made that conclusively revealed that the unapproved colchicine prescribed by physicians for the last several decades is not as safe or effective as COLCRYS®.

Your statement that colchicine is "governed by several USP monographs" is misleading and irrelevant. As I'm sure your clients know, the USP monographs for colchicine set standards for pharmaceutical test methods and standards of identity for drug substances (i.e., raw materials), *not* finished drug products such as the unapproved colchicine tablets manufactured and sold by West-Ward. USP standards are thus only a subset of what West-Ward would be required to comply with if it bothered to obtain FDA approval for its product. Accordingly, referring to USP monographs does nothing to justify West-Ward's sale of an unapproved and potentially dangerous finished drug product which, according to FDA, requires FDA approval.

Many patients continue to receive West-Ward's unapproved colchicine because their physicians are unaware that (1) new dosing regimens for COLCRYS® significantly decrease the most common side effects from colchicine use (*i.e.*, cramping, nausea, diarrhea, abdominal pain, and vomiting) and help to reduce the likelihood of potential negative interactions, (2) the labeling for Mutual's FDA-approved COLCRYS® product contains warnings on numerous drug-drug interactions, food interactions, contraindications, and the potentially dangerous accumulation of colchicine during chronic dosing, which are not included in the label for West-Ward's colchicine (*See* Pages 2-4 of my June 22, 2010 letter), and (3) their prescriptions are being filled at pharmacies with an unapproved colchicine product.

Although Hikma is apparently willing to turn a blind eye to the actions of its U.S. subsidiary, there is no question that West-Ward's colchicine product is illegal. The FDA has repeatedly stated that unapproved single-ingredient 0.6 mg colchicine products are "new drugs" within the meaning of the Federal Food, Drug, and Cosmetic Act ("FDCA") because they are not generally recognized as safe and effective for their labeled use and because a new drug can only be distributed in the United States if it has been approved by the FDA. *See* Pages 1-3 of my June 22, 2010 letter (citing two FDA warning letters to Sunrise Pharmaceutical, Inc. and Vision Pharma LLC and March 3, 2010 letter from Dr. Janet Woodcock, Director of the FDA's Center for Drug Evaluation and Research).

Hikma's and West-Ward's continued disregard of the very clear FDA pronouncements regarding unapproved colchicine undoubtedly exposes your clients to a similar fate as Forest Pharmaceuticals, Inc. ("Forest"). Forest recently pled guilty to several criminal charges and agreed to pay more than $300 million in a plea agreement with the FDA and Department of Justice stemming primarily from Forest's continued distribution of unapproved drugs. In the Forest case, the FDA announced that levothyroxine sodium products are "new drugs" within the meaning of the FDCA (as it did with colchicine) and that FDA approval was necessary to continue marketing and distributing the drugs. Forest ignored this information and continued to distribute its unapproved levothyroxine sodium product, which led to FDA enforcement action and criminal charges. Ms. Deborah M. Autor, Director of the Office of Compliance in the FDA's Center for Drug Evaluation and Research stated, "These charges should serve as a warning to industry that the FDA takes seriously its role to protect the public from unapproved drugs . . . Any company that operates in violation of the FDCA and ignores FDA's warnings should be aware that a criminal action could follow." *See* September 15, 2010 FDA News Release, Forest Pharmaceuticals Agrees to Guilty Plea for Violating FDA Laws (attached).

Hikma continues to bemoan the price of COLCRYS®, which is priced consistently with other FDA-approved prescription drugs on the market and reflects that Mutual has spent many tens of millions of dollars researching colchicine and educating health care professionals on Mutual's important discoveries (that serve to protect patients). Yet West-Ward has brazenly increased the price of its <u>unapproved</u> colchicine drug over 1000% since

Mutual obtained FDA-approval for COLCRYS® in July 2009. The timing of this dramatic price increase is obviously not coincidental and speaks volumes about the opportunistic nature of Hikma and its subsidiary West-Ward.

It is disappointing but not surprising that Hikma continues to endorse West-Ward's manufacturing and distribution of potentially dangerous unapproved colchicine. Presumably Hikma is taking this position because it reaps enormous profits each day that the FDA delays in taking the inevitable action to remove West-Ward's unapproved product from the market. In fact, Hikma's profits are higher now than they were before Mutual's false advertising and unfair competition lawsuit was filed because several of West-Ward's competitors have left the unapproved colchicine market altogether, either due to FDA Warning Letters or by voluntary compliance with the law, thus clearing the way for West-Ward to continue exploiting misinformed doctors, pharmacists, and patients at the expense of public health and safety.

I hope that my letters will help your clients to realize the error of their ways and prompt them to take appropriate steps to voluntarily cease the manufacture and distribution of unapproved colchicine. However, if Hikma and West-Ward cannot resist the opportunity to profit from selling a drug that is not FDA-approved and not generally recognized as safe and effective, we are confident that the FDA will take decisive action to protect the public health and remove West-Ward's illegal and potentially dangerous product from the market.

If your clients have any questions or comments, please let them know that I would be happy to receive correspondence from them.

Sincerely,

Richard H. Roberts, M.D., Ph.D.
President, CEO and Chairman
RHR/ph
Attachment

U.S. Department of Health & Human Services

U.S. Food and Drug Administration



## News & Events

### FDA NEWS RELEASE

**For Immediate Release:** September 15, 2010
**Media Inquiries:** Elaine Gansz Bobo, 301-796-7567, elaine.bobo@fda.hhs.gov
**Consumer Inquiries:** 888-INFO-FDA

**Forest Pharmaceuticals agrees to guilty plea for violating FDA laws**
*Company sold unapproved and misbranded drugs and obstructed agency investigation*

The U.S. Food and Drug Administration (FDA), working in close coordination with the U.S. Department of Justice (USDOJ), today announced that Forest Pharmaceuticals, Inc. entered into a plea agreement in which the company accepted responsibility for criminal actions including distribution of an unapproved new drug, distribution of a misbranded drug, and obstruction of an FDA inspection.

To resolve these charges and a related civil suit, Forest Pharmaceuticals, Inc. has agreed to pay more than $300 million, including $164 million in criminal penalties. This plea agreement is the culmination of a multiyear investigation conducted by FDA's Office of Criminal Investigations in cooperation with its law enforcement partners and the U.S. Attorney's Office for the District of Massachusetts.

Charges against Forest Pharmaceuticals, Inc. are primarily for its marketing of Levothroid (levothyroxine sodium tablets, USP), an unapproved drug used for the treatment of hypothyroidism. A 1997 Federal Register notice announced that these products are considered "new drugs" within the meaning of the Federal Food Drug and Cosmetic Act (FDCA) and that manufacturers who wished to continue marketing these products must obtain approved applications from the FDA by August 2000. Because levothyroxine was considered a medically necessary product, the FDA permitted a gradual phase-out with all distribution of unapproved levothyroxine sodium drug products to cease no later than August 2003.

Forest Pharmaceuticals did not obtain drug approval, increased its distribution of Levothroid rather than scaling down, and ignored a subsequent Warning Letter to stop the manufacture and distribution of Levothroid.

"These charges should serve as a warning to industry that the FDA takes seriously its role to protect the public from unapproved drugs," said Deborah M. Autor, director of the Office of Compliance in FDA's Center for Drug Evaluation and Research. "Any company that operates in violation of the FDCA and ignores FDA's warnings should be aware that a criminal action could follow."

Forest Pharmaceuticals, Inc. also is charged with distribution of a misbranded drug for its off-label promotion of Celexa for pediatric use when it was approved only for use in adults. Celexa is the brand name for the prescription drug citalopram, a selective serotonin reuptake inhibitor (SSRI) drug for the treatment of adult depression. In addition, Forest Pharmaceuticals, Inc. also is charged with obstructing an agency proceeding because of false statements made by its employees during a 2003 FDA inspection.

Under the terms of the plea agreement, Forest Pharmaceuticals, Inc. will plead guilty to all three counts brought against the company and will pay criminal penalties totaling $164 million. The Department of Justice also announced that Forest Pharmaceuticals, Inc. and its parent company, Forest Laboratories, Inc., have agreed to pay $149 million and to enter into a Corporate Integrity Agreement with the Office of Inspector General of the U.S. Department of Health and Human Services in order to resolve a related civil complaint against the companies.

Consumers should be aware that the Levothroid product currently marketed by Forest Pharmaceuticals, Inc. is not the subject of today's actions. Forest Pharmaceutical's guilty plea and criminal penalties relate to the marketing of the previously unapproved Levothroid product. The current Levothroid product now has an approved New Drug Application and is compliant with FDA regulations.

**For more information:**

- 1997 Federal Register Notice[1]
- 2001 Federal Register Notice[2]
- 2001 Guidance for Industry on Levothyroxine Sodium Products[3]
- Warning Letter[4]

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**Links on this page:**

1. http://www.gpo.gov/fdsys/pkg/FR-1997-08-14/pdf/97-21575.pdf
2. http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2001_register&docid=01-17538-filed.pdf
3. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079807.pdf
4. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2003/ucm147641.htm