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RESEARCH**

APPLICATION NUMBER:

21-543

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-543

Columbia Laboratories, Inc.
Attention: Susan Witham
Vice President, Regulatory Affairs
220 South Orange Avenue
Second Floor
Livingston, NJ 07039

Dear Ms. Witham:

Please refer to your new drug application (NDA) dated August 7, 2002, received August 19, 2002 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Striant™ (testosterone buccal system) mucoadhesive.

We acknowledge receipt of your submissions dated August 15, 28, September 3 and 16, October 2, 9, 10, and 16 (2), November 13 (2), December 3 (2), and 11, 2002, March 18 and 31, April 3 (2), 11, 14, and 22, May 1 and 28, June 4 (2), 6, 9, 16, 17 and 18, 2003.

This new drug application provides for the use of Striant™ for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) – testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone levels and gonadotropins (FSH, LH) above the normal range.

Hypogonadotropic hypogonadism (congenital or acquired) — idiopathic gonadotropin or LHRH deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation. These patients have low serum testosterone levels but have gonadotropins in the normal or low range.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (package insert and patient package insert submitted June 17, 2003). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, designate this

submission "FPL for approved NDA 21-543." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment in your submission dated June 16, 2003. This commitment is listed below:

To continue ongoing studies COL 1621-08 (Europe) and COL 1621-09 (US) in order to accumulate a total of 50 patients with at least two years of continuous treatment on Striant™.

During the conduct of these trials you have agreed that if there is evidence of a gum lesion, the investigator will perform a biopsy or will refer the patient for biopsy. You have also agreed that the case report forms for this trial will include a special listing in regard to whether there was lack of adhesion of the buccal system.

DESCRIPTION

Protocol Submission:	Within two weeks of the date of this letter
Study Start:	Ongoing as of the date of this letter
Final Report Submission:	Within 15 to 18 months of the date of this letter

Submit clinical protocols to your IND for this product and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of the commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and number of patients entered into each study. All submissions, including supplements, relating to this postmarketing study commitment must be prominently labeled "Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations. The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

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In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division, the Division of Reproductive and Urologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Eufrecina DeGuia, Regulatory Health Project Manager at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug
Products; HFD-580
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure: Labeling

**This is a representation of an electronic record that was signed electronically and
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/s/

Daniel A. Shames
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