

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 77N-0240; DESI 1786]

Certain Single-Entity Coronary Vasodilators Containing Isosorbide Dinitrate; Withdrawal of Approval of Abbreviated New Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing conditional approval of 25 abbreviated new drug applications (ANDA's) for certain single-entity coronary vasodilator drug products containing isosorbide dinitrate. FDA is withdrawing approval because there is a lack of substantial evidence that these drugs are effective for their labeled indications relating to the treatment and prevention of anginal attacks. The sponsors of these conditionally approved products failed to provide required adequate bioavailability/bioequivalence data on the products to support full approval of the applications.

DATES: Effective August 7, 2000.

ADDRESSES: Requests for an opinion on the applicability of this notice to a specific product should be identified with Docket No. 77N-0240 and reference number DESI 1786 and directed to the Division of Prescription Drug Compliance and Surveillance (HFD-330), Center for Drug Evaluation and Research, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

FOR FURTHER INFORMATION CONTACT: Mary E. Catchings, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2041.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of March 22, 1999 (64 FR 13802), FDA published a notice offering an opportunity for a hearing (NOOH) on a proposal to withdraw approval of 25 conditionally-approved ANDA's. The proposal was based on a lack of adequate bioavailability/bioequivalence data to support a finding of substantial evidence of effectiveness as required by section 505(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(e)), 21 CFR 314.126, and 21 CFR part 320.

In response to the NOOH, Zeneca Pharmaceuticals requested a hearing for Sorbitrate Chewable Tablets (ANDA 86-

388) and Sorbitrate Oral Tablets (ANDA 88-074). Zeneca later withdrew its hearing request for these products. No other sponsor of the products listed in the March 22, 1999, NOOH requested a hearing. As stated in the NOOH, the failure of an applicant or any other person subject to the notice to request a hearing constitutes an election by that person not to use the opportunity for a hearing and a waiver of any contentions concerning the legal status of that person's drug product(s). Accordingly, this notice withdraws conditional approval of the following ANDA's:

1. ANDA 85-783; Isordil Chewable Tablets containing 10 milligrams (mg) of isosorbide dinitrate per tablet; Wyeth-Ayerst Laboratories, (formerly held by Ives Laboratories, Inc.), P.O. Box 8299, Philadelphia, PA 19101.

2. ANDA 86-045; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Bolar Pharmaceutical Co., Inc., 130 Lincoln St., Copiague, NY 11726.

3. ANDA 86-186; Isosorbide Dinitrate (controlled release, colored) Capsules containing 40 mg of the drug per capsule; Eon Labs Manufacturing, Inc. (formerly held by The Vitarine Co., Inc.), 227-15 North Conduit Ave., Laurelton, NY 11413.

4. ANDA 86-191; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Bolar.

5. ANDA 86-224; Isosorbide Dinitrate (controlled release) Tablets containing 40 mg of the drug per tablet; Geneva Pharmaceuticals, Inc. (formerly held by Cord Laboratories, Inc.), 2555 West Midway Blvd., P.O. Box 446, Broomfield, CO 80038-0446.

6. ANDA 86-362; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Bolar.

7. ANDA 86-388; Sorbitrate (chewable) Tablets containing 10 mg of isosorbide dinitrate per tablet; Zeneca Pharmaceuticals (formerly held by Stuart Pharmaceuticals), 1800 Concord Pike, Wilmington, DE 19897.

8. ANDA 86-788; Isosorbide Dinitrate (controlled release, green) Tablets containing 40 mg of the drug per tablet; Forest Laboratories, Inc., 919 Third Ave., New York, NY 10022.

9. ANDA 86-790; Isosorbide Dinitrate (controlled release, yellow) Tablets containing 40 mg of the drug per tablet; Forest.

10. ANDA 87-314; Isosorbide Dinitrate (chewable) Tablets containing 10 mg of the drug per tablet; D. M. Graham Laboratories, Inc., 58 Pearl St., P.O. Box P, Hobart, NY 13788.

11. ANDA 87-414; Isosorbide Dinitrate (controlled release, scarlet/clear) Capsules containing 40 mg of the drug per capsule; Eon Labs.

12. ANDA 87-461; Isosorbide Dinitrate (controlled release orange/clear) Capsules containing 40 mg of the drug per capsule; Eon Labs.

13. ANDA 87-477; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Ascot Hospital Pharmaceuticals, Inc., 8055 North Ridgeway Ave., Skokie, IL 60076.

14. ANDA 87-482; Isosorbide Dinitrate (controlled release) Tablets containing 40 mg of the drug per tablet; Ascot.

15. ANDA 87-507; Isosorbide Dinitrate (controlled release, white/amethyst) Capsules containing 40 mg of the drug per capsule; Eon Labs.

16. ANDA 87-558; Isosorbide Dinitrate (controlled release) Tablets containing 40 mg of the drug per tablet; Par Pharmaceutical, Inc., One Ram Ridge Rd., Spring Valley, NY 10977.

17. ANDA 87-680; Isosorbide Dinitrate (controlled release, white/clear) Capsules containing 40 mg of the drug; Eon Labs.

18. ANDA 87-694; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Vanguard Labs, Inc., P.O. Box 1268, Glasgow, KY 42142-1268.

19. ANDA 87-700; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Vanguard.

20. ANDA 88-074; Sorbitrate Tablets containing 20 mg of isosorbide dinitrate per tablet; Zeneca.

21. ANDA 88-428; Isosorbide Dinitrate (controlled release) Tablets containing 20 mg of the drug per tablet; Forest.

22. ANDA 88-589; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Barr Laboratories, Inc., Two Quaker Rd., P.O. Box 2900, Pomona, NY 10970-0519.

23. ANDA 88-590; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Barr.

24. ANDA 88-591; Isosorbide Dinitrate Tablets containing 20 mg of the drug per tablet; Barr.

25. ANDA 88-592; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Barr.

The effectiveness conclusions and conditions for marketing described in a notice published in the **Federal Register** of August 3, 1984 (49 FR 31151), also applied to the drug products described below. Although approval of these products was withdrawn previously based on the written requests of the applicants, who no longer market the products, this notice constitutes FDA's final conclusions on the effectiveness of these products.

1. NDA 17-226; Sorbitrate (controlled release) Tablets containing 40 mg isosorbide dinitrate per tablet; Zeneca.

2. ANDA 84-473; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Zenith Goldline Pharmaceuticals, 140 Legrand Ave., Northvale, NJ 07647.

3. ANDA 84-474; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Zenith Goldline.

4. ANDA 86-035; Isosorbide Dinitrate Tablets containing 10 mg of the drug per tablet; Zenith Goldline.

5. ANDA 86-044; Isosorbide Dinitrate Tablets, containing 10 mg of the drug per tablet; Circa Pharmaceuticals (formerly held by Bolar Pharmaceutical Co., Inc.), 15 Grand Park Blvd., Athens, OH 45701.

6. ANDA 86-048; Isosorbide Dinitrate Tablets containing 20 mg of the drug per tablet; Bolar.

7. ANDA 86-051; Isosorbide Dinitrate (controlled release) Tablets containing 40 mg of the drug per tablet; Bolar.

8. ANDA 86-071; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Chelsea Laboratories, Inc., 896 Orlando Ave., West Hempstead, NY 11552.

9. ANDA 86-072; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Chelsea.

10. ANDA 86-073; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Chelsea.

11. ANDA 86-078; Isosorbide Dinitrate Tablets containing 10 mg of the drug per tablet; Chelsea.

12. ANDA 86-302; Isosorbide Dinitrate Tablets containing 10 mg of the drug per tablet; Purepac Pharmaceutical Co., 200 Elmora Ave., Elizabeth, NJ 07207.

13. ANDA 86-304; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Purepac.

14. ANDA 86-855; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Lederle Laboratories, North Middletown Rd., Pearl River, NY 10965.

15. ANDA 86-858; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Lederle.

16. ANDA 86-861; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Lederle.

17. ANDA 86-862; Isosorbide Dinitrate Tablets containing 10 mg of the drug per tablet; Lederle.

18. ANDA 86-922; Isosorbide Dinitrate (sublingual) Tablet containing 5 mg of the drug per tablet; Par.

19. ANDA 86-924; Isosorbide Dinitrate (sublingual) Tablets containing 2.5 mg of the drug per tablet; Par.

20. ANDA 87-163; Isosorbide Dinitrate (chewable) Tablets containing

5 mg of the drug per tablet; D. M. Graham.

21. ANDA 87-344; Isosorbide Dinitrate (controlled release) Capsules containing 40 mg of the drug per capsule; Inwood Laboratories, Inc., 909 Third Ave., New York, NY 10022-4731.

22. ANDA 87-415; Isosorbide Dinitrate (controlled release, green/clear) Capsules containing 40 mg of the drug per capsule; Eon.

23. ANDA 87-469; Isosorbide Dinitrate (sublingual) Tablets containing 10 mg of the drug per tablet; Chelsea.

24. ANDA 87-474; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Ascot.

25. ANDA 87-475; Isosorbide Dinitrate Tablets containing 10 mg of the drug per tablet; Ascot.

26. ANDA 87-476; Isosorbide Dinitrate Tablets containing 20 mg of the drug per tablet; Ascot.

27. ANDA 87-478; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Ascot.

28. ANDA 87-486; Isosorbide Dinitrate (controlled release) Capsules containing 40 mg of the drug per capsule; Ascot.

29. ANDA 87-490; Isosorbide Dinitrate Tablets containing 20 mg of the drug per tablet; Chelsea.

30. ANDA 87-491; Isosorbide Dinitrate Tablets containing 30 mg of the drug per tablet; Chelsea.

31. ANDA 87-618; Isosorbide Dinitrate Tablets containing 10 mg of the drug per tablets; Vanguard.

32. ANDA 87-673; Isosorbide Dinitrate Tablets containing 5 mg of the drug per tablet; Vanguard.

33. ANDA 87-933; Isosorbide Dinitrate (sublingual) Tablets containing 10 mg of the drug per tablet; Par.

34. ANDA 88-005; Isosorbide Dinitrate (sublingual) Tablets containing 5 mg of the drug per tablet; Unit Dose Laboratories, 1718 Northrock Court, Rockford, IL 61103.

35. ANDA 88-006; Isosorbide Dinitrate (sublingual) Tablets containing 10 mg of the drug per tablet; Unit Dose Labs.

36. ANDA 88-123; Sorbitrate (sublingual) Tablets containing 10 mg of isosorbide dinitrate per tablet; Zeneca.

Any drug product that is identical, related, or similar to the drug products named above and is not the subject of an approved new drug application (NDA) is covered by the applications listed above and is subject to this notice (21 CFR 310.6). Any person who wishes to determine whether a specific product is covered by this notice should write to the Division of Prescription Drug Compliance and Surveillance (address above).

The Director of the Center for Drug Evaluation and Research, under the act (section 505) and under authority delegated to her (21 CFR 5.82), finds that, on the basis of new information on the drugs and the evidence available when the applications were approved, there is a lack of substantial evidence that the products named above will have the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

Therefore, based on the foregoing finding, approval of the applications listed above and all their amendments and supplements is withdrawn effective August 7, 2000. Shipment in interstate commerce of these products or of any identical, related, or similar product that is not the subject of a fully approved NDA will then be unlawful.

Dated: June 20, 2000.

Janet Woodcock,

Director, Center for Drug Evaluation and Research.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99D-2145]

International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH); Final Guidance on "Impurities in New Veterinary Medicinal Products" (VICH GL11); Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a final guidance for industry (#92) entitled "Impurities in New Veterinary Medicinal Products" (VICH GL11). This guidance document has been developed for veterinary use by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). The guidance is intended to assist in developing registration applications for approval of veterinary medicinal products submitted to the European Union, Japan, and the United States.

DATES: Submit written comments at any time.