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2553 '03 MAY 14 A9:02

May 12, 2003

BY FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20857

Re: Citizen Petition 03P-0160: Genpharm's Reply to Comments by L. Perrigo Company

Ladies /Gentlemen:

On behalf of our client Genpharm Inc. of Etobicoke, Ontario, Canada, we submit the following reply to the attached April 29, 2003 comments by L. Perrigo Company on Genpharm's Citizen Petition, filed April 16, 2003, requesting that FDA refuse to approve Perrigo's Section 505(b)(2) NDA for loratadine tablets, 10 mg. Genpharm requests that this reply be incorporated as part of its Citizen Petition.

1. FDA's Guidance Flatly Prohibits Approval of Perrigo's Duplicate Product Via a Section 505(b)(2) NDA

FDA's *Guidance for Industry: Applications Covered by Section 505(B)(2)* (October 1999) explicitly prohibits the approval of a duplicate of a previously approved drug under a Section 505(b)(2) NDA. (Genpharm's Citizen Petition, pp. 4-5).

Perrigo openly admits that its loratadine product is a duplicate of Claritin® brand of loratadine tablets, 10 mg. (Perrigo comments at 2, 4). Hence, Perrigo's loratadine product **must be approved** via an ANDA.

That Perrigo's application might have been deemed appropriately submitted as a 505(b)(2) application, because at the time Claritin® was available upon prescription only (Perrigo comments at 2), is beside the point. Since then, Claritin® has been switched to OTC status, and Perrigo's loratadine product is now identical in all respects to Claritin® tablets, 10 mg. As such, Perrigo's product can only be approved via the ANDA that Perrigo has also filed for the same product. (Genpharm's Petition, pp. 4, 5).

03P-0160 RC 1

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2. FDA's 505(b)(2) Approval of Alavert® Is Clearly Distinguishable

Perrigo's further contention that its loratadine product must be treated like Wyeth's Alavert®, which was approved under a 505(b)(2) NDA (Perrigo comments at 4) is plainly incorrect.

Wyeth's loratadine product is an **orally-disintegrating tablet**, which begins dissolving on the tongue and may be taken without water (see attached label and Wyeth release). This property, permitting absorption of Wyeth's loratadine product before it passes through the gut, is precisely the kind of significant difference from a previously approved drug that FDA directs be approved via a Section 505(b)(2) NDA. (FDA's 505(b)(2) Guidance at 2-6; Genpharm's Citizen Petition, pp.2-4). Wyeth evidently submitted additional studies to FDA demonstrating that its orally-disintegrating tablet is safe and effective, thereby warranting 505(b)(2) approval.

3. Any Court Decision Shortening Perrigo's 30-Month Stay Must Be Rendered in the Same Action Involving Perrigo's 505(b)(2) NDA

Perrigo's final argument -- that its 30-month stay was truncated by a separate decision of patent invalidity in a paragraph IV patent infringement action between Schering and Geneva -- does not withstand scrutiny.

As pointed out in Genpharm's Citizen Petition, the Hatch-Waxman Amendments and FDA regulations provide for a shortening of a 505(b)(2) applicant's 30-month stay only when there has been a decision of patent invalidity or non-infringement **in the paragraph IV action brought against the 505(b)(2) applicant.** (21 U.S.C. § 355(c)(3)(C)(i); 21 C.F.R. § 314.107(b)(3); Genpharm Petition, pp. 7-8).

The *Mylan v. Shalala* and *Mylan v. Henney* cases cited by Perrigo (comments at 6-7) are inapposite because (i) they involved ANDAs, not 505(b)(2) NDAs, and (ii) their holdings were directed to a triggering event for 180-day generic market exclusivity, not the shortening of a 30-month stay.

Similarly, FDA's March 2000 Guidance cited by Perrigo (comments at 7-8) is inapplicable, because (i) the guidance does not pertain to 505(b)(2) NDAs, and (ii) Perrigo misinterprets the guidance. FDA's statement in the March 2000 Guidance that the agency will henceforth interpret the term "court" to mean "the first court that renders a decision finding the patent at issue invalid, unenforceable or non-infringed" refers to the first court decision **in a particular paragraph IV action.** This is obvious not only from the statement itself, but from the Guidance as a whole, which clarifies the triggering-effect distinction between a district court decision and

which clarifies the triggering-effect distinction between a district court decision and an appellate court decision **in the same action**. Plainly, the above statement does not mean that a decision in another applicant's paragraph IV action which happens to be decided earlier can serve to shorten a given applicant's 30-month stay in its own action.

Finally, that certain courts may have determined 180-day exclusivity to be triggered by a decision in another paragraph IV action is certainly no basis for concluding that "a company should be able to obtain approval of its 505(b)(2) NDA or ANDA based upon a patent case in which it is not a party" (Perrigo comments at 8). This is wishful thinking on Perrigo's part. No court has ever held, and FDA has never ruled, that a 505(b)(2) applicant's 30-month stay can be ended by a decision in another applicant's case.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP

By_____
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Attorneys for Petitioner GENPHARM INC.

CJR/bav

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PERRIGO®

2336 '03 MAY -1 A9:12

April 30, 2003

Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20857

RE: Submission of Electronic Documents

To Whom It May Concern:

Please find attached one original and one copy of the document CP 03P-0160 (Comments On Citizen Petition Submitted by Genpharm Inc.) that was sent to the FDA by electronic submission on Tuesday, April 29, 2003.

If you have any questions regarding this material, please contact Brian R. Schuster by phone at 269-673-9745.

Best Regards,

Tricia Pasek

Tricia Pasek
RA, Administrative Assistant

Encl.

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April 29, 2003

2337 '03 MAY -1 A9:12

Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane
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Re: CP 03P-0160

COMMENTS ON CITIZEN PETITION SUBMITTED BY GENPHARM INC.

L. Perrigo Company ("Perrigo") submits the following response to the Citizen Petition submitted by Genpharm Inc. ("Genpharm") on April 15, 2003. The Genpharm petition asks that FDA refuse to approve Perrigo's 505(b)(2) new drug application ("NDA") for loratadine tablets, 10 mg.

Each of the reasons that Genpharm advances as a basis for its requested relief is either wrong or immaterial to the question of whether Perrigo's 505(b)(2) NDA should be approved.[1]

[1] Genpharm says in a footnote that a Perrigo communication about the status of the various loratadine applications "appears to constitute pre-approval promotion." Perrigo's communication was intended to shed light on the confusing regulatory issues surrounding the switch of Claritin from Rx to OTC and the various 505(b)(2) NDAs and ANDAs that had been submitted. Perrigo made no safety or effectiveness claims for its product that would raise questions of pre-approval promotion. As the attached "Loratadine Update" shows, Genpharm's marketing partner has disseminated materials that go beyond the referenced communication from Perrigo. Perrigo's communication was in direct response to the attached materials and was intended to correct inaccuracies therein.

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Genpharm contends that Perrigo's loratadine product may not be approved as a 505(b)(2) NDA because it is not sufficiently different, in Genpharm's view, from Claritin®, 10 mg. Therefore, Genpharm argues that Perrigo may only obtain approval of an abbreviated new drug application ("ANDA") rather than a 505(b)(2) NDA.

The simple answer is that there is no support in the statute, FDA's regulations or its 505(b)(2) guidance document (*Guidance for Industry: Applications Covered by Section 505(b)(2)*) for the proposition Genpharm advances. Section 505(b)(2) does not restrict the types of drug products for which an application may be submitted. Similarly, while the ANDA section of the law, § 505(j), does limit the types of products for which an ANDA may be submitted, it contains no corresponding limitation on those products which may properly be the subject of a 505(b)(2) NDA.

While FDA's regulations, 21 C.F.R. § 314.101(d)(9), and the 505(b)(2) guidance document do say that one may not submit a 505(b)(2) NDA for a product that is a duplicate of the listed drug and is eligible for approval under § 505(j), the facts of this case do not support the argument Genpharm advances. At the time Perrigo submitted its 505(b)(2) NDA for an over-the-counter ("OTC"), 10 mg. loratadine tablet product, the reference listed drug, Claritin®, was a prescription drug. Therefore, Perrigo could not have submitted an ANDA for an OTC 10 mg. loratadine product. As Genpharm is well aware, an ANDA drug must bear the same labeling as the reference listed drug. A prescription drug and an OTC drug cannot bear the same labeling. Moreover, the

505(b)(2) guidance document specifically says that a 505(b)(2) application may be submitted to change a prescription indication to an OTC indication.

The fact that FDA approved Schering-Plough's supplemental NDA to convert Claritin® from prescription to OTC status while Perrigo's 505(b)(2) NDA was pending does not change the fact that Perrigo's application was properly submitted as a 505(b)(2) NDA.

Genpharm conveniently ignores the fact that FDA has already approved Wyeth's 505(b)(2) NDA for Alavert, a 10 mg. orally disintegrating tablet version of loratadine. That 505(b)(2) NDA was approved on December 19, 2002 after FDA had already approved Schering's supplemental NDA to convert its orally disintegrating tablet to OTC status. Moreover, it is our understanding that Wyeth also has a pending ANDA for an orally disintegrating tablet.[2] If Genpharm's arguments had any legal merit -- which they do not -- FDA would not have been able to approve Wyeth's 505(b)(2) NDA.

[2] Indeed, a citizen petition has been filed by Andrx Pharmaceutical Inc. arguing that Wyeth's marketing of its 10 mg. orally disintegrating tablet under § 505(b)(2) constitutes commercial marketing of generic loratadine within the meaning of § 505(j)(5)(B)(iv)(I), therefore triggering Wyeth's exclusivity for its ANDA for the same product. While we take no position on the merits of Andrx's petition, it is a further example that Perrigo's 505(b)(2) NDA was properly filed.

Perrigo is in the same position as Wyeth. The only difference is that Perrigo is seeking approval for a tablet as opposed to an orally disintegrating tablet. FDA cannot treat Perrigo differently than it has treated Wyeth.

Genpharm makes much of Perrigo's supposed "motivation" for submitting a 505(b)(2) NDA. Those arguments are irrelevant. Perrigo submitted a 505(b)(2) NDA because that was a regulatory option available to it. Recent reports in the trade and lay press have indicated that the price of loratadine at the consumer level has remained high notwithstanding the switch of some loratadine products to OTC status. Approval of Perrigo's product will improve competition and result in lower costs to consumers.

Finally, Genpharm argues that even if Perrigo's 505(b)(2) NDA was properly submitted, FDA may not approve Perrigo's 505(b)(2) application until the end of the 30-month stay or a court decision of invalidity or non-infringement in an action brought by Schering against Perrigo. First, there has been a court decision in a patent case between Schering and Perrigo that satisfies the court decision requirement of the statute. Second, Genpharm's contention that a court decision must be one between Schering and Perrigo is not supported by FDA or the courts.

1. There is a Court Decision of Invalidity in a Paragraph IV Lawsuit Brought by Schering Against Perrigo.

As Genpharm is well aware, on August 8, 2002, Judge Bissell of the U.S. District Court for the District of New Jersey ruled that claims 1 and 3 of Schering's Patent No. 4,659,716 (the '716 patent) were invalid. Schering Corp. v. Geneva Pharmaceuticals, Inc., 64 U.S.P.Q. 2d 1032 (D.N.J. 2002). Subsequently, in a separate case brought by Schering against Perrigo as a result of Perrigo's paragraph IV certification in its ANDA for loratadine tablets, Judge Bissell issued an order finding claims 1 and 3 of the '716 patent invalid. See attached order of August 29, 2002. Therefore, there has been a court order of invalidity in a paragraph IV lawsuit brought by Schering against Perrigo.

Schering also brought another lawsuit against Perrigo as a consequence of Perrigo's 505(b)(2) NDA. That case was filed on December 2, 2002. In its complaint, a copy of which is attached, Schering acknowledged that the '716 patent had already been declared invalid in the earlier case against Perrigo but stated that it was filing this lawsuit "to preserve Schering's rights . . . ." (¶ 23). Schering also stated that the lawsuit should be stayed pending a ruling by the Federal Circuit in Schering's appeal in the Geneva case. Accordingly, Schering and Perrigo agreed to a stay which was signed by Judge Bissell on January 21, 2003, a copy of which is attached.

The stay in the 505(b)(2) case is predicated upon the incontrovertible fact that there is nothing to litigate between Schering and Perrigo. Perrigo already has obtained a

district court order finding that the '716 patent is invalid. If Schering sought now to relitigate that issue in the 505(b)(2) case, the complaint would be promptly dismissed on res judicata or collateral estoppel grounds. Therefore, similar to Teva Pharmaceuticals, USA, Inc. v. FDA, 182 F.3d 1003 (D.C. Cir. 1999) (dismissal on grounds of lack of subject matter jurisdiction equivalent to a court order of non-infringement), there is a court order of patent invalidity that requires FDA to approve Perrigo's 505(b)(2) NDA.

2. There is No Requirement for a Court Decision Between Schering and Perrigo

Even if there was not already a decision of invalidity in a case involving Schering and Perrigo, there is no such statutory requirement. Genpharm quotes 21 U.S.C. § 355(c)(3)(C)(i) and highlights the words "the court" and "the court decision." Genpharm argues that the use of the definite article "the" as opposed to the indefinite article "a" means that the only court decision that can terminate the 30-month period is a court decision involving Perrigo's 505(b)(2) NDA. The case law demonstrates that the word "the" does not carry the weight Genpharm would like it to.

In Mylan Pharmaceuticals, Inc. v. Shalala, 81 F. Supp. 2d 30 (D.D.C. 2000), Judge Roberts recognized that the "180-day exclusivity provision in clause (iv) of section 355 (j)(5)(B) must be read in conjunction with the 30-month stay provision in clause (iii). The regulation at issue recognizes this fundamental point by defining 'court' in precisely

the same way for both clauses."[3] Judge Roberts further noted that "[t]he chief linguistic difference between clause (iii) and clause (iv) is that the former refers to 'the court' while the latter refers to 'a court.'" Contrary to the weight Genpharm attaches to the word "the," Judge Roberts held that "[t]his difference is of no great moment in light of the interplay between the clauses."

After the Mylan decision and a second case also involving Mylan, Mylan Pharmaceuticals, Inc. v. Henney, 94 F. Supp. 2d 36 (D.D.C. 2000), FDA issued its court decision guidance document (*A Guidance for Industry: Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*). In that document FDA said that it "will interpret the term *court* as found in § 505(j)(5)(B)(iii)(I) [the approval provision for ANDAs] and 505(j)(5)(B)(4) [the 180-day exclusivity provision] to mean the first court that renders a decision finding the patent at issue invalid, unenforceable or non-infringed. When it is the district court that renders such a decision, FDA may approve the ANDA as of the date the district court enters its decision." As Genpharm notes, this guidance document does not specifically deal with 505(b)(2) applications, but there is absolutely no reason to apply a different meaning of the terms "court" or "court decision" for 505(b)(2) NDAs and ANDAs. Indeed, the definition of "court decision" that was challenged in the two Mylan cases and that was the subject of the court decision guidance

[3] Judge Roberts held that the regulation, 21 C.F.R. § 314.107(e), was invalid because it defined court to mean "the court that enters final judgment from which no appeal can be taken."

document was set forth in 21 C.F.R. § 314.107. The title of that regulation is: "Effective date of approval of a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act." Therefore, the definitions of "court" or "court decision" are the same for both ANDAs and 505(b)(2) NDAs.

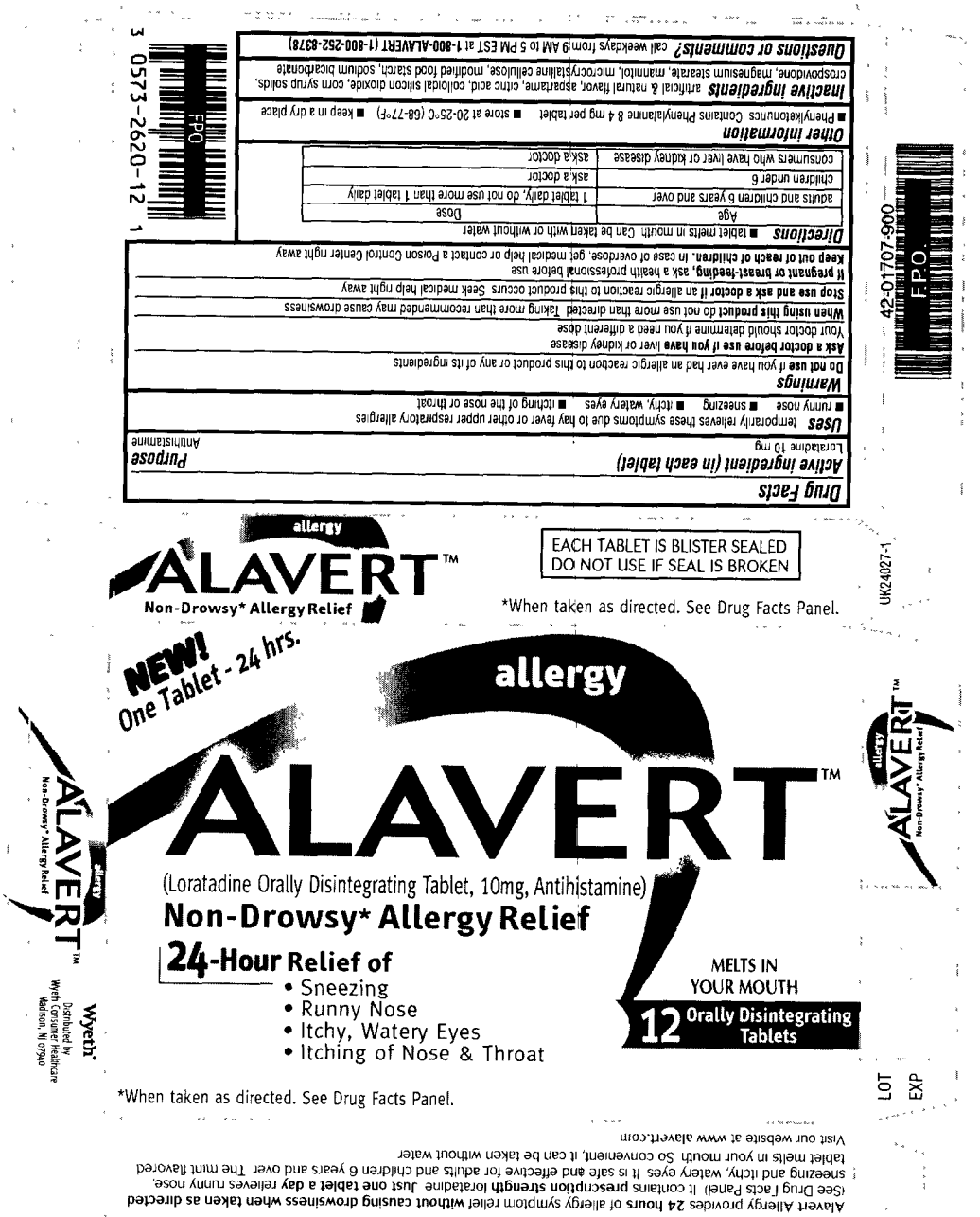
As FDA has long ruled, the 180-day exclusivity of a first ANDA filer can be triggered by a decision of non-infringement or invalidity in an unrelated patent case. That position has been upheld in the courts. Teva Pharmaceuticals USA, Inc. v. FDA, 182 F.3d 1003 (D.C. Cir. 1999); Minn. Mining and Mfg. Co. v. Barr Labs, Inc., 289 F.3d 775 (Fed. Cir. 2002). If an unrelated patent case triggers exclusivity and if "court" and "court decision" mean the same thing for approval and exclusivity purposes, a company should be able to obtain approval of its 505(b)(2) NDA or ANDA based upon a patent case in which it is not a party.

Therefore, the decision rendered by the district court in Schering v. Geneva Pharmaceuticals Inc. finding the relevant patent claims to be invalid is, by itself, a "court decision" that permits approval of Perrigo's 505(b)(2) NDA, notwithstanding the fact that the 30-month period has not run. Even if that was not the case, however, the district court's finding of invalidity in the Schering v. Perrigo ANDA case establishes beyond any doubt that the court decision requirement has been satisfied.

In conclusion, Genpharm's petition is nothing but a thinly veiled attempt to delay approval of Perrigo's 505(b)(2) NDA at the eleventh hour. FDA should reject the petition and promptly approve Perrigo's 505(b)(2) NDA.

Sincerely,

John R. Nichols
General Counsel, L. Perrigo Company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Warnings
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Ask a doctor before use if you have liver or kidney disease
Your doctor should determine if you need a different dose
When using this product do not use more than directed Taking more than recommended may cause drowsiness
Stop use and ask a doctor if an allergic reaction to this product occurs Seek medical help right away
If pregnant or breast-feeding, ask a health professional before use
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away
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Age
Dose
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1 tablet daily, do not use more than 1 tablet daily
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12/20/2002

Wyeth Consumer Healthcare Receives Final Approval For Over-The-Counter Loratadine; Alavert™ Shipments Will Begin Today

Madison, N.J., December 20, 2002 - Wyeth Consumer Healthcare announced today th the U. S. Food and Drug Administration (FDA) has granted final approval to the company's application for over-the-counter (OTC) Alavert(tm) (10mg loratadine orally disintegrating tablets). Wyeth Consumer Healthcare, a division of Wyeth (NYSE:WYE), will immediately begin shipping 12-, 24- and 48-count quantities of Alavert to retailers, grocery stores and pharmacies around the country. The company will begin shipping a six-count trial size package next week.

Alavert Provides Convenience and Value in One Package

One dose of Alavert offers non-drowsy, 24-hour allergy relief in a quick-dissolving form that can be taken with or without water.

Wyeth Consumer Healthcare's suggested retail price for a 48-count Alavert package is approximately $27, which equates to a cost of approximately 57 cents per tablet. This pricing offers consumers all of the benefits of non-drowsy, 24-hour allergy relief at 20 percent less than the current retail price per tablet of the other comparable OTC loratadi product that is being sold.

It is expected that a one-month supply of Alavert could cost consumers as little as $18, which compares favorably to the $15 - $20 co-payment that many consumers paid for loratadine when it was dispensed as a prescription.

In the future, the monthly cost of Alavert is expected to compare even more favorably to the possibly increased prescription co-payments that consumers may see in 2003 for other leading prescription non-sedating antihistamines.

Alavert - Brought to You By a Respected Leader in OTC Medications

Wyeth Consumer Healthcare currently markets many leading OTC brands that have become household names for millions of consumers, including Advil(r), Robitussin(r), Centrum(r), and Chap Stick(r). The company also conducted what is widely believed to be the "gold standard" for prescription to OTC switches when it brought Advil (ibuprofen) to the non-prescription market in 1984.

Wyeth Consumer Healthcare has also been a pioneer in making OTC loratadine availab to consumers, as it was the first company to submit an application to the FDA to have th orally disintegrating tablet form of loratadine switched from prescription to OTC status.

Alavert is the second loratadine product to be approved by the FDA for sale without a prescription.

Wyeth Consumer Healthcare

Wyeth Consumer Healthcare, a division of Wyeth, is one of the world's leaders in the development, manufacture and marketing of non-prescription medicines, vitamins and nutritional products including such established brands as Advil(r), Centrum(r), Chap Stick (r), Dimetapp(r) and Robitussin(r).

About Wyeth

Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing, and marketing of pharmaceuticals, vaccines, biotechnology products and non-prescription medicines that improve the quality of life for people worldwide. The Company's major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare and Fort Dodge Animal Health.

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