

Buchanan Ingersoll

ATTORNEYS

1776 K Street, N.W.
Suite 800
Washington, DC 20006-2365

T 202 452 7900
F 202 452 7989

www.buchananingersoll.com

HAND DELIVERY - RETURN RECEIPT REQUESTED

September 19, 2005

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

9644 05 SEP 19 04:57

CITIZEN PETITION

The undersigned, on behalf of Savient Pharmaceuticals, Inc., submits this petition in accordance with § 505(j) of the Federal Food, Drug and Cosmetic Act ("FFDCA")¹, as well as 21 C.F.R. §§10.20, 10.30, 320.32, and 320.33, requesting that the Commissioner of Food and Drugs verify the scope of Savient's three year exclusivity for geriatric dosing information and geriatric studies data for its Oxandrin® drug product. This verification requires that the Food and Drug Administration ("FDA") refuse to approve any Abbreviated New Drug Application ("ANDA") for generic oral products containing oxandrolone until the expiration of that exclusivity period on June 20, 2008.

Savient was recently granted a three-year period of market exclusivity under §505(j) of the FFDCA for changes to the labeling of its Oxandrin® drug product regarding use of lower initial dose of Oxandrin® in geriatric patients. These labeling changes were supported by data

¹ 21 U.S.C. §§ 201 et seq. (hereinafter all citations will be to the FFDCA).

2005P-0383

CPI

from clinical studies performed by Savient, and submitted to FDA in response to the Agency's initiative to obtain clinical data on drug effects in geriatric patients. The changes consist of revised dosing instructions for geriatric patients, as well as additional information in the clinical pharmacology section regarding the effects of Oxandrin® on the elderly. As mentioned in Savient's February 17, 2004 Citizen Petition² (concerning issues related to safety, drug interaction, and bioequivalence), geriatric patients comprise a significant portion of the total Oxandrin® patient population.³ In accordance with FFDCA § 505(j)(5)(F)(iv), no generic version of oxandrolone which contains the protected labeling changes may be approved during the three years of market exclusivity. The new precaution and dosing labeling information⁴ are essential to the safe use of the drug in geriatric patients, and any oxandrolone drug product lacking such labeling is presumed less safe for any indication where elderly patients may be expected to use the drug. FDA is prohibited from approving any ANDA where the generic drug product is less safe than the pioneer reference listed drug ("RLD"). Further, should FDA approve a generic version of oxandrolone, which lacks the necessary (and exclusive) geriatric dosing and safety information, the generic drug product will have less restrictive dosage information in its labeling when compared to Oxandrin®. This situation would result in the legally untenable situation where Savient's Oxandrin® drug product, with its statutory grant of three years of market exclusivity for important novel geriatric dosing information, would be at a disadvantage when compared to generic oxandrolone drug products that are prohibited from containing such labeling. The public would be at greater risk.

² Docket number 204P-0074.

³ "Approximately 40% of the Oxandrin® using population are patients in long term healthcare facilities. Most of this population consists of elderly patients." February 17, Citizen Petition, page 6.

⁴ The supplement to the Oxandrin® new drug application (number 013718) was approved on June 20, 2005.

Therefore, for reasons listed above, and more fully described in this petition, FDA may not approve any generic oxandrolone drug product that lacks Savient's protected geriatric dosage information.

A. ACTION REQUESTED

The Drug Price Competition and Patent Term Restoration Act of 1994 (the "Waxman-Hatch Amendments")⁵ created § 505(j) of the FDCA, which provides a sponsor with the opportunity to receive FDA approval to market a new drug that is the same⁶ as a previously approved drug without submitting substantial evidence of the drug product's safety and effectiveness. Instead, the ANDA mechanism relies upon the FDA's prior finding that the RLD is safe and effective and upon evidence to show that the ANDA is bioequivalent to the RLD. In order for a drug to be the "same" as the RLD, it must include labeling that is identical (with narrow exceptions) to that of the RLD. The FDCA specifically permits "changes required ... because the new [generic] drug and the listed drug are produced or distributed by different manufacturers."⁷ Additionally, FDA regulations allow the generic drug labeling to omit labeling information that is protected by grants of statutory market exclusivity⁸ *provided* that any omission does not render the generic drug product less safe than the RLD for any indications not protected by patent or exclusivity.⁹

The protected geriatric labeling for Oxandrin® is necessary for the safe use of the drug for its labeled indications, and therefore cannot be omitted from the labeling of any generic

⁵ Drug Price Competition and Patent Term Restoration Act of 1984, PL 98-417 (Sept. 24, 1984).

⁶ Statutory requirements for determining whether a drug is the "same" as a previously approved drug are found in FDCA § 505(j)(2)(A).

⁷ FDCA § 505(j)(2)(C).

⁸ 21 C.F.R. § 314.94(a)(8)(iv).

⁹ 21 C.F.R. § 314.127(a)(7).

oxandrolone drug product. As a result, no generic oxandrolone drug product may be approved until the expiration of Savient's exclusivity.

The grant of exclusivity periods for pioneer drugs is an important intellectual property right that was intended by Congress to reward innovative drug companies for developing new clinical data for pharmaceuticals, and to stimulate drug development.¹⁰ In many cases FDA has dramatically restricted the benefit of the exclusivity by approving generic drugs with labeling that contain all the labeling of the RLD's except that protected by the exclusivity. As a practical matter, complete substitution occurs in the marketplace despite the differences in labeling, and the benefit of the exclusive label indication has been vitiated.

However, the instant situation is unique. In response to a request from the Agency for data on the safe use of drugs in the elderly, who are subject to every indication for use for Oxandrin®, the company generated clinical data that led to unique labeling for safer drug use. This new labeling provides no market advantage, because it is actually more restrictive than the original label. If generic versions of oxandrolone are approved without Oxandrin's® protected geriatric labeling, such drugs would have labeling that is less restrictive and less safe than that of Oxandrin®, and Savient's protected (and the public's) interest in the Oxandrin® geriatric labeling would be directly harmed.

Therefore, we respectfully request that FDA verify the scope of Savient's three-year exclusivity period for the geriatric labeling for Savient's Oxandrin® drug product exclusivity, and take steps to ensure that this exclusivity is properly protected. No ANDA for a generic oxandrolone drug product can be approved until after the expiration of that exclusivity period.

¹⁰ H.R. Rep. 98-857.

Only such a decision is consistent with the statute and FDA's interpretation of the statute in specific prior decisions in analogous situations.¹¹

B. STATEMENT OF GROUNDS

I. Introduction

Oxandrin® is an oral tablet, which contains oxandrolone, USP as the active pharmaceutical ingredient ("API"), indicated as adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain weight or to maintain normal weight, to offset the protein catabolism associated with prolonged administration of corticosteroids, and for the relief of the bone pain frequently accompanying osteoporosis.

The product was developed and marketed by G.D. Searle and Co. (now Pfizer, Inc.) in the 1960s and has been marketed by Savient in 1995. Since then, Savient has undertaken an intensive development effort to ensure complete compliance with current regulatory and clinical requirements and initiatives including evaluation of clinical data on the use of the drug in geriatric patients. In 2004, Savient filed a Citizen Petition with FDA requesting that FDA determine specific bioequivalence requirements for generic oxandrolone drug products due to certain complex biochemical properties of the drug, and due to very significant interactions with the anti-coagulant drug product, warfarin.¹² That petition is still pending with FDA. The issues raised in that petition presented several potential safety issues with generic versions of

¹¹ See discussion of ribavirin and tramadol *infra*.

¹² Citizen Petition to FDA, February 17, 2004, docket number 2004P-0074.

oxandrolone, and several of those issues were either primarily related to elderly patients, or could be expected to have their greatest impact in that patient population (e.g. warfarin interaction, where elderly patients make up a significant portion of the at risk population). Those issues would be exacerbated should a generic oxandrolone be permitted on the market without the geriatric labeling information.

Savient was recently granted a three-year period of market exclusivity under s505(j) of the FDCA for changes to the labeling of its Oxandrin® drug product regarding use of Oxandrin® in geriatric patients. The labeling changes included additions to the clinical pharmacology section, a new geriatric use statement under the precautions section, and a new geriatric use statement under the dosing and administration section. The labeling change established a new lower and safer initial dose for geriatric patients. These changes were made based upon analysis of data from clinical studies of Oxandrin®. The labeling changes and supporting data were submitted to FDA in a supplement to NDA 013718, and that supplement was approved on June 20, 2005. FDA's approval of the supplement, which contained clinical data that was necessary for said approval, resulted in three years of market exclusivity for Oxandrin® during which no generic version of the drug containing the new geriatric precautions and dosing information may be approved by law.¹³ This precaution and dosing labeling information is essential to the safe use of the drug in geriatric patients, and any oxandrolone drug product lacking such labeling must be presumed less safe for any indication where elderly patients may be expected to use the drug. Significant use by the elderly is expected for all indications for Oxandrin®. As discussed below, under FDA regulations, generic drugs that have labeling which would make the drug less safe than the RLD cannot be approved

¹³ FDCA § 505(j)(5)(F)(iv).

II. Geriatric Studies

FDA has been evaluating the need for specific studies in the geriatric patient population for over a decade. In 1997, the Agency established the final rule for geriatric use labeling.¹⁴ This section established specific requirements for the geriatric labeling of pharmaceuticals, and it requires that approved products contain specific geriatric use information. The geriatric labeling requirement reflects a growing awareness in the medical/scientific community that the pharmacology of special patient populations are unique, and that these populations require special consideration in the drug development, review, and approval process. Concern for certain patient populations is evidenced by the special statutory and regulatory considerations for not only geriatric patients, but also in pediatric and in certain ethnic populations.

This increased attention to special patient populations, including geriatric patients, has resulted in specific regulatory initiatives such as regulation and guidance intended to enhance the safety and effectiveness of drugs intended for these patients. Savient's submission of clinical data and revised labeling for use of Oxandrin® in geriatric patients represents the company's response to FDA's initiatives to increase the clinical/scientific knowledge regarding use of drugs for elderly patients.

III. Market Exclusivity for Geriatric Labeling

Section 505(j)(5)(F)(iv) of the FDCA provides that if a supplement filed under § 505(b) contains reports of new clinical investigations essential to the approval of that supplement and that are conducted or sponsored by the drug sponsor, FDA may not approve any ANDA filed under § 505(j) that contains the change that was approved in the supplement:

¹⁴ 62 Fed. Reg. 45313, (August 27, 1997) found at 21 C.F.R. § 201.57(f)(10)

If a supplement to an application approved under subsection (b) is approved after the date of enactment of this subsection, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).

Savient was granted exclusivity under this section of the Act for supplement S-023 to NDA number 013718 for Oxandrin®. The supplement was approved on June 20, 2005.

Among other things, the supplement contained information from four clinical studies conducted with Oxandrin® in 339 patients, 172 of which were geriatric patients. These studies were the basis of changes to the labeling for Oxandrin®, including changes to the precautions as well as the dosing and administration sections. These changes are the following:

PRECAUTIONS

***Geriatric Use:** Oxandrin, at daily doses of 5 mg bid and 10 mg bid, was evaluated in four clinical trials involving a total of 339 patients with different underlying medical conditions. The maximum duration of treatment was 4 months with the average duration of treatment from 68.5 days to 94.7 days across the studies. A total of 172 elderly patients (≥ 65 years of age) received Oxandrin treatment. Mean weight gain was similar in those ≥ 65 and those < 65 years of age. No significant differences in efficacy were detected between the 5 mg bid and 10 mg bid daily doses. The adverse event profiles were similar between the two age groups although the elderly, particularly in women, had a greater*

sensitivity to fluid retention and increases in hepatic transaminases. A single dose pharmacokinetic study in elderly volunteers revealed an increased half-life when compared to younger volunteers. (see CLINICAL PHARMACOLOGY) Based on greater sensitivity to drug-induced fluid retention and transaminase elevations, a lower dose is recommended in the elderly (see DOSAGE AND ADMINISTRATION).

and:

DOSING AND ADMINISTRATION

Geriatric Use: *Recommended dose for geriatric patients is 5 mg bid.*

The clinical studies in Savient's supplement to NDA 013718 were necessary for approval of the new geriatric labeling, and in accordance with § 505(j)(5)(F)(iv), FDA granted Savient three years of market exclusivity for this new labeling. The labeling change involved more than merely a strengthening of warning or precautions. Such limited safety labeling changes of that type do not require a FDA pre-approval,¹⁵ and they are not eligible for market exclusivity under the FFDCA. For Oxandrin®, the change, while relating to safe use of the drug, involved a change to the drug's dosing regimen. This change, supported by clinical data, required pre-approval, and is of the sort that is eligible for the three-year exclusivity.¹⁶ Such a warning cannot be unilaterally added to the safety or precautions section of the drug's labeling.

¹⁵ 21 C.F.R. § 314.70(c).

¹⁶ The preamble to FDA's regulation on drug exclusivity states:

"FDA declines to define in the regulations the kinds of supplemental applications that, if supported by clinical investigations, would warrant 3-year exclusivity. Although the preamble to the proposed rule identified certain types of changes in a product that would normally warrant exclusivity (changes in active ingredient, strength, dosage form, route of administration, or conditions of use), the agency did not intend to suggest that other types of changes would not qualify. For example, changes in dosing regimen have resulted in grants of 3-year exclusivity. Changes that would not warrant exclusivity are, as discussed in the proposed rule, change in labeling that involve warnings

The Oxandrin® geriatric exclusivity expires on June 20, 2008, and it is published in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"). The code assigned to the exclusivity is M-42, which is defined as "addition of geriatric use subsection to the precautions section of the package insert and geriatric dosing information."

As a result of the granted exclusivity, no ANDA that uses Oxandrin® as a RLD may be approved with the new geriatric labeling until after June 20, 2008.

IV. Generic Drug Labeling Must be "the Same" as the Labeling for the RLD

The FDCA and FDA's implementing regulations require that ANDA's contain the "same" labeling as the RLD that they are copying. Nevertheless, certain allowances are made in the law for changes necessary for differences such as different manufacturer or distributor names, or for differences mandated by market exclusivity granted to the sponsor of the RLD. Section 505(j)(2)(C) required that ANDA's include "information to show that the labeling proposed for the new [generic] drug is the same as the labeling approved for the listed drug ... except for the changes required ... because the new [generic] drug and the listed drug are produced or distributed by different manufacturers." FDA expanded on this section of the FDCA in its implementing regulations, and specifically addresses changes from the label of the RLD that result from either patent protection or exclusivity granted under the FDCA. These regulations provide that the labeling for the RLD and the generic drug must be the same except for:

or other risk information that must be included in the labeling of generic competitors. Applicants obtaining approval for such changes in labeling would, in any event, have no valid interest in precluding such information from the labeling of other products." 59 Fed. Reg. 50388 (emphasis added).

*differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(4)(D) of the Act.*¹⁷

Thus, ANDA applicants are generally permitted to exclude from the labeling for their generic drug those labeling changes that are protected by exclusivity granted to the sponsor of the RLD. However, such omissions of exclusivity-protected labeling are only permitted where such changes do not render the generic drug product less safe than the RLD for any indications not protected by patent or exclusivity.¹⁸

This section of the regulations permits generic drug manufacturers to obtain approval of ANDA's where some indications of the RLD are protected by exclusivity. The generic drug applicant merely excludes those protected indications from its labeling. FDA and the courts have supported this "carving out" of protected indications on many occasions, so long as the carved out language does not "render the proposed drug product less safe or effective than the listed drug for all remaining, non-protected conditions of use."¹⁹

Although FDA recently reaffirmed this position with regard to carve outs in a response to a Citizen Petition from Valeant Pharmaceuticals Inc.,²⁰ the Agency's response established the inappropriateness of approving any ANDA for oxandrolone without the specific language for which Oxandrin® has been granted market exclusivity. In its petition, Valeant asserted that approval of any generic version of its Rebetol® (rebavirin) drug product would require removal

¹⁷ 21 C.F.R. § 314.94(a)(8)(iv).

¹⁸ 21 C.F.R. § 314.127(a)(7).

¹⁹ 21 C.F.R. § 314.127(a)(7).

²⁰ April 6, 2004 letter to docket number 2003P-0321.

of protected labeling that referred to combination use with the drug PEG-Intron®. FDA responded that removal of this language was appropriate for a generic drug, since there was another, non-protected, use for the drug, and that the removal of the protected language would not render the drug less safe for the other non-protected indication. In its response, FDA also stated (in support of the regulation discussed above) that it would not be permitted to approve an ANDA if omission of protected labeling language would result in the generic drug being less safe for the remaining indication. This precise situation exists with Oxandrin®.

Furthermore support for the proposition that FDA cannot approval an ANDA that carves out protected labeling information that is necessary for the safe use of the drug product is found in FDA's resolution of petitions by various generic drug manufacturers to obtain approval of generic versions of R.W. Johnson Pharmaceutical Research Institute's ("Johnson") tramadol hydrochloride drug products.²¹ In that situation, Johnson obtained exclusivity for new dosing regimens for its drug based on an escalating dose titration. The original dosage instructions for the drug did not provide for dose titration, but subsequent clinical investigations by Johnson resulted in two amendments to the labeling for escalating dose titration levels. The first change provided for increasing the drug dose by 50 mg per day, and the second provided for increasing the drug dose by 25 mg per day. At the time FDA responded to the petitions, the exclusivity period for the 50 mg dose titration regimen had expired. Nevertheless, FDA found that "the 10-day, 50 mg trial provided essential safety information that can and should remain in the labeling." Had any exclusivity remained for the 50 mg dose titration labeling, FDA would have been precluded from approving any ANDA for the drug until that exclusivity expired. In contrast, the 25 mg dose titration regimen (for which there was remaining exclusivity) was found

²¹ FDA docket numbers 02P-0252, 02P-0191, and 01P-0495.

by FDA to be unnecessary for the safe use of the drug, and thus, the Agency was permitted to approve ANDA's for the drug with the protected language removed.

FDA's position with regard to tramadol hydrochloride provides additional precedent for Savient's position that FDA is precluded from approving any ANDA for oxandrolone until the expiration of the exclusivity period for Oxandrin's® geriatric dosage information in June 2008. Therefore, FDA, through precedent established in the Citizen Petition process confirms the position set forth in its regulations, that it cannot approve an ANDA where omission of labeling information that is protected by exclusivity would result in a drug that is less safe for the labeled indications.

V. New Geriatric Labeling is Necessary for the Safe Use of the Drug

The oxandrolone situation is unique. Unlike Valeant's Rebetol® or other drugs where FDA has approved ANDA's that carve out or exclude labeling for indications protected by patent or exclusivity under the FDCA, the protected geriatric precaution and dosing labeling for Oxandrin® apply to all intended uses for the drug. This labeling is essential to the safe use of oxandrolone for all of the labeled indications when the drug is used in geriatric patients. Further, the instant situation is also distinguishable from the tramadol situation, where the new dosage regimen did not implicate drug safety or effectiveness. As noted in the company's February 17, 2004 Citizen Petition, geriatric patients constitute a very significant portion of the drug's patient population. Therefore, the drug cannot be safely used for any of its labeled indications unless the protected labeling is included. As a result, under the FDCA and FDA regulations, specifically 21 C.F.R. § 314.127, and FDA precedent, no ANDA for oxandrolone may be approved until the expiration of exclusivity for the geriatric precaution and dosing information on June 20, 2008.

Under the FDCA and its implementing regulations, a drug product is considered to be misbranded unless its labeling bears adequate directions for its safe and effective use.²² For prescription drugs, adequate directions for use requires, in part, that the labeling include dosage information and any relevant warnings or precautions for any labeled indication.²³ FDA has determined through rulemaking and guidance that geriatric use information can be fundamental to the safe use of pharmaceuticals, and in the case of oxandrolone, FDA has concluded that labeling changes for geriatric use precautions and dosing information were necessary for the safe and effective use of the drug for all labeled indications. As a result, oxandrolone drug products cannot be deemed to bear adequate directions for use for any indication without the approved geriatric precaution and dosing information.

Further support for the proposition that generic drugs must include the same geriatric labeling as the RLD is found in FDA guidance. As discussed under section 2 (Marketing Exclusivity for Geriatric Labeling), above, approved drugs have specific geriatric use labeling requirements, which are found at 21 C.F.R. § 201.57(10). In October of 2001, FDA issued specific guidance on this geriatric labeling.²⁴ In that guidance, FDA stated that ANDA applicants must include geriatric labeling that is based on the RLD's geriatric use section. Thus, FDA specifically refers to geriatric labeling as a section of ANDA labeling that is required to be "the same" as that of the RLD. FDA is required to follow its guidance in this matter.²⁵

Oxandrin® is indicated for use as an adjunctive therapy to promote weight gain after weight loss due to a variety of causes. A very significant number of patients who suffer such

²² FDCA § 502(f)(1).

²³ 21 C.F.R. § 201.200(d).

²⁴ Guidance for Industry - Content and Format for Geriatric Labeling - October 2001.

²⁵ See, Alaska Professional Hunters Association, Inc. v. Federal Aviation Administration, 177 F. 3d 1030 (D.C. Cir. 1999); Paralyzed Veterans of America v. D.C. Arena, 117 F.3d 579, 586 (D.C. Cir. 1997).

weight loss, and who are treated with Oxandrin® are geriatric patients. Savient's clinical data (which formed the basis for its exclusivity) with regard use of the drug in this patient population demonstrate that elderly patients do not metabolize the drug as quickly as do younger patients, and exhibit significantly increased fluid retention in response to the drug. Therefore geriatric patients require lower initial dose than do these younger patients, which is a vital safety issue.

The results of these data and the contents of the protected labeling provide a concrete example of the general understanding in the scientific and medical community that 1) geriatric patients have different pharmacological reactions to drugs, and 2) specific study data in this patient population are critical to safe use of pharmaceuticals. This requirement is particularly important for those drugs for which use by the elderly represent a significant segment of the intended patient population according to product labeling. The FDA's guidance on geriatric labeling supports this position by specifically requiring that ANDA's contain the same geriatric labeling as the RLD. FDA is required to follow its regulations and guidance, and there is no exception to this requirement for generic drug approval.

As noted above, geriatric dosage information is a required by regulation to be included in drug labeling.²⁶ In the preamble to the geriatric labeling regulation, FDA acknowledged (in agreement with the general medical community) that geriatric labeling is important to the safe use of prescription drugs. The preamble provides that:

This final rule furthers FDA efforts to promote safe and effective prescription drug use in the elderly by requiring that information on the safe and effective use of drugs in the

²⁶ 21 C.F.R. § 201.57(f)(10).

elderly be included in labeling, and by specifying a location and format for presenting this information.

According to FDA, geriatric labeling *must* include known information about geriatric use:

The final rule is intended to make geriatric labeling format and content more consistent by requiring that there be a "Geriatric use" statement in prescription drug labeling, that the statement reflect all information available to the sponsor that is relevant to the appropriate use of the drug in elderly patients ... The "Geriatric use" statement will give practitioners and others easier access to more information about prescription drug use in elderly patients.

Not only have FDA and the medical community become more aware of the differences in drug metabolism between different patient populations, the changing demographics of the United States and the significantly higher drug use among the elderly when compared to the general population increases the importance of including geriatric information where such information is available. Again, FDA acknowledged this in its preamble to the geriatric labeling regulations:

Geriatric labeling information is of increasing importance because of the growing proportion of the population that is over 65 years of age, and the significant use of medications by this age group. People over age 65 constitute only 12 percent of the U.S. population, but they consume over 30 percent of the prescription drug products sold in this country. The elderly are expected to constitute 22 percent of the U.S. population by the year 2030.

and;

Because older people take about three times as many prescription drugs as younger individuals and because taking several drugs together substantially increases the risk of drug interactions, unwanted effects, and adverse reactions labeling addressing this information should result in fewer adverse reactions. A number of studies have indicated that adverse drug reactions and patient noncompliance contribute to costly emergency room and hospital visits.

These statements in the preamble provide significant evidence that FDA intended geriatric labeling information, where available, to be a mandatory part of a drug's label. This is particularly true in situations, such as with oxandrolone, where, due to particular safety concerns, the dosage information for geriatric patients is different than that for younger patients.

VI. Approval of Generic Oxandrolone without Geriatric Labeling is Contrary to the Intent of the FDCA

The FDCA as amended by the Waxman-Hatch Amendments creates a carefully structured system of limited reward for innovative pharmaceutical companies. The act provides for five years of market exclusivity against generic competition upon approval of new drug applications ("NDA") for new chemical entities, and three years of market exclusivity upon approval of NDA's or NDA supplements where approval of that application requires clinical data. Once any exclusivity expires, generic drug companies are then permitted to rely upon the development work done by the pioneer drug companies, and obtain approval of their drugs

through the ANDA process. Congress, in drafting the Waxman-Hatch Amendments, sought to balance the intellectual property rights of the pioneer companies with the public interest lower cost pharmaceuticals. The system is intended to provide the pioneer drug company with the benefit of exclusivity as an incentive to create and improve pharmaceuticals, for the ultimate benefit of the public health. If generic oxandrolone drug products are permitted on the market prior to the expiration of Savient's exclusivity period for the Oxandrin® geriatric labeling (a valuable proprietary right), the careful system of limited incentive that was created by Congress will be turned on its head.

If a generic version of oxandrolone is approved without the necessary geriatric dosing and safety information, the result will be that the pioneer Oxandrin® drug product, that has been granted label exclusivity, will contain dosing information that provides limited dosing levels for the elderly, along with additional adverse event clinical data. Any generic oxandrolone will not have this information, and will be less restricted in its use by its label. This results in a legally and logically untenable situation where the generic drug is not only less safe than the pioneer, but where the generic has "better" or less restrictive labeling when compared to the pioneer Oxandrin® drug product. The statutory grant of three years of market exclusivity for labeling changes requiring clinical data was designed as an incentive for innovation. In Savient's unique situation, permitting a carve-out of the protected information would have the opposite effect.

C. CONCLUSION

The FDCA, as interpreted by case law and FDA regulations and precedent permit approval of generic drugs for certain indications that are not protected by patent or market

exclusivity. However, FDA regulations and guidance do not permit such an approval where the carve out of protected labeling language would potentially jeopardize the safety of a large segment of the intended patient population of the drug when used according to the labeled indications. Based on the requirement for the above referenced geriatric safety labeling, no generic oxandrolone drug product can be safely used without the protected geriatric labeling, and therefore, FDA is precluded under 21 C.F.R. § 314.127 and relevant guidance from approving any such generic version of oxandrolone. Further, in the instant situation, if generic versions of oxandrolone are approved without Oxandrin's® protected geriatric labeling, such drugs would have labeling that is less restrictive and less safe than that of Savient's pioneer drug product.

Therefore, in view of the precedents recited above, we respectfully request that FDA confirm that no ANDA for a generic oxandrolone can be approved until after the expiration of the geriatric labeling exclusivity granted to Oxandrin on June 20, 2005

D. ENVIRONMENTAL IMPACT

In accordance with 21 C.F.R. § 25.31(c), an environmental impact analysis is not required.

E. CERTIFICATION

The undersigned certified, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Edward John Allera

Signature 

Theodore Sullivan

Signature 

Counsel to Savient Pharmaceuticals, Inc.
Buchanan Ingersoll P.C.
1776 K Street, N.W.
Suite 800
Washington, DC 20006
Phone number: 202-452-7985