

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
200045Orig1s000

ENVIRONMENTAL ASSESSMENT

**Environmental Assessment
Finding of No Significant Impact**

NDA 200-045

**(b) (4) Tablets
(aliskiren/amlodipine/hydrochlorothiazide)**

**Food and Drug Administration
Center for Drug Evaluation and Research**

December 08, 2010

FINDING OF NO SIGNIFICANT IMPACT

NDA 200-045

(b) (4)

Tablets

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions. The Food and Drug Administration (FDA) is required under NEPA to consider the environmental impact of approving certain drug product applications as an integral part of the regulatory process.

NDA 200-045 requests approval for (b) (4) film-coated combination tablets (aliskiren/amlodipine/hydrochlorothiazide: 150/5/12.5 mg, 300/5/12.5 mg, 300/5/25 mg, 300/10/12.5 mg and 300/10/25 mg) for the treatment of hypertension. In support of the application, Novartis Pharmaceuticals Corporation prepared an environmental assessment (EA; attached) in accordance with 21 CFR Part 25, which evaluates the potential environmental impacts of aliskiren, amlodipine, and hydrochlorothiazide.

The Food and Drug Administration, Center for Drug Evaluation and Research, has carefully considered the potential environmental impact due to approval of this application and has concluded that this action is not expected to have a significant impact on the environment. Therefore, an environmental impact statement will not be prepared.

PREPARED BY:

Raanan A Bloom, Ph.D.
Senior Environmental Officer
Office of Pharmaceutical Science

CONCURRED BY:

Nakissa Sadrieh, Ph.D.
Associate Director for Research Policy and Implementation
Office of Pharmaceutical Science

CONCURRED BY:

Moheb Nasr, Ph.D.
Director, Office of New Drug Quality Assessment
Office of Pharmaceutical Science

Attachment: January 08, 2010, Environmental Assessment

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(CCI/TS) immediately following this page

Global Pharma Environment

Aliskiren / Amlodipine / Hydrochlorothiazide (SAH100)

150/5/12.5 mg, 300/5/12.5 mg, 300/5/25 mg, 300/10/12.5 mg
and 300/10/25 mg aliskiren/amlodipine/HCT
film-coated tablets

Aliskiren / Amlodipine / Hydrochlorothiazide_ABBR_EA

Environmental assessment

Authors: Hoeger B.
Date: 27-Jan-2010
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Property of Novartis

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(b) (4)

1 Date

08-Jan-2010

Aliskiren / Amlodipine /Hydrochlorothiazide New Drug Application (NDA)

Reference is also made to Environmental Assessment submitted to related aliskiren, amlodipine and Diovan HCT NDAs:

Tekturna Tablets, NDA 21-985

Original NDA submission: document dated 24-Jan-2006

Norvasc (amlodipine besylate) Tablets, NDA 19-787

Original NDA submission: approved 5-12-1995

Diovan HCT Tablet Original NDA 20-818:

Original NDA submission: approved 06-Mar-1998

All environmental fate and effects study reports for aliskiren, amlodipine and hydrochlorothiazide drug substances previously submitted in the Rasilez/Tekturna Tablet NDA 21-985, Pfizer's Norvasc (amlodipine besylate) Tablets Original NDA 19-787 (approved 5-12-1995) and Diovan HCT Tablet Original NDA 20-818 (submitted 18-Mar-1997; approved 06-Mar-1998), respectively and reviewed by the Agency have not been included in this assessment.

2 Name of applicant/petitioner

Novartis Pharmaceuticals Corporation

3 Address

One Health Plaza
East Hanover, NJ 07936-1080

4 Description of proposed action

4.1 Requested approval

Novartis has filed a new drug application pursuant to section 505b of the FD&C Act for aliskiren / amlodipine / hydrochlorothiazide fixed dose combination film-coated tablets. An Environmental Assessment (EA) is submitted pursuant to 21 CFR part 25.

4.2 Need for action

Aliskiren, amlodipine and hydrochlorothiazide (HCT) are currently approved separately in various dosage forms and strengths for the treatment of hypertension. This NDA provides for fixed combinations of aliskiren, amlodipine and HCT in the form of 150/5/12.5 mg, 300/5/12.5 mg, 300/5/25 mg, 300/10/12.5 mg and 300/10/25 mg aliskiren/amlodipine/HCT film-coated tablets. SAH100 is intended for the treatment of essential hypertension in adults. Approval of this submission is expected to benefit patients with hypertension whose blood pressure is not adequately controlled on monotherapy.

4.3 Locations of use

Patients with hypertension will use aliskiren / amlodipine / HCT film-coated tablets in their homes, in clinics and in hospitals.

4.4 Disposal sites

Hospitals, pharmacies and clinics will dispose of empty or partially empty packages of drug product according to their internal established procedures. In the home, empty or partially empty containers will typically be disposed of by the community's solid waste management system, which may include landfills, incineration and recycling. Minimal quantities of the unused drug may potentially be disposed of directly into the sewer system.

5 Identification of substances that are the subject of the proposed action

Aliskiren

5.1 Nomenclature

5.1.1 Established name (U.S. Adopted name – USAN)

Aliskiren hemifumarate

5.1.2 Brand/proprietary name/trade name

Rasilez[®]/Tekturna[®]

5.1.3 Chemical names

5.1.3.1 Chemical Abstracts Index name

Benzeneoctanamide, δ -amino-N-(3-amino-2,2-dimethyl-3-oxopropyl)- γ -hydroxy-4-methoxy-3-(3-methoxypropoxy)- α,ζ -bis(1-methylethyl)-, (α S, γ S, δ S, ζ S)- (E)-2-butenedioate (2:1) (salt)

5.1.3.2 Systematic chemical name (IUPAC)

(2S,4S,5S,7S)-5-Amino-4-hydroxy-2-isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy)-benzyl]-8-methyl-nonanoic acid (2-carbamoyl-2-methyl-propyl)-amide; ½ (E)-but-2-enedioic acid

5.1.4 Other names

SPP100, CGP60536B

5.2 Chemical Abstracts Service (CAS) registration number

173334-58-2 (hemifumarate)

173334-57-1 (free base)

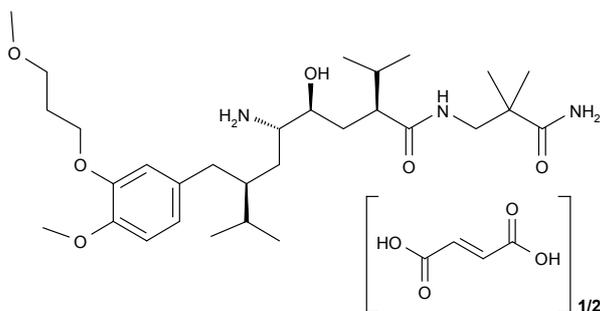
5.3 Molecular formula

$C_{30}H_{53}N_3O_6 \cdot 1/2 C_4 H_4 O_4$

5.4 Molecular weight

609.8 g/mol

5.5 Structural formula



Amlodipine

5.6 Nomenclature

5.6.1 Established name (U.S. Adopted Name – USAN)

Amlodipine besylate

5.6.2 Chemical name

5.6.2.1 Chemical Abstracts Index name

3-Ethyl 5-methyl 2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate benzenesulphonate

5.6.2.2 Systemic chemical name (IUPAC)

Benzenesulfonate 2-[4-(2-chloro-phenyl)-3-ethoxycarbonyl-5-methoxycarbonyl-6-methyl-1,4-dihydro-pyridin-2-ylmethoxy]-ethyl-ammonium

5.6.3 Other names

UK 48340-26

5.7 Chemical Abstract Service (CAS) registration number

111470-99-6

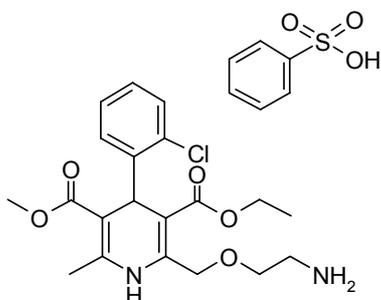
5.8 Molecular formula

C₂₀ H₂₅ Cl N₂ O₅ · C₆ H₆ O₃ S

5.9 Molecular weight

567.06 g/mol

5.10 Structural formula



Hydrochlorothiazide

5.11 Nomenclature

5.11.1 Established name (U.S. Adopted Name – USAN)

Hydrochlorthiazide

5.11.2 Trade name

Esidrix®

5.11.3 Chemical name

5.11.3.1 Chemical Abstracts Index name

2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-chloro-3,4-dihydro-1,1-dioxide

5.11.3.2 Systemic chemical name (IUPAC)

6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide

5.11.4 Other names

HCT

HCTZ

5.12 Chemical Abstract Service (CAS) registration number

58-93-5

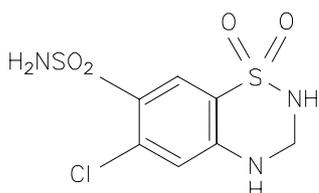
5.13 Molecular formula

C₇H₈N₃ClO₄S₂

5.14 Molecular weight

297.7 g/mol

5.15 Structural formula



6 Environmental issues

6.1 Physical and chemical characterization

Aliskiren hemifumarate

Based on its low log P [$\log K_{ow}$] value and very high water solubility, aliskiren hemifumarate is not expected to significantly bioconcentrate in living organisms (Table 4, Table 5). Henry's Law Constant was not determined, as aliskiren hemifumarate is not expected to be released into air or have a significant vapor pressure, based on its molecular weight and melting point

of > 95°C. The aliskiren hemifumarate information is summarized in Data Summary Table (Table 1) at the end of this report.

Amlodipine besylate

Based on its low log P [$\log K_{ow}$] value, amlodipine is not expected to significantly bioconcentrate in living organisms or to sorb to organic particles. Since the $\log K_{ow}$ was less than 3, no further sorption/desorption properties ($\log K_{oc}$) were considered. Amlodipine has been stated to display negligible vapour pressure and would thus not be expected to be released into the air.

Hydrochlorothiazide

Hydrochlorothiazide shows moderate solubility in water. Based on its low octanol-water partition coefficient [$\log K_{ow}$], HCT is not expected to bioconcentrate in aquatic organisms.

6.2 Environmental depletion mechanisms

Aliskiren hemifumarate

Environmental fate and effects study reports for Rasilez[®]/Tekturna[®] drug substance have been initially reported to the agency in aliskiren film-coated tablets Original NDA 21-985 (submitted 13-Feb-2006). This information has been previously submitted to and reviewed by the Agency, and is not included in the present assessment. The information is summarized in Data Summary Table (Table 1) located at the end of this report.

Aliskiren hemifumarate has been determined to be hydrolytically stable to 83% within forced decomposition testing conducted over a 3-day period in an aqueous medium at 100°C. Based on these results, a half-life of several months up to a year at 25°C was estimated. Aliskiren has not been found to be biodegradable to a significant extent. Based on the UV/VIS absorption spectra [Drug substance elucidation of structure and other characteristics, Module 3], no significant absorption was found above 290 nm for aliskiren. Hence photodegradation is not regarded as a significant source of depletion for this substance. Results are reported in the Data Summary Table (Table 1).

Based on the results of a batch equilibrium test, aliskiren shows moderate sorption to sludge and significant removal from the water phase during sewage treatment plant passage is therefore not expected.

Amlodipine besylate

Environmental fate and effects study reports for amlodipine drug substance have been initially reported to the agency in Pfizer's Norvasc (amlodipine besylate) Tablets Original NDA 19-787 (approved 5-12-1995) and numerous submitted and approved supplement NDAs (not listed individually). This information has been previously submitted to and reviewed by the

Agency, and is not included in the present assessment. The information is summarized in a Data Summary Table (Table 2) located at the end of this report.

Amlodipine is not readily biodegradable. It is not expected to bioaccumulate, based on its physico-chemical properties and its high susceptibility to oxidative metabolism in higher organisms [Module 2.5 Clinical Overview]. According to the original manufacturer, it has a tendency to sorb to sludge and sediments [Pfizer MSDS 2003]¹.

Based on the UV/VIS absorption spectra [Drug substance elucidation of structure and other characteristics, Module 3], significant absorption is seen above 290 nm for amlodipine and photolability has actually been found for this compound. Hydrolytically, amlodipine has been found to be stable at environmental pH [Abdoh et al. 2004]².

Hydrochlorothiazide

HCT is not readily biodegradable. Based on a batch equilibrium test, HCT shows low sorption to sludge and significant removal from the water phase during sewage treatment plant passage is therefore not expected.

6.3 Environmental concentration

6.3.1 Expected Introduction Concentration (EIC)

As described in the July 1998 Guidance for Industry: Environmental Assessment of Human Drugs and Biologics Applications³, the Expected Introduction Concentration (EIC) of an active moiety into the aquatic environment may be calculated as follows:

$$\text{EIC-Aquatic (ppb)} = A \times B \times C \times D$$

where:

A = kg / yr produced for direct use (as active moiety)

B = 1 / 1.214 x 10¹¹ liters per day entering POTWs [1996 Needs Survey, Report to Congress]

C = 1 year / 365 days per year

D = 10⁹ µg/kg (conversion factor)

The EIC of aliskiren, amlodipine and HCT have been calculated for the peak production year estimates of the drug substance requirements for all Novartis products containing aliskiren, amlodipine and HCT, including the new aliskiren / amlodipine / HCT formulations, and for all approved indications. An estimate of drug substance production requirements for the peak year (2015, 2010 and 2010, for aliskiren, amlodipine and HCT, respectively) is presented in [Confidential Appendix 11.2.1]. The calculated EICs for aliskiren, amlodipine and HCT are provided in [Confidential Appendix 11.2.2].

Novartis is confident that the actual EICs will not exceed these estimates by an order of magnitude.

As set forth in 21 CFR Part 25.31(b), action on an New Drug Application is categorically excluded from the requirement to prepare an Environmental Assessment or an Environmental Impact Statement if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be less than 1 part per billion (ppb). “Increased use”, as defined in 21 CFR Part 25.5(a), will occur if the drug is “administered at higher dosage levels, for longer duration or for different indications than were previously in effect, or if the drug is a new molecular entity.”

Novartis certifies that this submission for SAH100 film-coated tablets, for the treatment of hypertension qualifies for a categorical exclusion in accordance with 21 CFR Part 25.31(b) as the EICs of the active moiety amlodipine and hydrochlorothiazide will be less than 1 ppb.

Further, Novartis states that, to the best of its knowledge, no extraordinary circumstances exist which may significantly affect the quality of the human environment and would thus require the preparation of at least an Environmental Assessment for amlodipine and hydrochlorothiazide.

6.4 Summary

6.4.1 Aliskiren - aquatic environment

Studies were conducted to accurately determine the water solubility and partition coefficient of aliskiren hemifumarate. The results of the water solubility study indicate that aliskiren hemifumarate would be highly soluble in water over the environmental pH range. The n-octanol/water partition coefficient, which indicates the tendency of a non ionized organic chemical to accumulate in fatty tissue, suggests that aliskiren hemifumarate would not be expected to bioconcentrate substantially in aquatic organisms. The calculated results presented in [Table 4](#) and [Table 5](#) for the bioconcentration factor (BCF) support the conclusion that aliskiren hemifumarate would not be expected to bioconcentrate or bioaccumulate. A batch equilibrium test with aliskiren revealed moderate sorption of this API to sludges. Significant removal of aliskiren from the water phase during sewage treatment plant passage is therefore not expected.

Investigations of environmental depletion mechanisms demonstrated that aliskiren hemifumarate does not biodegrade or hydrolyze rapidly in the aquatic environment.

Five-year production estimates for aliskiren indicate that during the peak year, the EIC of aliskiren hemifumarate at the point of entry into the aquatic environment will be greater than 1 ppb. Novartis is confident that the actual EIC will not exceed these estimates by an order of magnitude.

Based upon these factors, the evaluation of the environmental effects of aliskiren hemifumarate was limited to the aquatic environment.

6.5 Environmental effects of released substances

Aliskiren hemifumarate

The environmental effects of aliskiren hemifumarate were evaluated in the aquatic environment following the “Tiered Approach to Fate and Effects Testing” (Figure 1, July 1998 EA Guidance for Industry³). Aliskiren did not show any inhibitory activity in microorganisms which may be found in activated sludge. Acute toxicity in the aquatic species tested was low with daphnia being the most sensitive species with an EC₅₀ of 56 mg/L. Results are reported in the Data Summary Table (Table 1).

6.5.1 Aliskiren assessment factor

As described in the July 1998 Guidance for Industry: Environmental Assessment of Human Drugs and Biologics Applications³, an assessment factor is a toxicity ratio which provides a consistent regulatory basis for determining if and when additional ecotoxicity testing should be performed, using a tiered approach. The assessment factor may be calculated by dividing an appropriate acute toxicity test endpoint by the MEEC (Maximum Expected Environmental Concentration). An assessment factor greater than 1000 would not require additional ecotoxicity testing.

6.5.1.1 Aliskiren - assessment factor

In the case of aliskiren, by applying the 48-hour EC₅₀ from the *Daphnia magna* immobilization study and the EIC from [Confidential Appendix 11.2.2], an assessment factor of 20'934 is obtained. (Calculation of the assessment factor is provided in [Confidential Appendix 11.2.3]). Thus, no additional ecotoxicity testing would be required for aliskiren. Since the assessment factor calculated for aliskiren is a magnitude greater than that reported in the Guidance Document, the results suggest aliskiren is unlikely to be toxic in the aquatic environment.

7 Mitigation measures

Based upon the information and data presented in this environmental assessment, Novartis has concluded that no potential adverse environmental impacts are anticipated with the packaging, distribution, use or disposal of aliskiren/amlodipine/HCT film-coated tablets within the United States. No mitigation measures are considered necessary.

8 Alternatives to the proposed action

No alternatives to the proposed action are suggested, as no potential adverse environmental impacts have been identified for the packaging, distribution, use or disposal of aliskiren/amlodipine/HCT film-coated tablets. The use of aliskiren/amlodipine/HCT film-coated tablets will directly benefit patients with hypertension.

It is our conclusion that approval of this application is therefore preferable to non-approval.

9 List of preparers

Curriculum vitae, documenting the qualifications and credentials of the contributors to this environmental assessment, are provided in [Non-confidential Appendix 11.1.1].

10 References

1. Pfizer MSDS 2003. Official Material Safety Data Sheet for Amlodipine besylate. Last Revision Date: Jan 31 2003.
2. Abdoh, A., Al-Omari, M.M., Badwan, A.A., Jaber, A.M.Y. 2004. Amlodipine Besylate–Excipients Interaction in Solid Dosage Form. *Pharmacol Dev Technol* 9: 15-24 (2004).
3. US Food and Drug Administration, Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), July 1998. Guidance for Industry: Environmental Assessment of Human Drugs and Biologics Applications. CMC 6, Revision 1.
4. Annex V to EU Directive 67/548/EEC, Part C. Available online at: <http://ecb.jrc.it/testing-methods/> (accessed January 2006).
5. Kumar, K.A., Ganguly, K., Mazumdar, K., Dutta, N.K., Dastidar, S.G., Chakrabarty, A.N. 2003. Amlodipine: a cardiovascular drug with powerful antimicrobial property. *Acta Microbiol Pol* 52: 285-92 (2003).
6. Kenaga, E.E., Goring, C.A.I., 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. *American Society for Testing and Materials Spec. Tech. Publ. 707, Aquat. Toxicol.*, pp. 78-115.

11 Appendices

11.1 Non-confidential appendices

[11.1.1] Curriculum vitae of contributor

11.2 Confidential appendices

(b) (4)

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Appendix 11.1.1 Curriculum vitae of the contributor

Birgit Hoeger, Ph.D.
Global Pharma Environment

Relevant Professional Experience

- 2006 - Environmental Risk Assessment Officer at Novartis Pharma AG.
- 2005-2006 Contractual Agent at the European Commission - Joint Research Centre, Ispra, Italy, European Centre for the Validation of Alternative Methods (ECVAM), Task Officer for Environmental Toxicology.
- 2004-2005 Postdoctoral student, Environmental Toxicology, University of Konstanz (Prof. Dr. D.R. Dietrich). Toxicological investigations on bioconcentration of human pharmaceuticals and their effects on the immune system in brown trout (*Salmo trutta f. fario*).

Education

- 2004 Ph.D. Biology (Environmental Toxicology) at the University of Konstanz, Germany (Prof. Dr. D.R. Dietrich). Effects of sewage treatment plant effluent on the immune system of rainbow trout (*Oncorhynchus mykiss*).
- 2000 Diplom in Biology, University of Konstanz, Germany.

Publications

- > 6 peer reviewed publications
- Co-author of several project reports and a book chapter on effects of pollution of the aquatic environment on the immuno-competence of fishes.

Professional Memberships

- SETAC (Society of Environmental Toxicology and Chemistry (2006 -)
- Reach Implementation Project 3.3-2, Endpoint Working Group 10 (Aquatic Bioaccumulation and Avian Toxicity) (2006 - 2007)

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/s/

RAANAN A BLOOM
12/08/2010

NAKISSA SADRIEH
12/08/2010

MOHEB M NASR
12/09/2010



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmaceutical Science/Immediate Office

Memorandum

Date: December 8, 2010

From: Raanan A. Bloom, Ph.D.
OPS/IO/SRS

To: Don Henry
OPS/ONDQA

Through: Nakissa Sadrieh, Ph.D.
OPS/IO/SRS

Subject: NDA 200-045 / (b) (4) Environmental Assessment Review

Submission Date: February 25, 2010

Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080

Background

An Environmental Assessment (EA) dated January 08, 2010, has been submitted for new drug application NDA 200-045 / (b) (4) film-coated tablets (aliskiren hemifumarate / amlodipine besylate / hydrochlorothiazide: 150/5/12.5 mg, 300/5/12.5 mg, 300/5/25 mg, 300/10/12.5 mg and 300/10/25 mg).

Review of the Current Submission

Aliskiren hemifumarate was previously approved for use in NDA 21-985 (Tekturna Tablets) 150 mg and 300 mg (Original NDA submission document dated 24-Jan-2006). An EA was submitted and reviewed and a FONSI issued April 27, 2006. All environmental fate and effects study reports for the drug substances were previously submitted and reviewed by the agency. Aliskiren, amlodipine and hydrochlorothiazide (HCT) are currently approved (see below) separately in various dosage forms and levels (including the levels provided for in this application) for the treatment of hypertension.

Tekturna: Aliskiren Hemifumarate NDA 021985

Tekamlo: Aliskiren Hemifumarate, Amlodipine Besylate NDA 022545

Tekturna HCT: Aliskiren Hemifumarate; Hydrochlorothiazide NDA 022107

No new information, except for changes in total estimated production values, are submitted with this application.

The total production value for direct use for aliskiren hemifumarate (all dosage forms sold by Novartis) under NDA 21-985 was estimated at (b) (4). The present submission provides a maximum estimate of (b) (4) aliskiren hemifumarate in 2015. The corresponding EIC values are (b) (4), respectively. Since there is no increase in the EIC or changes in toxicity parameters, the FONSI prepared for 21-985 is applicable to this submission.

Amlodipine and hydrochlorothiazide qualify for exclusions under 21CFR25.31(b). Provided toxicity information indicates that environmental impacts are not expected.

The following production and EIC values are provided in the EA:

Amlodipine (peak year 2010): production: (b) (4); EIC (aquatic) (b) (4).
Hydrochlorothiazide (peak year 2010): production: (b) (4); EIC (aquatic): (b) (4).

Cumulative Impacts

A cumulative impacts analysis considers environmental introductions from all drug product APIs under consideration in this application (NDAs, ANDAs and OTC, if applicable). IMS National Sales Perspectives data provides a listing of sales volumes by API.

Sales data:

Aliskiren: (b) (4) (Aliskiren is sold only by Novartis. Predicted production values are provided by Novartis)

Amlodipin: (b) (4) (IMS National Sales Perspectives)

Hydrochlorothiazide: (b) (4) 9 IMS National Sales Perspectives)

A literature search (environmental concentrations, fate and effects) was conducted.

Aliskiren:

No environmental information was located.

Amlodipine

No information on environmental concentrations was located.

A toxicity study evaluating effects of amlodipine was assessed using the cnidarian *Hydra vulgaris*. In a 7 day exposure period there were no effects on survival at concentrations up to 1.0 mg/L and after 17 days neither feeding nor bud formation were adversely

affected. The ability of dissected polyps to regenerate a hypostome, tentacles and foot was inhibited by amlodipine at 10ug/L.
(Chemosphere 51 (2003) 521–528)

Hydrochlorothiazide

Information on environmental concentrations was located

Po and Lambro rivers in Northern Italy: 0.53 - 255.80 ng/L
(Environ. Sci. Technol., 2003, 37 (7), pp 1241–1248)

WWTP effluent in Italy: 439.1 ng/l

(Journal of Hazardous Materials 122 (2005) 205–209)

WWTP primary effluent Spain: 2.3–4.8 ug/L

(Water Research 43 (2009) 831-841)

Ecotoxicity studies were not located.

Current available information does not indicate a need for preparation of a cumulative EA.

Comments and Conclusions

Based on FDA EA guidance and an evaluation of the information provided in this and previous EAs for [REDACTED]^{(b) (4)}, no adverse effects are expected from the introduction of aliskiren hemifumarate / amlodipine besylate / hydrochlorothiazide into the environment due to the use of [REDACTED]^{(b) (4)} tablets.

A Finding of No Significant Impact (FONSI) is recommended.

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RAANAN A BLOOM
12/08/2010

NAKISSA SADRIEH
12/08/2010