

Review of Proposed Proprietary Name - May 19, 2009 - Hiberix

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research
MEMORANDUM

Date:

May 19, 2009

From:

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OCBQ/DCM/APLB, HFM-602

Through:

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Through:

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To:

Jason Humbert, RPM, OVRP/DVRPA/CMC (HFM-481)
Jay Slater, M. D., Committee Chair, OVRP/DDBPAP (HFM-422)
Karen Farizo, M. D., Clinical Reviewer, OVRP/DVRPA/CRB1 (HFM-475)

Subject:

Review of Proposed Proprietary Name **HIBERIX**
[Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)]
BLA STN: 125347
Sponsor: Glaxo SmithKline
Recommendation:
Acceptable with Concerns

Executive Summary:

APLB recommends that the proposed proprietary name, **HIBERIX**, [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)], be found **Acceptable with Concerns**.

Background:

On March 17, 2009 Glaxo SmithKline (GSK) submitted BLA STN 125347 for Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate).

On March 31, 2009, the sponsor submitted a request for a review of the proposed proprietary name, HIBERIX, for review.

The PDUFA action date for the BLA for HIBERIX is August 1, 2009.

HIBERIX is a trademark developed by GlaxoSmithKline. The name HIBERIX represents components of the vaccine (Hib- for *Haemophilus influenzae* type b) combined with -rix

which is commonly used by GlaxoSmithKline's vaccine portfolio trademarks. HIBERIX is currently licensed in 98 countries worldwide and there have been no reports of safety concerns.

HIBERIX is proposed for active immunization as a booster dose for the prevention of invasive disease caused by *Haemophilus influenzae* type b (Hib) in children 15 months through 4 years of age (prior to fifth birthday). The booster dose is critical in boosting antibody titers and ensuring continued protection.

HIBERIX has the potential to provide an additional source of monovalent Hib vaccine to the US market for the booster dose in the current shortage to avoid break-through Hib disease.

There are currently two licensed *Haemophilus influenzae* type b vaccine products: ActHIB, *Haemophilus b* Conjugate Vaccine (Tetanus Toxoid Conjugate) vaccine combined with Sanofi Pasteur Inc. DTP vaccine by reconstitution is indicated for the active immunization of infants and children 2 through 18 months of age for the prevention of invasive disease caused by *H influenzae* type b and/or diphtheria, tetanus and pertussis.

PedvaxHIB, *Haemophilus b* Conjugate Vaccine (Meningococcal Protein Conjugate) for routine vaccination against invasive disease caused by *Haemophilus influenzae* type b in infants and children 2 to 71 months of age. Merck suspended production and the distribution is not expected before mid-2009.

GSK submitted the results of a study conducted by the -----b(4)-----, a subsidiary of ----b(4)----- conducted a Proprietary Name Analysis and a Proprietary Name Promotional Assessment which was completed in March 2009. -b(4)- concluded that when HIBERIX is compared to other product names, seven names were identified as potentially similar to Hiberix (e.g., Havrix, Hexabrix, Hibiclens, Hiprex, Iferex 150, Imitrex, and Niferex). Based on the -b(4)- analysis, no names were considered an apparent issue for the prescribing/ dispensing of HIBERIX. The Proprietary Name Promotional Assessment confirmed that HIBERIX is not promotional or misleading. APLB reviewed the -b(4)- report, which was included in the sponsor's request for a proprietary name review.

Overview of the Proposed Indication, Dosage Form, Dose, Administration, and Storage Information:

HIBERIX will be indicated for active immunizations as a booster dose for the prevention of invasive disease caused by *Haemophilus influenzae* type b (Hib) for use in children 15 months through 4 years of age (prior to fifth birthday).

HIBERIX is a sterile, lyophilized powder which is reconstituted at the time of use with the accompanying saline diluent. Each vial of lyophilized vaccine injection will contain 10 mcg of purified capsular polysaccharide (PRP) covalently bound to approximately 25 mcg tetanus toxoid (TT) and 12.6 lactose as a stabilizer to be reconstituted with the accompanying saline diluent supplied in prefilled syringes. HIBERIX 0.5 mL will be administered via intramuscular injection after reconstitution.

The lyophilized vaccine vials require refrigeration at temperatures between 2° and 8° C (35° and 46° F) and protected from light. The diluent requires refrigeration between 2° and 8° C (35° and 46° F) or at a controlled room temperature between 20° and 25° C (68° and 77° F) and should be discarded if frozen. The reconstituted product should be stored between -----b(4)-----

-b(4)- and should be used within 24 hours of reconstitution. HIBERIX should be discarded if frozen.

-b(4)- conducted a safety study with 150 healthcare professionals and identified eight proprietary names, Clarinex, Havrix, Heparin, Herplex, Hiprex, histineex HC, Imitrex, and Pediarix as having sound-alike, look-alike characteristics with HIBERIX. The -b(4)- Safety Evaluators. assessed the product profiles of these names compared to that of HIBERIX, and concluded that minimal overlapping drug profile characteristics were identified that would contribute to a medication error.

APLB completed an independent review of existing proprietary and established/proper names.

1. False or Misleading [21 U.S.C. section 321(n)]:

The proposed proprietary name, HIBERIX, is not regarded to be false or misleading.

2. Fanciful [21CFR 201.10 (c)(3)]:

The proposed proprietary name, HIBERIX, is not regarded to be fanciful.

3. Similarity in Spelling or Pronunciation [21 CFR 201.10 (c) (5)]:

HIBERIX may be confused with the proprietary names for other marketed products of similarity in spelling or pronunciation. Since drug products are prescribed through written, verbal, and /or electronic orders, similarity in spelling or pronunciation via such forms of communication may lead to medication errors. Even when proprietary names are only slightly similar, overlapping product characteristics may contribute to a greater potential for confusion.

APLB acknowledges that there is a minimal potential for medication error due to similarity in spelling and pronunciation between HIBERIX and other marketed products. Some of the marketed products whose names share many phonetic and orthographic similarities to HIBERIX include Havrix, Hexabrix, Hiprex, and Imitrex.

There is a slight potential for confusion with other GSK vaccines because they end in "rix": Boostrix, Fluarix, Engerix B, Havrix, Infanrix, Twinrix, Pediarix, and Kinrix but the beginnings of their proprietary names are not similar to HIBERIX.

APLB also considers the following risk factors to evaluate the degree to which HIBERIX may be of concern for medication errors:

Strength/Dose/Dosage Form/Route of Administration

Indications and/or Pharmacological-Therapeutic Categories

Marketing Status (prescription – RX or over-the-counter – OTC)

Storage Location (room temperature or refrigerator)

Products are listed in the table below from the highest to lowest potential for causing a medication error.

Proprietary name (established/proper name)	Dosage Form	Dose & Administration	Indication	RX/OTC	Storage	Potential for medication error
HIBERIX [Haemophilus b Conjugate Vaccine	IM injection (lyophilized vaccine vial with saline	Single 0.5 mL dose IM	Active immunization as a booster dose for the prevention of invasive disease	RX	Lyophilized vials refrigerator	N/A

Proprietary name (established/ proper name)	Dosage Form	Dose & Administration	Indication	RX/OTC	Storage	Potential for medication error
(Tetanus Toxoid Conjugate)]	diluent in prefilled syringe		caused by Haemophilus influenzae type b (Hib) in children 15 months through 4 years of age.		and protect from light	
Havrix Hepatitis A Virus Vaccine	Suspension for IM injection in vials & syringes	Children & Adolescents 0.5mL and 0.5 mL booster dose administered between 6 & 12 months later. Adults: 1 mL dose and 1mL booster dose between 6 & 12 months later.	Active immunization against hepatitis A for persons ≥ 12 months of age.	RX	Refrigerator	Moderate
Hexabrix ioxaglate meglumine and ioxaglate sodium	Solution for IV injection	5-15 mL	Pediatric angiocardiology; arteriography; angiography; venography; urography; arthrography; hysteroqram	RX	Below 30°C (86) Do not freeze	low
Imitrex sumatriptan succinate	Subcutaneous injection Tablet Intranasal spray	Injection 6 mg/day; oral 25-200mg/day nasal 5-40 mg/day	treatment of migraine attacks with or without aura and 2) cluster headaches	RX	Refrigerator and protect from light	low
Hiprex methenamine hippurate	tablet	1 g twice daily	Urinary tract infections prophylaxis	RX	Room temperature	low

When the product profiles of the above products were compared to that of HIBERIX, overlapping characteristics were identified that were regarded as an issue for prescribing/ dispensing of HIBERIX.

Havrix and HIBERIX have a similar sound alike and look-alike characteristics and overlapping product characteristics. Both products are IM injectable products and are stored in the refrigerator. Both products are indicated as immunization for children, HIBERIX for haemophilus vaccine in children 15 months through 4 years of age and Havrix for hepatitis for hepatitis A for persons 12 months of age and older. There is a

potential risk of medication error, i.e., a child could receive a hepatitis immunization instead of a haemophilus vaccine booster dose at 15 months through 4 years of age, thereby decreasing the child's continued Haemophilus protection. Therefore, the risk of medication error is moderate. We recommend that packaging for **HIBERIX** be distinct from Havrix to help mitigate the potential for confusion between these products. Hexabrix and Imitrex have a similar sound like and look alike characteristic and are injectable products, however the dosage and administration schedule and indications are not similar to HIBERIX. Therefore the risk of medication error is low. In addition, Hexabrix has a different storage condition than HIBERIX. Hiprex has similar sound like and look alike characteristics with HIBERIX. However, HIBERIX but does not have any overlapping product characteristics with Hiprex. Therefore, the risk of medication error is low.

In conclusion, HIBERIX has similar sound alike and look-alike characteristics and overlapping product characteristics with Havrix and therefore appears to be at risk for medications errors.

The Office of Biostatistics and Epidemiology/Division of Epidemiology/Vaccine Safety Branch provided VAERS reports of ActHIB and PedvaxHIB errors. In the last 5 years, there have been 10 reports of Havrix, Comvax, Pneumovax, Infanrix, and Vaqta being administered instead of Pedvax HIB.

Recommendations:

APLB recommends that the proposed proprietary name HIBERIX be found Acceptable with Concerns. There is a potential risk that HIBERIX and Havrix may be mixed up, thereby causing medication errors. Therefore, we recommend that the HIBERIX packaging be sufficiently distinct from Havrix to avoid medication errors.

If OVRB accepts our recommendation that the proposed proprietary name HIBERIX be found acceptable with concerns, please include the following text in your letter to the manufacturer:

In consultation with CBER's Advertising and Promotional Labeling Branch (APLB), we have considered your proposed proprietary name HIBERIX and conclude that under 21 CFR Part 201 the proposed proprietary name is acceptable with concerns. There is a potential risk for medication errors with Havrix, however, these risks may be minimized by providing packaging that will differentiate HIBERIX from Havrix.

If you have any questions with regards to this review, please contact Maryann Gallagher, Consumer Safety Officer at 301-827-3028.

References:

- Acronymfinder.com (<http://www.acronymfinder.com>)
- MediLexicon (<http://www.medilexicon.com/>)
- CBER product website (<http://www.fda.gov/cber/products.htm>)
- Drugs @ FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)
- DailyMed (<http://dailymed.nlm.nih.gov/dailymed/about.cfm>)
- PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) (<http://cdspoca.cder.fda.gov/POCA/default.aspx>)
- Drug Facts and Comparisons
- Micromedex Integrated Index (<http://csi.micromedex.com/fraMain.asp?Mnu=0>)
- RxList (<http://www.rxlist.com/script/main/hp.asp>)
- The Orange Book (<http://www.fda.gov/cder/ob/>)

- USAN Adopted Names (<http://www.ama-assn.org/ama/pub/category/2956.html>)
- CDRH Medical Device Approvals website (<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/MDA/mda-list.cfm?list=1>)
- Internet search engines (e.g., Google, Dog Pile)
- USP Dictionary Online
- Medical dictionaries
- Physicians Desk Reference
- United States Patent and Trademark Office (<http://www.uspto.gov>)
- VAERS
- Linguistics folder in APLB eRoom
 - Firm name: Glaxo Smithkline