CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125011

PROPRIETARY NAME REVIEW(S)

MEMORANDUM

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

Date: June 4, 2003

From: Nancy Chamberlin, PharmD., CSO
Advertising and Promotional Labeling Branch (HFM-602)
Division of Case Management

Through: Glenn N. Byrd, MBA, RAC, Chief, Advertising & Promotional Labeling Branch (HFM-602)

Through: Mary A. Malarkey, Director
Division of Case Management (HFM-610)

To: Terrye Zaremba, Ph.D., Primary Reviewer, DMA/OTRR, (HFM-596)
Karen Jones, RPM, DARP/OTRR, (HFM-588)

Subject: Updated Review of Proposed Proprietary Name **BEXXAR**
BLA 125011

Recommendation: Proposed proprietary name "**BEXXAR**" Acceptable With Concerns

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Executive Summary:

APLB recommends that the proposed proprietary name "**BEXXAR**" is Acceptable with Concerns.

Background:

Corixa Corporation submitted an amendment to their BB-IND 3323 on September 24, 2002, requesting a review of the proposed proprietary name "**BEXXAR**" by the FDA Center for Biologics Evaluation and Research (CBER) Office of Therapeutics Research and Review and APLB. That review was completed on January 27, 2003, and recommended that Bexxar was Acceptable with Concerns (review memo attached).

APLB was recently requested to re-review the proprietary name because substantial time had past since our last review and to ensure that our review was within 90 days of approval.

Conclusion:

No recently approved products whose names resemble **BEXXAR** were found; therefore, there are no new risks for medication error beyond those identified in our previous review of January 27, 2003.

*The following references were used:

1. 2002 American Drug Index.
2. 2003 Physicians' Desk Reference.
3. http://www.fda.gov/cder/ob/default.htm (Electronic Orange Book).
4. http://www.rxlist.com.(RxList).
5. http://www.fda.gov/cder/approval/index.htm (CDER New and Generic Drug Approvals: 1998 to 2002). Also, looked at CBER New BLA, NDA and ANDA approvals lists ending June 1, 2003.
6. https://www.factsandcomparisons.com/efacts.asp (Drug Facts and Comparisons)
7. http://www.ama-assn.org (American Medical Association Website-Newly Approved USAN stems through April 14, 2003

Firm name: Corixa Corporation.

Letter type: Memorandum

Bcc: HFM-602
HFM-602
HFM-610
HFM-610
HFM-99

N. Chamberlin
G. Byrd
M. Malarkey
DCM Files
DCC
APLB Proprietary Name File

History:
Prepared by: N. Chamberlin 6/3/03
Comments by G Byrd: 6/4/03
Reviewed by M Malarkey:
Finalized by: N. Chamberlin 6/4/03

File name: Bex2name.rev (P030114001)

Concurrence box:

MailCode or Office	Name	Date
602	[signature]	6/4/03
602	[signature]	6/4/03
610	[signature]	6/4/03

MailCode or Office	Name	Date

APLB file

MEMORANDUM

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

Date: January 27, 2003

From: Nancy Chamberlin, Pharm.D., Regulatory Review Officer,
Advertising and Promotional Labeling Branch (HFM-602)
Division of Case Management

Through: Glenn N. Byrd, MBA, RAC, Chief, Advertising and Promotional Labeling Branch
(HFM-602)

Through: Mary A. Malarkey, Director
Division of Case Management (HFM-610)

To: Terrye Zaremba, Ph.D., Primary Reviewer, DMA/OTRR, (HFM-596)
Karen Jones, RPM, DARP/OTRR, (HFM-588)

Subject: Review of Proposed Proprietary Name **BEXXAR**
BB-IND 3323, Amendment No.625
BLA 125011

Recommendation: Acceptable With Concerns

Executive Summary:

Proprietary name review has recently come under the scrutiny of the FDA Office of Chief Counsel (OCC) due to significant concerns associated with the potential infringement on 1st Amendment constitutional rights when disapproving proposed names. In December 2002, a meeting was held with OCC, CBER, and CDER participants to discuss this issue. One of the messages received by CBER and CDER at this meeting was that in order to

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In consideration of the potential 1st Amendment concerns associated with evaluating the proposed proprietary name **BEXXAR**, the Advertising and Promotional Labeling Branch (APLB) recommends that the proprietary name **BEXXAR** be found *acceptable with concerns*. There

appears to be a risk for a medication error of **BEXXAR** with proprietary names for other marketed products (**Bextra, Benicar,** and **Bexarotene**) taking into account similarity in spelling, pronunciation, handwriting, marketing status, and safety concerns. This risk may be reduced due to the differences in the dosage form, dosing interval, route of administration, and limited distribution of the radiolabeled **BEXXAR** products to commercial or hospital radiopharmacy locations. However, the unlabeled **BEXXAR** products may be shipped anywhere and given in hospital or in clinics which may increase the risk of a mix-up with these products.

In addition, there are 4 products with the proposed **BEXXAR** proprietary name: **BEXXAR D** and **BEXXAR T** which are labeled radioisotopes, and **BEXXAR QS** and **BEXXAR N** which are unlabeled (not radioactive) products. A potential for medication errors exists between these products. With the addition of suffixes (single letter) to the **BEXXAR** proprietary name, the wrong **BEXXAR** product may be dispensed due to confusion in hearing or reading the medication orders, interpreting which product is given at a particular sequence in the regimen, misreading the labeling, and storage of the products resulting in a medication error.

Background:

Corixa Corporation submitted an amendment to their BB-IND 3323 on September 24, 2002, requesting a review of the proposed proprietary name "**BEXXAR**" by the FDA Center for Biologics Evaluation and Research (CBER) Office of Therapeutics Research and Review and APLB.

The approved USAN name is tositumomab for the therapeutic **BEXXAR** package containing unlabeled ("cold") Anti-B1 antibody and labeled antibody with iodine I^{131} (hot) Anti-B1 antibody.

Since the initial APLB review of the proprietary name, **BEXXAR** has continued to be under development and a other products with similar names have been approved for marketing in the interim. In addition, it is noted that a review of this name was conducted in February 2002; however, the concerns raised herein were not identified at that time.

Chronological History :

- January 6, 1999, APLB reviewed the proposed proprietary name **BEXXAR** and regarded the proposed name to be acceptable.
- January 29, 1999, Agency issued an acceptability letter to Corixa for the **BEXXAR** proprietary name.
- 1999, Corixa submitted a BLA that was classified as refuse to file.
- December 29, 1999, **Bexarotene** capsule approved
- May 15, 2000, APLB reviewed the proposal for proprietary name change to add suffixes to **BEXXAR** and determined that it was acceptable with concerns.
- June 28, 2000, **Bexarotene** topical gel approved

- September 15, 2000, Corixa submitted BLA 125011 with clinical trials in the phase III stage.
- September 21, 2001, Corixa submitted a request for another review of the proposed **BEXXAR** proprietary name.
- November 16, 2001, **Bextra** approved
- February 11, 2002, APLB reviewed the proposed proprietary name **BEXXAR** and issued a memo to OTRR with a recommendation of acceptable with concerns.
- April 25, 2002, **Benicar** approved
- September 24, 2002, Corixa requested another review of the proposed proprietary name "**BEXXAR**" and in this submission they explained their limited distribution procedure for the radiolabeled product to distribution only to commercial or hospital radiopharmacy. However, the unlabeled products would not have limited distribution.

The BB-IND 3323 for "**BEXXAR**" was originally submitted for the treatment of relapsed/refractory low grade or follicular B-Cell non-Hodgkin's Lymphoma. The BLA is currently under review.

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

The proposed indication for "**BEXXAR**" is for the treatment of patients with relapsed or refractory low-grade or transformed low-grade, CD20-positive, B-cell non-Hodgkin's lymphoma (NHL). The dosages for "**BEXXAR**" are individualized and therapy consists of a combination of base monoclonal antibody and radiolabeled monoclonal antibody therapy. The unlabeled first dose may be administered by IV infusion in the doctor's office, clinic or hospital setting. However, qualified staff in nuclear/radio-oncology or hospital settings must administer the radio-labeled **BEXXAR** products by IV infusions. There are four injectable products with the proposed **BEXXAR** proprietary name, **BEXXAR D**, and **BEXXAR T** are radio-labeled products in glass vials within lead pots stored in the freezer and **BEXXAR QS** and **BEXXAR N** are unradio-labeled (cold) products that are injectable solutions in glass vials stored in the refrigerator.

Proposed Proprietary Name Evaluation

1) **False or Misleading [21 CFR 201.6 (a)]:**
The proposed proprietary name **BEXXAR** is not regarded to be false or misleading.

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

The proposed proprietary name **BEXXAR** is not regarded to be fanciful. It does not appear to imply that the drug or ingredient has some unique effectiveness or composition beyond that supported by the data.

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

BEXXAR may be confused with the proprietary name or the established name of a different marketed drug product because of similarity in spelling or pronunciation. Since, drug products are prescribed through written, verbal, and /or electronic orders, such forms of communication may lead to medication errors, particularly if proprietary and /or established names sound or look alike. Even when proprietary names are only slightly similar, overlapping product characteristics may create a greater potential for confusion. The names are listed in the table below from the highest to lowest potential for causing a medication error.

APLB also has concern with similar letters in the first part of a proprietary or established name because the prescriber's handwriting may become less legible at the end of the name making these names undistinguishable with sound-alike, look-alike names for products that already exist in the U.S. marketplace. Such names include **Benicar, Bextra,** and **Bexarotene.**

- There are four products with the proposed **BEXXAR** proprietary name: **BEXXAR N,** which is unlabeled product and is used for the first dose; **BEXXAR D,** which is labeled and used for the dosimetric dose; **BEXXAR T,** which is labeled and used for the therapeutic dose; and **BEXXAR QS,** which is unlabeled and not given directly to the patient but used to adjust the therapeutic dose. The term "qs" has been used in pharmacy compounding practices to mean for "a sufficient quantity" and the sponsor intends for the **BEXXAR QS** product to be used to adjust the dose of **BEXXAR D** and **BEXXAR T.** Due to these products having the same root name and modified only by a single letter suffix there is the potential for dispensing errors between these products due to misinterpretation of handwritten or verbal medication orders.
- **BEXXAR** is spelled and sounds similar to **Bextra** since both names begin with the "bex" and even though the ends of the names, "xar" in **BEXXAR** and "tra" in **Bextra** are different, both products contain 2 syllables there appears to be a potential for medication error between **BEXXAR** and **BEXTRA** due to the similar spelling and pronunciation of these names.
- **BEXXAR** is spelled and sounds similar to **Benicar** since both names begin with "Be" and end with "xar" and "car". Even though **BEXXAR** contains 2 syllables while **Benicar** is 3 syllables there is a potential for medication error due to similarity in spelling and pronunciation.
- **BEXXAR** sounds similar to **Bexarotene** since both names begin with the "bex". However, the "xar" in **BEXXAR** and "**arotene**" in **Bexarotene** are very different. **BEXXAR** contains 2 syllables while **Bexarotene** is 4 syllables so there may be a lesser potential for medication error.
- **BEXXAR** ending "xar" sounds similar to "XR" which is a suffix for extended

release products such as: Effexor XR, Adderal XR, Voltaren XR, Dilacor XR, Tegretol XR and Glucophage XR. However, these products have different spelling and pronunciation and have more syllables than **BEXXAR.** Therefore, the potential for medication errors with these products is low.

Proprietary Name	Dosage Form	Rx / OTC	Dose & Administration	Indication	Storage	Potential
BEXXAR (tositumomab and iodine I^{131} tositumomab) is a combination of base monoclonal antibody and radiolabeled monoclonal antibody	For Injection: 4 different products (see below)	Rx	Individualized: Given as 4 intravenous infusions. First give unlabeled BEXXAR N, then labeled dosimetric dose of BEXXAR D, followed 7-14 days later by another dose of BEXXAR N and labeled therapeutic dose of BEXXAR T	Non-Hodgkin's Lymphoma	I^{131} labeled product is stored in freezer (– °C), while unlabeled product is stored in the refrigerator	N/A
BEXXAR QS (tositumomab)	35mg/ 3 ml in glass vial	Rx	2.5mL vial of unlabeled tositumomab to adjust the amount of tositumomab in BEXXAR D and BEXXAR T	Non-Hodgkin's Lymphoma	Refrig.	High
BEXXAR N (tositumomab)	225mg/ 16.1 ml in glass vial	Rx	450 mg of unlabeled tositumomab given IV	Non-Hodgkin's Lymphoma	Refrig.	High
BEXXAR D (I^{131} tositumomab)	Dosimetric **lead pot** with activity concentration: not less than 0.61 mCi/ mL; Tositumomab : not less than 0.1 mg/mL; volume not less than 20 mL	Rx	Recommended dosimetric dose of 35 mg tositumomab Labeled with 5 mCi of I^{131} Tositumomab given iv. Then followed by gamma scans 1 hour after completion of dose and 2, 3 or 4 days; and 6 or 7 days after the	Non-Hodgkin's Lymphoma	Frozen (– °C)	High

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Proprietary Name	Dosage Form	Rx / OTC	Dose & Administration	Indication	Storage	Potential
			BEXXAR D dose. Dose is individualized based on total body residence time, patient's mass and height.			
BEXXAR T (I^{131} tositumomab)	Therapeutic **lead pot** with activity conc. Not less than 5.6 mCi/mL; Tositumomab : not less than 1.1 mg/mL; volume not less than 20 mL	Rx	Recommended dose: 35 mg tositumomab Labeled with an appropriate amount of activity (mCi) of I^{131} Tositumomab given iv to deliver 75 cGY. (Specified total body radiation dose is individualized by platelet count and lean body weight)	Non-Hodgkin's Lymphoma	Frozen (— °C)	High
Bextra (valdecoxib) Approved 11/01	Tablets: 10 and 20 mg	Rx	Osteoarthritis and rheumatoid arthritis: 10 mg once daily; Primary dysmenorrhea: 20 mg twice daily, as needed	Relief of the signs and symptoms of osteoarthritis and rheumatoid arthritis. Treatment of primary dysmenorrhea	Room temp	Medium
Benicar (olmesartan medoxomil) Approved 4/02	Tablets: 5, 20 and 40 mg	Rx	Dosage is individualized. The usual starting dose is 20 mg once daily with or without food when used as monotherapy in patients who are not volume-contracted. For patients requiring further reduction in blood pressure after 2 weeks of	Treatment of hypertension	Room temp	Medium

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Proprietary Name	Dosage Form	Rx / OTC	Dose & Administration	Indication	Storage	Potential
			therapy, the dose may be increased to 40 mg.			
Bexarotene *established name* for Targretin Approved 6/00	Topical: 1% Gel	Rx	Initially apply sufficient gel to cover the lesion once every other day for the first week. Increase the application frequency at weekly intervals to once daily, then twice daily, then 3 times daily, and finally 4 times daily according to individual lesion tolerance. Use as long as deriving a benefit.	Cutaneous T-cell lymphoma (CTCL) lesions that are refractory to other therapies	Room temp	Medium
Bexarotene *established* for Targretin Approved 12/99	Capsule: 75 mg	Rx	Initial dose: 300 $mg/m^2/day$ adjusted for body surface area as a single oral daily dose with a meal. Increase 8 weeks later if a response to $400mg/m^2/day$ if tolerated or decrease dose.	Cutaneous T-cell lymphoma (CTCL) lesions that are refractory to other therapies	2 to 25°C	Medium
BuSpar (buspirone)	Tablets: 5, 10, 15, 30 mg	Rx	Initial dose: 15 mg daily (5 mg 3 times a day) & increase by 5mg at 2-3 day intervals if needed. Not to exceed 60 mg/ day.	Management of anxiety disorders	Room temp	Low

Proprietary Name	Dosage Form	Rx / OTC	Dose & Administration	Indication	Storage	Potential
Effexor (venlafaxine)	Tablets 25, 37.5, 50, 75, 100 mg	Rx	Starting dose 75mg/day administered in 2 or 3 divided doses, taken with food. May increase dose at 4 to 7 day intervals up to a maximum of 375 mg/day, generally in 3 divided doses. To discontinue therapy taper off over 2 weeks.	Treatment of depression.	Room temp	Low
Effexor XR (venlafaxine)	Capsules, extended release: 37.5mg, 75, and 150mg	Rx	Starting dose 75mg/day administered in 2 or 3 divided doses, taken with food. May increase dose at 4 to 7 day intervals up to a maximum of 275 mg/day, generally in 3 divided doses. To discontinue therapy taper off over 2 weeks.	Treatment of generalized anxiety disorder .	Room temp	Low

The following risk factors should also be considered when evaluating the degree to which **BEXXAR** may be of concern for medication errors:

Strength:

Two different products with similar or identical strengths and with proprietary names that sound or look alike could be more easily confused than two products with very different strengths. The risk of confusion increases substantially if two products with similar proprietary names have identical strengths and dosing intervals.

The **BEXXAR** regimen consists of four different **BEXXAR** products. The non-radiolabeled injectable liquid products are supplied as 35mg/ ~mL l (**BEXXAR QS**) and 225mg/ 16.1 ml **(BEXXAR N).** The frozen radiolabeled products are supplied with activity concentration: not less than 0.61 mCi/ mL, Tositumomab: not less than 0.1 mg/mL, volume not less than 20 mL **(BEXXAR D);** and with activity concentration of not less than 5.6 mCi/mL, Tositumomab: not less than 1.1 mg/mL; volume not less than 20 mL **(BEXXAR T).**

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Bextra is supplied as 10 mg and 20 mg tablets, while **Benicar** is supplied as 5 mg, 20 mg and 40 mg tablets. **Bexarotene** is supplied as 1% topical gel and as a 75 mg capsule. These strengths are different from **BEXXAR**. Therefore, the risk of possible confusion of these marketed products with **BEXXAR** due to strength is negligible.

Dosing Interval/Dosage Form/Route of Administration:

The risk of a medication error is increased when products with similar proprietary names are dosed or prescribed in an identical manner (i.e., once a day). In addition, there is evidence that medication errors can occur even between different dosage forms (capsule vs. injection) and between products with similar routes of administration when similar proprietary names exist.

BEXXAR QS is supplied as an injectable liquid in glass vials, and **BEXXAR N** as injectable liquid in glass vials for intravenous infusion. **BEXXAR D** and **BEXXAR T** are supplied as frozen, labeled injectable dosage forms in glass vials in lead pots. The first unlabeled dose may be given in the doctor's office, hospital, or radiation oncology facility. While the subsequent doses administered in a hospital, freestanding nuclear medicine or radiation oncology facility.

The regimen consists of 4 different intravenous infusions utilizing the various **BEXXAR** products. On the first day of therapy the patient receives an infusion of **BEXXAR N** which consists of 450 mg of unlabeled tositumomab diluted in 50 mL of 0.9% Sodium Chloride Injection, USP and infused over 1 hours. Followed by the **BEXXAR D** dose of 35 mg of tositumomab containing 5mCi of I-131 tositumomab diluted to a final volume of 30 mL with 0.9% Sodium chloride Injection, USP and infused over 20 minutes. Then 7 to 14 days later the patient receives another **BEXXAR N** dose infused over 1 hour, followed by the patient specific dose of **BEXXAR T** as 35 mg of tositumomab containing 5mCi of I-131 tositumomab diluted to a final volume of 30 mL of 0.9% Sodium Chloride Injection, USP and infused over 20 minutes. While **BEXXAR QS** is not given directly to the patient, it is used to adjust the amount of tositumomab in **BEXXAR D** and **BEXXAR T**.

Bextra is supplied as oral tablets. The dose and dosing interval for **Bextra** is 10 mg once a day in osteoarthritis and adult rheumatoid arthritis, and 20 mg twice daily if needed in primary dysmenorrhea. It may be administered in the hospital or outpatient settings.

Benicar is supplied as oral tablets. The dose and dosing interval for **Benicar** is individualized, with a starting dose of 20 mg once daily with or without food when used as monotherapy in patients who are not volume-depleted. For patients requiring further reduction in blood pressure after 2 weeks of therapy, the dose may be increased to 40 mg. It may be administered in the hospital or outpatient settings.

Bexarotene is supplied as topical gel and as a capsule. The dosage for the topical **Bexarotene** is cover the lesions once every other day for the first week and increase the application frequency at weekly intervals to once daily, then twice daily, then 3 times daily, and finally 4 times daily according to individual lesion tolerance. While the oral dose and dosing interval

for **Bexarotene** capsules is initially 300 mg/m^2/day as a single oral daily dose with a meal and decrease or increase this dose in 8 weeks later if a response up to 400mg/m^2/day.

The dosing interval, dosage form, dose, and route of administration for **BEXXAR, Bextra, Benicar**, and **Bexarotene** are very different; therefore, the risk of medication error might appear to be minimized. However, since these medications may be administered together in inpatient and outpatient settings the potential for medication errors does exist.

In addition, the four products with the proposed **BEXXAR** proprietary name, **BEXXAR D, BEXXAR T, BEXXAR QS,** and **BEXXAR N**, could be confused with each other and the marketed products. A potential for medication errors in verbal and written medication orders, interpreting the dose, resulting in administration of the wrong dose and product exists with these products by adding suffixes (single letter) to the **BEXXAR** proprietary name.

Marketing Status:
Two products with similar proprietary names that are in the same marketing arena (e.g., prescription drug products) could more easily be confused than two products with similar names in different markets (one Rx and the other OTC).

The unradiolabeled **BEXXAR** products, **Benicar, Bextra and Bexarotene** will be readily available by prescription; therefore the potential for medication errors does exist due to marketing status. The labeled **BEXXAR products** will be available by prescription to radiopharmacy/hospitals on a limited distribution and administered by qualified staff in a hospital or nuclear/radio-oncology setting, thus minimizing the risks for error.

Indications and/or Pharmacological-Therapeutic Categories:

The proposed indication for **BEXXAR** is for the treatment of B-Cell non-Hodgkin's Lymphoma. **Bexarotene** is used in oncology patients for treatment of topical cutaneous T-cell lymphoma lesions. The other products in the chart above do not have similar indications or similar pharmacological/ therapeutic category as **BEXXAR.**

However, different indications will not decrease the risk of confusion since the intended use or indication is not routinely written on a prescription or medication order, and the patient may have more than one pre-existing illness/ disease state (i.e. cardiac disease, arthritis, and cancer). Therefore, the possibility of a medication error exists between the various **BEXXAR** products and **Bextra, Benicar,** and **Bexarotene** if a verbal or written order is received for **BEXXAR.**

Storage Location:

The use of a different storage location (i.e., refrigerator vs. room temperature, oral dosage form location vs. intravenous dosage form location) for two different products with similar names does not significantly decrease the risk of wrong product selection by the health care professional. Therefore, the use of different storage locations for drugs with names that look or sound alike may not mitigate the potential risk of medication errors.

BEXXAR QS and **BEXXAR N** are stored in glass vials in the refrigerator (without the

radioactive warning label). While **BEXXAR D** and **BEXXAR T** are I^{131} products stored in lead pots frozen at [redacted]°C with a radioactive material warning label. The sponsor proposed to have a limited distribution for the radioactive labeled **BEXXAR** products; however, any pharmacy may order the unlabeled (non-radioactive) **BEXXAR** products. b(4)

Bextra and **Benicar** are stored at room temperature. **Bexarotene** topical gel is stored at room temperature; however, the capsule is stored at 2 to 25°C (refrigerator and room temperature). Therefore, the potential for medication errors with the **BEXXAR** products due to storage exists but the risks are minimal.

Packaging and Labeling:

When the container labels, carton labeling, and/ or packaging is similar for two different drug products with similar proprietary names, the risk for confusion with similar proprietary names is increased.

The packaging labeling of the marketed products **Benicar, Bextra** and **Bexarotene** was not available therefore the risk of confusion due to packaging labeling could not be ascertained. The draft packaging, carton and container labeling for the BEXXAR products dated March 16, 2000 titled as final vender prep were provided. The non-radiolabeled products, **BEXXAR QS** is supplied as injectable liquid in [redacted] mL glass vials in cartons of [redacted] vials and **BEXXAR N** is supplied as 20 mL glass vials in single cartons ([redacted]. While **BEXXAR D** and **BEXXAR T** are I^{131} products supplied in single use vials frozen in lead pots with a [redacted] b(4)

A significant risk for medication errors or confusion with the four **BEXXAR** products exists. Safety considerations should be addressed in designing and reviewing the labels with the **BEXXAR** products to try to prevent dispensing errors and at the appropriate sequence in the therapy.

Safety Concerns:

The sponsor for **BEXXAR** did not conduct drug interaction studies, so it is difficult to predict if **BEXXAR** and **Bextra** could be safely administered simultaneously in an oncology patient that might have arthritis. However, due to the serious life-threatening nature of the potential adverse events that might occur from incorrect product administration, the sponsor should ensure that all steps should be taken to educate caregivers and/or alter the planned distribution scheme to prevent incorrect dispensing of these sound alike name products.

Recommendations:

APLB recommends that the proposed proprietary name **BEXXAR** be found ***acceptable with concerns***. There appears to be a risk for a medication error with proprietary names for other marketed products **Benicar, Bextra** and **Bexarotene** due to similarity in spelling, handwriting, pronunciation, storage, marketing status, and safety concerns.

In addition, we have concerns on the similar naming of the four different **BEXXAR** vials (**BEXXAR QS, BEXXAR N, BEXXAR D, and BEXXAR T** and the resulting potential for medication errors. A potential for medication errors exists with these products by adding suffixes (single letter) to the **BEXXAR** proprietary name, to be confused with each other by verbal orders, in interpretation of the medication orders, dosing regimen, storage and package labeling.

To mitigate the potential medication errors that might occur from incorrect product administration, the sponsor should ensure that all steps be taken to educate caregivers and/or alter the planned distribution scheme to prevent incorrect dispensing of these sound alike name products and prevent incorrect dispensing of BEXXAR products.

APLB recommends that the product office consider the following actions in relation to this product and proprietary name:

1. Accept our recommendation on the **BEXXAR** product names but ask the sponsor to develop creative ways to restrict the product by unique procedures, distribution, and designing labels for the **BEXXAR** products to ensure that the correct product would be administered and to minimize the potential for medication errors, or
2. Accept our recommendation on the general **BEXXAR** name, but request the manufacturer to develop new "sub-names" for the 4 respective **BEXXAR** versions (**N, D, QS,** and **T**) to ensure that the correct product would be administered and to minimize the potential for medication errors.
3. Reject our recommendation and determine that the **BEXXAR** product names are unacceptable. It is recommended that items 1 and/or 2 above be thoroughly evaluated prior to choosing this item. Should the product office reject our recommendation, a detailed, written justification is recommended to document that decision.

The following references were used:

1. 2002 American Drug Index.
2. 2002 Physicians' Desk Reference.
3. http://www.fda.gov/cder/ob/default.htm (Electronic Orange Book).
4. http://www.rxlist.com (RxList)
5. http://www.fda.gov/cder/approval/index.htm CDER New and Generic Drug Approvals: 1998 to 2002. In addition, the CBER New Approval lists though January 3, 2003 for BLAs, NDA and ANDAs was also reviewed.
6. http://www.factsandcomparisons.com/efacts.asp (Drug Facts and Comparisons)
7. http://www.ama-assn.org (American Medical Association Website-Newly Approved
8. USAN stems through September 23, 2002
9. APhA Handbook of Nonprescription Drugs, 13th Edition, ©2002

Please refer to the attached prior APLB proprietary review memos for BEXXAR:

1. February 11, 2002
2. May 15, 2000
3. January 6, 1999

Firm name: Corixa Corporation.

Letter type: Memorandum

Bcc:	HFM-602	N. Chamberlin
	HFM-602	C. Broadnax
	HFM-602	G. Byrd
	HFM-99	DCC
	HFM-610	M. Malarkey
	HFM-602	APLB Proprietary Name File

History:
Prepared by N Chamberlin: 1/8/3, 1/10/3, 1/14/3,1/15/3, 1/16/3, 1/21/3, 1/27/3
Comments by C Broadnax: 1/13/03, 1/14/3
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Comments by G Byrd: 1/13/03, 1/22/03
Reviewed by M Malarkey: 1/22/3
Finalized by: N Chamberlin

File name: (P030114001)
\\Cbsfs03\oc\APLB\APLB\Proprietary Name Reviews\Acceptable with concerns\ BEXXAR - 27 Jan 03 -
Concurrence box:

MailCode or Office	Name	Date
HFM-602		1-29-03
HFM-602		1-29-03

MailCode or Office	Name	Date

MEMORANDUM

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

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From: Carole Broadnax, Maryann Gallagher and Yongkai Weng
Advertising and Promotional Labeling Branch (HFM-602)
Division of Case Management

Through: Mary A. Malarkey, Director
Division of Case Management (HFM-610)

To: Terrye Zaremba, Chairperson, DMA/OTRR, (HFM-596)
George Mills, Clinical Reviewer, DCTDA/OTRR, (HFM-573)
Michael Noska, CSO, DARP/OTRR, (HFM-588)

Subject: Review of Proposed Proprietary Name **BEXXAR™**
IND 3323, Amendment No. 590/ Serial No. 590
BLA 125011

Recommendation: ACCEPTABLE with concerns

Corixa Corp. submitted an amendment to their IND 3323 on September 21, 2001, and requested another review of the proposed proprietary name, BEXXAR™, to determine if a product with a similar sounding name could have been approved since Corixa received an acceptability letter from the agency dated January 29, 1999.

The Advertising and Promotional Labeling Staff previously reviewed the proposed proprietary name BEXXAR on January 6, 1999, and the name was regarded to be acceptable. The review is attached. The current BLA 125011 was submitted on September 15, 2000 and the present clinical trial is in the phase III stage.

The proposed indication of BEXXAR™ therapy is for the treatment of patients with B cell non-Hodgkins lymphoma. The approved USAN name is tositumomab for the therapeutic package containing both an unlabeled ("cold") Anti-B1 antibody and a labeled antibody with iodine I-131 (hot) Iodine-131 Anti-Bi antibody.

Recommendation: APLB recommends that the proposed proprietary name "**BEXXAR**" be found **acceptable with concerns.** There appears to be a risk for a medication error taking into account dosage form, route of administration, marketing status and indication. However, this risk may be minimized due to the difference in the dosing interval, limited access to the radiolabeled component

of the BEXXAR therapy and the fact that the carton label for the unlabeled BEXXAR component indicates that it is for combination use with the radiolabeled component. These risk factors should be considered since there still appears to be a potential for a medication error.

1) **False or Misleading [21 CFR 201.6 (a)]:**
The proposed brandname is not regarded to be false or misleading.

2) **Fanciful [21CFR 201.10 (c)(3)]:**
The proposed brandname is not regarded to be fanciful. It does not appear to imply that the drug or ingredient has some unique effectiveness or composition beyond that supported by the data.

3) **Similarity in Spelling or Pronunciation [21 CFR 201.10 (c) (5)]:**
There are potential problems due to similarity in spelling and pronunciation with a proprietary name and an established name for two other marketed products as outlined below.

Proprietary/*Established Name*	**Dosage Form**	**Rx/OTC**	**Indication**	**Potential**
BEXXAR	IV	Rx	**Non-Hodgkin's Lymphoma**	**N/A**
BEXTRA	Tablet	Rx	Arthritis and Menstrual Cramping	High
Bexarotene	Capsule and Gel	Rx	Cutaneous T-Cell Lymphoma	High

- BEXTRA (Valdecoxib) tablets was recently approved by Center for Drug Evaluation and Research on November 16, 2001, for the signs and symptoms of osteoarthritis and adult rheumatoid arthritis and for the treatment of pain associated with menstrual cramping.

- Targretin® (Bexarotene) capsules, 75 mg was approved on December 29, 1999, for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractory to at least one prior systemic therapy.

- Targretin® (Bexarotene) gel 1% was approved June 28, 2000, for the topical treatment of cutaneous lesions in patients with CTCL who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

There appears to be a high potential for medication error between BEXXAR and BEXTRA. Both names contain the same prefix "Bex" and the last two letters "ar" and "ra" which are transposed. The pronunciation of the two proprietary names is similar.

The following risk factors associated should also be considered when evaluating the degree to which BEXAAR and BEXTRA and Bexarotene may be of concern for medication errors:

Dosing Interval/Dosage Form/Route of Administration:
The dosing interval between BEXXAR vs. BEXTRA and Bexarotene are very different, therefore, the risk of a medication error appears to be minimal.
BEXXAR is dosed specifically for each patient as a one hour infusion of the unlabeled antibody followed by a 20 minute infusion of the radio labeled antibody over a 7 to 14 day regimen; BEXTRA is dosed once daily for arthritis and twice daily for menstrual cramping;
TARGRETIN ® (Bexarotene) capsules are dosed daily and the gel is initially applied once every other day up to an application frequency of four times daily. Both the Bexarotene capsules and gel are dosed for as long as the patient is deriving benefit. **Minimal Risk**

Since there is considerable evidence that medication errors can occur even between different dosage forms and route of administration (capsule vs. injection and oral vs. intravenous) this risk has to be taken into account when considering the risk of a medication error between BEXXAR (IV), BEXTRA (tablets) and Bexarotene (capsules and gel). **Major Risk**

Marketing Status :
Two products with similar proprietary names that are in the same marketing arena (e.g., prescription rug products) could more easily be confused than two products with similar names in different markets (one Rx and the other OTC). BEXXAR, BEXTRA and Bexarotene are all prescription drug products. **Major Risk**

Indications and/or Pharmacological-Therapeutic Categories:
BEXXAR and BEXTRA have different indications. The agency has considerable evidence that drug products with different indications will not decrease the risk of confusion because of similar proprietary names, since the intended use or indication is not routinely communicated on a prescription. **Major Risk**

BEXXAR and Bexarotene are within the same therapeutic category (oncology), however, BEXXAR is not available to general access since it is a radiolabeled product. The use of similar proprietary names in products that have similar indications or are within the same therapeutic/pharmacological category (e.g., two oncological products) may increase the risk of a medication error. However, certain products in therapeutic categories that are not available to general access may decrease the potential for an error to occur (e.g. radiological products). **Minimal Risk**

Storage Location:
FDA has found that the use of a different storage location (i.e., refrigerator vs. room temperature, oral dosage form location vs. intravenous dosage form location) for two different products with similar names does not significantly decrease the risk of wrong product selection by the health care professional.

Therefore, the use of different storage locations for drugs with names that look or sound alike may not mitigate the potential risk of medication errors. **Major Risk**

However, the risk may be minimized for BEXXAR vs. BEXTRA and Bexarotene since the radiolabeled BEXXAR is stored frozen (– C) with a radioisotope caution label and BEXTRA and Bexarotene are stored at room temperature. A risk still exists for the unlabeled BEXXAR to be confused with BEXTRA or Bexarotene since it is only stored refrigerated (4°C), however, the risk may be minimized because the unlabeled BEXXAR carton label indicates that it is for use in combination with the radiolabeled BEXXAR. **Minimal Risk** b(4)

The following references were used:

1. 2002 American Drug Index.
2. 2001 Physicians' Desk Reference.
3. http://www.fda.gov/cder/ob/default.htm (Electronic Orange Book).
4. http://www.rxlist.com.(RxList).
5. http://www.fda.gov/cder/approval/index.htm (CDER New and Generic Drug Approvals: 1998 to 2001).
6. https://www.factsandcomparisons.com/efacts.asp (Drug Facts and Comparisons)
7. http://www.rxmed.com (ReMed)

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C. Broadnax
M. Gallagher
Y. Weng
DCC
APLB Proprietary Name File

History
Prepared by Y Weng: 1/16/02, 1/22/02, 2/1/02, 2/4/02
Comments by Carole Broadnax,1/30/02, 2/1/02, 2/6/0, 2/8/02
Comments by M Gallagher: 1/25/02, 2/1/02,2/7/02
Comments by K Smith: 1/25/02
Comments by B Conner: 12/19/01
Finalized by M. Gallagher 2/11/02

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Concurrence box:

MailCode or Office	Name	Date
HFM-602	Gallagher	2/11/02
HFM-602	Broadnax	2/11/02
HFM-602	Weng	2/12/02

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