

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

Date: September 03, 2013

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

Through: Lisa L. Stockbridge, Ph.D.
Branch Chief
Advertising and Promotional Labeling Branch (APLB) (HFM-602)
Division of Case Management

To: Edward Thompson OMPT/CBER/OBRR/DBA/RPMB
Mitchell Frost, M.D. OMPT/CBER/OBRR/DH/CRB

Subject: Labeling Review
ANAVIP (*Crotalidae* (Pit-Viper) Immune F(ab')₂ (Equine)) Injection
BLA 125488/0

Sponsor: Instituto Bioclon S.A. de C.V. and Rare Disease Therapeutics, Inc.

Background: The sponsor submitted:

☒ New Approval

☐ Changes Being Effectuated (CBE) supplement

☐ Prior Approval Supplement (PAS)

☐ Major Amendment

Submission Date: March 16, 2013

Submission action due date: March 18, 2014

Submission contains revised:

- X** Prescribing Information (PI)
- Patient Package Insert (PPI)
- Carton and/or container labels
- Other

APLB Comments/Recommendations

APLB has reviewed a proposed PI and provides the following comments and recommendations to OBRR from a promotional and comprehension perspective. At this time, the recent Anascorp prescribing information (PI) is being used as the standard. In this review, unless otherwise stated, all comments are intended to make the Anavip PI similar to the Anascorp PI.

General

Please do not use terms like “mild”, “moderate”, or “severe” without adding qualifying contextual information.

HIGHLIGHTS

- Upon approval, please include the year in the **Initial U.S. Approval** section.
- In the INDICATIONS AND USAGE section of the PI, please delete the following statement regarding practice of medicine:

“Early use of Anavip[®] is advised to prevent clinical deterioration and the occurrence of systemic coagulation abnormalities.”

Also note that the term “early” is vague and would require quantification if used.

- In the DOSAGE AND ADMINISTRATION section, please revise the final bullet point to state:

“Close patient monitoring is necessary.”

Delete the phrase, “As with all antivenom products,” as it minimizes the importance of this directive for Anavip.

- In the WARNINGS AND PRECAUTIONS section, please address subsections 5.3 and 5.4.
- In the ADVERSE REACTION section, please include the cutoff frequency (e.g., incidence rate greater than x%).

FULL PRESCRIBING INFORMATION

- See above comment regarding the INDICATIONS AND USAGE statement.
- In the DOSAGE AND ADMINISTRATION section, please delete:
“Additional Patient Care (Supportive and Adjunctive Therapy): Supportive measures are often utilized to treat certain manifestations of crotalid snake envenomation, such as pain, swelling, hypotension, and wound infection. Poison control centers are helpful resource for individual treatment advice.”

Also, please delete:

- “Pre-hospital care: Perform envenomation (lesion) assessment. Mark the leading edge of edema on the patient’s skin indicating proximal leading edge of lesion. Continue to monitor local injury.”*
- For ease of readability, please revise and move the statement regarding laboratory analysis,
“Perform laboratory analyses, including complete blood count, platelet count, PT, PTT, serum fibrinogen level and routine serum chemistries. Complete labs regularly to gauge response to therapy and anticipate additional dosing.”

to the end of the DOSAGE AND ADMINISTRATION section.

- In the WARNINGS AND PRECAUTIONS section, please delete,
*“The following precautions should be used to manage acute hypersensitivity reactions:
Emergency medical care (e.g., epinephrine, intravenous antihistamines and/or albuterol) should be readily available.”*
- In the WARNINGS AND PRECAUTIONS section, please delete,
“Provide patients with signs and symptoms of delayed allergic reactions or serum sickness (e.g., rash, fever, myalgia, arthralgia), so they can seek appropriate follow-up care.”

This information is already in the PATIENT COUNSELING INFORMATION section.

- Subsection 5.3 of the WARNINGS AND PRECAUTIONS section is missing. Please include the following information in the WARNINGS AND PRECAUTIONS section:

“5.3 Transmissible Infectious Agents

Anavip is made from equine (horse) plasma, it may therefore carry a risk of transmitting infectious agents, e.g., viruses.”

- In the ADVERSE REACTIONS section, please include the cutoff frequency for the common adverse reactions (e.g., incidence rate greater than x%).
- Only include adverse reactions in section 6 ADVERSE REACTIONS.
- Do not include 6.2 POSTMARKETING EXPERIENCE if there is no postmarketing experience to report.
- Since there are no drug interactions studies, please delete section 7 DRUG INTERACTIONS.
- Do not address clinical studies by study number. Describe the study instead.
- Do not use the terms Phase 1, Phase 2, etc. This is not valuable information to the end user of the PI.
- Do not use the terms primary or secondary endpoint. Only include information for which there is substantial evidence or substantial clinical experience.

If you have any questions, please contact Michael Brony, Pharm.D., Regulatory Review Officer at 301-827-6342.

Firm name: Instituto Bioclon S.A. de C.V.

Prepared: Michael Brony 09/03/13

Concur w/ Comments by: Lisa Stockbridge 09/03/13

Finalized by: Michael Brony 09/03/13

Bcc: HFM-602 Lisa Stockbridge

HFM-602 Chron File

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