CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-941 / S-002

Trade Name: EMLA Cream

Generic Name: Lidocaine 2.5% and prilocaine 2.5%

Sponsor: AstraZeneca LP

Approval Date: April 11, 1994
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NDA 19-941/S-002

Astra USA, Inc.
P.O. Box 4500
Westborough, MA 01581-4500

Attention: James G. Baumann, Jr.
Regulatory Affairs

Dear Mr. Baumann:

Please refer to your supplemental new drug application dated December 10, 1993 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for EMLA (lidocaine 2.5% and prilocaine 2.5%) Cream.

The supplemental application provides for minor changes to the originally approved package insert.

We have completed our review of this supplemental application with draft labeling and it is approved effective as of the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling approved effective as of the date of this letter and the Instructions for Use approved December 30, 1992. Marketing the product with FPL that is not identical to this draft labeling and the approved Instructions for Use may render the product misbranded and an unapproved drug.

Please submit twelve copies of the FPL as soon as available. Please individually mount seven of the copies on heavy weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved supplemental NDA 19-941/S-002. Approval of this FPL is not required before it is used.

Should additional information relating to the safety and effectiveness of the drug become available prior to our receipt of the FPL, revision of that labeling may be required.
Should you have any questions, please contact Leslie Vaccari, Project Manager, 301-443-3741.

We remind you that you must comply with the requirements for an approved NDA as set forth under 21 CFR 314.80 and 314.81.

Sincerely yours,

Review Team
Pilot Drug Evaluation Staff, HFD-007
Center for Drug Evaluation and Research

Robert Bedford, M.D.          Dennis Bashaw, Pharm.D.
Medical Officer               Pharmacokineticist

Leslie Vaccari
Project Manager
cc: Orig. NDA19-941/S-002  
HFD-007/Div. File  
HFD-007/BBedford  
HFD-007DBashaw  
DO  
HFD-85  
HFD-007/LVaccari/4-1-94  
R/D Init. by: Fran LeSane 4/1/94  
F/T by: J.Veach 4/5/94  

DOC wp:Emla.02  

APPROVED SUPPLEMENT
APPLICATION NUMBER:

19-941 / S-002

LABELING
**TABLE 1**

<table>
<thead>
<tr>
<th>EMLA (g)</th>
<th>Area (cm²)</th>
<th>Time on (hrs)</th>
<th>Drug Content (mg)</th>
<th>Absorbed (mg)</th>
<th>Cmax (µg/mL)</th>
<th>Tmax (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>400</td>
<td>3</td>
<td>Iodocaine 1500</td>
<td>54</td>
<td>0.12 µg/mL</td>
<td>4</td>
</tr>
<tr>
<td>60</td>
<td>400</td>
<td>24*</td>
<td>Prilocaine 500</td>
<td>32</td>
<td>0.07 µg/mL</td>
<td>10</td>
</tr>
</tbody>
</table>

*Maximum recommended duration of exposure is 4 hours.*

When EMLA cream is used according to the recommended dosing instructions, peak blood levels of lidocaine are approximately 1/20 the systemic toxic level. Likewise, the maximum prilocaine peak is about 1/30 the toxic level. The application of EMLA cream to broken or infected skin, or to 2,000 mg/cm² or more, may cause an increased amount of lidocaine and prilocaine to be absorbed. The maximum recommended duration of exposure is 4 hours. If this maximum duration is exceeded, the drug should be discontinued.

**INDICATION AND USAGE**

EMLA cream is a topical anesthetic cream for the painless administration of intradermal or intramuscular injections, and for the painless performance of dermal procedures.

**CONTRAINDICATIONS**

EMLA cream is contraindicated in patients with a known history of sensitivity to the ingredients of the cream or to any other component of the product.

**WARNINGS**

Application of EMLA cream to larger areas or for longer times than those recommended could result in significant amounts of lidocaine and prilocaine being absorbed, leading to systemic toxicity. Patients should be instructed to avoid occlusive dressing (plastic wrap) over the injection site, and to wash EMLA cream from the skin before making injections.

**INSTRUCTIONS FOR APPLICATION**

1. Apply 2.5 g of cream (1/2 to 1 tube) per 20 cm² (approx. 2 in. by 2 in.) to skin in a thick layer at the site of the procedure.

2. Take off occlusive dressing (plastic wrap) with the 5 g tubes only and remove the center cut-out piece.

3. Peel the paper liner from the paper framed dressing.
4. Cover the EMLA® Cream so that you get a thick layer underneath. Do not squeeze the tube. Smooth down the dressing edges carefully and ensure it is secure to avoid leakage. (It is exposed when a child is a patient.)

5. Remove the protective paper. The time of application can easily be marked directly on the patient’s skin. EMLA® Cream must be applied at least 1 hour before the start of a routine procedure and for a maximum of 2 hours after the start of a painful procedure.

6. Remove the occlusive dressing, wipe off the EMLA® Cream, clean the entire area with an antiseptic solution and prepare the patient for the procedure. The duration of effective skin anaesthesia will be uninterrupted after removal of the occlusive dressing.

PRECAUTIONS

1. Do not apply near eyes or on open wounds.

2. Do not use in children under one month of age.


- Manufactured by: Astra Pharmaceutical Production, AB

- Manufactured in: Sweden

- Manufactured for: Astra Pharmaceutical Products Inc., Westborough, MA 01581

- 030019366. 1Ou922

- For professional use only.
CSO REVIEW OF LABELING

NDA 19-941/S-002

TRADE NAME: EMLA (lidocaine 2.5% and prilocaine 2.5%) Cream

SPONSOR: Astra USA, Inc.

SUBMISSION DATE: December 10, 1993
    Amendment: March 18, 1994

This labeling supplement provides for minor labeling changes which either clarify or update information already in the insert. Two of the changes provide additions which provide for safer use of the product. The additions are as follows:

1. PRECAUTIONS section

   [Signature]

2. DOSAGE AND ADMINISTRATION

   [Signature]

I have checked this draft labeling with the last approved labeling dated December 30, 1992. The only differences noted between the proposed draft labeling and the last approved labeling are those proposed which are acceptable. Therefore, this supplement should be approved.

The medical officer and pharmacokineticist concur that the labeling should be approved.

Leslie Vaccari
Project Manager

4-1-94

Attachment

cc: ORIG. NDA 19-941/S-002
    HPD-007/DIV FILE
    HPD-007/CLVaccari/4-1-94
    initialed by peer CSO (Date)
NDA 19-941

'Astra USA, Inc.
P.O. Box 4500
Westborough, MA 01581-4500

Attention: James G. Baumann, Jr.
Regulatory Affairs Specialist

Dear Mr. Baumann, Jr.,

We acknowledge receipt of your supplemental application for the following:

Name of Drug: EMLA Cream (Lidocaine 2.5% and Prilocaine 2.5%)

NDA Number: 19-941

Supplement Number: S-002

Date of Supplement: December 10, 1993

Date of Receipt: December 16, 1993

Should you have any questions, please contact

Leslie Vaccari
Project Manager
(301) 443-3741

Sincerely yours,

For Project Manager
Pilot Drug Evaluation Staff,
HFD-007
Center for Drug Evaluation and Research