

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

***APPLICATION NUMBER:***  
**006488Orig1s027**

***Trade Name:*** Xylocaine (lidocaine hydrochloride) Solutions for  
Local Anesthesia in Dentistry

***Generic or  
Proper Name:*** lidocaine hydrochloride with or without epinephrine

***Sponsor:*** Astra Pharmaceutical Products Inc.

***Approval Date:*** 12/12/1984

***Indication:*** Xylocaine (lidocaine hydrochloride) Solutions for Local  
Anesthesia in Dentistry are indicated for production of local  
anesthesia by nerve block or infiltration techniques.

# CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:  
NDA 006488/S-027**

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**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**NDA 006488/S-027**

**APPROVAL LETTER**

NDA 6-488/S-027

DEC 12 1984

Astra Pharmaceutical Products Inc.  
Otis Street  
Westborough, MA 01581

Attention: Bruce R. Nanning

Gentlemen:

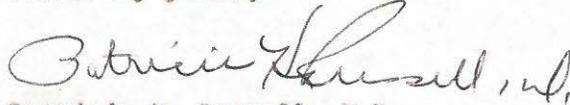
Please refer to your supplemental new drug application dated April 30, 1981, resubmitted January 27, 1983 pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xylocaine (lidocaine HCl) Solutions for Local Anesthesia in Dentistry.

We acknowledge your final printed labeling dated September 21, 1984 and received by the Division on September 25, 1984.

The supplement (S-027) provides for revised labeling to conform with 21 CFR 201.56 and 201.57 (Labeling Format Revision) and with the Local Anesthetic Human Prescription Drugs Class Labeling Guideline for Professional Labeling.

We have completed our review of this supplemental application and it is approved. Our letter of December 4, 1982 detailed the conditions relating to the approval of this application.

Sincerely yours,



Patricia H. Russell, M.D.  
Acting Director  
Division of Surgical-Dental  
Drug Products  
Office of Drug Research and Review  
Center for Drugs and Biologics

cc: BOS-DO (HFR-1100)

NDA 6-488

HFN-160

HFN-240

HFN-83

Doc. Room 160

R/D: JPHannan 12/6/84

R/D init by PHRussell 12/10/84, CPHoiberg 12/7/84, JKInscoe 12/7/84,

HLDickstein 12/10/84, GBoyer 12/7/84

FT td W1416Y 12/10/84

APPROVAL

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**NDA 006488/S-027**

**LABELING**

# Xylocaine (lidocaine hydrochloride)

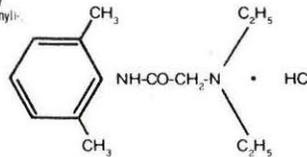
## Solutions for Local Anesthesia in Dentistry

APPROVED DEC 12 1984

### DESCRIPTION

Xylocaine (lidocaine HCl) solutions are sterile isotonic solutions that contain a local anesthetic agent with and without epinephrine (as bitartrate) and are administered parenterally by injection. See INDICATIONS AND USAGE for specific uses. The quantitative composition of each available solution is shown in Table 1.

Xylocaine solutions contain lidocaine HCl which is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-monohydrochloride and has the following structural formula:



Epinephrine is (1-3,4-Dihydroxy-5-(methylamino) methyl) benzyl alcohol and has the following structural formula:

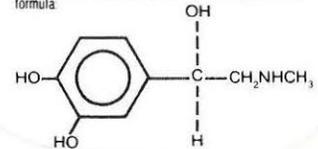


Table 1. Composition of Available Solutions

PRODUCT IDENTIFICATION		FORMULA						
Xylocaine (lidocaine HCl) Concentration %	Epinephrine (as the bitartrate) (dilution)	SINGLE DOSE CARTRIDGES			MULTIPLE DOSE VIALS			
		Citric Acid (mg/ml)	Sodium Chloride (mg/ml)	Sodium Metabisulfite (mg/ml)	Citric Acid (mg/ml)	Sodium Chloride (mg/ml)	Methylparaben (mg/ml)	Sodium Metabisulfite (mg/ml)
2	None	None	6.0	None	None	6.0	1.0	None
2	1:100,000	0.2	6.0	0.5	0.2	6.0	1.0	0.5
2	1:50,000	0.2	6.0	0.5	NS	NS	NS	NS

NS — Not Supplied

NOTE: The pH of all solutions is adjusted to USP limits with sodium hydroxide and/or hydrochloric acid.

### CLINICAL PHARMACOLOGY

**Mechanism of action:** Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action.

**Onset and duration of anesthesia:** When used for infiltration anesthesia in dental patients, the time of onset averages less than 2 minutes for Xylocaine 2% Solution and Xylocaine 2% Solutions with epinephrine. Xylocaine 2% Solution provides an average pulp anesthesia of 5 minutes. Xylocaine 2% Solutions with epinephrine 1:100,000 or 1:50,000 provide an average pulp anesthesia of at least 60 minutes with an average duration of soft tissue anesthesia of approximately 2.5 hours.

When used for nerve block in dental patients the time of onset of Xylocaine 2% Solution with epinephrine averages 2-4 minutes. Xylocaine 2% Solutions with epinephrine 1:100,000 or 1:50,000 provide an average pulp anesthesia of at least 90 minutes with an average duration of soft tissue anesthesia of 3.25 hours.

**Hemodynamics:** Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system and/or the beta-adrenergic receptor stimulating action of epinephrine when present.

**Pharmacokinetics and metabolism:** Information derived from diverse formulations, concentrations and usages reveals that lidocaine is completely absorbed following parenteral administration, its rate of absorption depending, for example, upon various factors such as the site of administration and the presence or absence of a vasoconstrictor agent. Except for intravascular administration, the highest blood levels are obtained following intercostal nerve block and the lowest after subcutaneous administration.

The plasma binding of lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 µg of free base per ml, 60 to 80 percent of lidocaine is protein bound. Binding is also dependent on the plasma concentration of the alpha-1-acid glycoprotein.

Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinyloxide and glycinyloxide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline.

Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half-life of this agent is typically 1.5 to 2.0 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 µg free base per ml. In the rhesus monkey, arterial blood levels of 18-21 µg/ml have been shown to be threshold for convulsive activity.

### INDICATIONS AND USAGE

Xylocaine (lidocaine HCl) Solutions are indicated for production of local anesthesia by nerve block or infiltration techniques. Only accepted procedures for these techniques as described in standard textbooks are recommended.

### CONTRAINDICATIONS

Lidocaine HCl is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type.

### WARNINGS

DENTAL PRACTITIONERS WHO EMPLOY LOCAL ANESTHETIC AGENTS SHOULD BE WELL VERSED IN DIAGNOSIS AND MANAGEMENT OF EMERGENCIES WHICH MAY ARISE FROM THEIR USE. RESUSCITATIVE EQUIPMENT, OXYGEN AND OTHER RESUSCITATIVE DRUGS SHOULD BE AVAILABLE FOR IMMEDIATE USE.

To minimize the likelihood of intravascular injection, aspiration should be performed before the local anesthetic solution is injected. If blood is aspirated, the needle must be repositioned until no return of blood can be elicited by aspiration. Note, however, that the absence of blood in the syringe does not assure that intravascular injection will be avoided.

### PRECAUTIONS

**General:** The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Standard textbooks should be consulted for specific techniques and precautions for various regional anesthetic procedures. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use. (See WARNINGS and ADVERSE REACTIONS.) The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical condition. Lidocaine should also be used with caution in patients with severe shock or heart block.

Local anesthetic solutions containing a vasoconstrictor should be used cautiously in areas of the body supplied by end arteries or having otherwise compromised blood supply. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result. Preparations containing a vasoconstrictor should be used with caution in patients during or following the administration of potent general anesthetic agents, since cardiac arrhythmias may occur under such conditions.

Cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be monitored after each local anesthetic injection. Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness should alert the practitioner to the possibility of central nervous system toxicity. Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position, placing the patient in the recumbent position is recommended when an adverse response is noted after injection of a local anesthetic. (See ADVERSE REACTIONS, Cardiovascular System.) Since amide-type local anesthetics are metabolized by the liver, lidocaine should be used with caution in patients with hepatic disease.

Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations. Lidocaine should also be used with caution in patients with impaired cardiovascular function.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it is not known whether amide-type local anesthetics may trigger this reaction and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs of tachycardia, tachypnea, labile blood pressure and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and prompt treatment, including oxygen therapy, dantrolene (consult dantrolene sodium intravenous package insert before using) and other supportive measures.

Lidocaine should be used with caution in persons with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine.

**Use in the Head and Neck Area:** Small doses of local anesthetics injected into the head and neck area, including retrobulbar, dental and stellate ganglion blocks, may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Confusion, convulsions, respiratory depression and/or respiratory arrest, and cardiovascular stimulation or depression have been reported. These reactions may be due to intra-arterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their circulation and respiration monitored and be constantly observed. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded. (See DOSAGE AND ADMINISTRATION.)

**Information for Patients:** The patient should be informed of the possibility of temporary loss of sensation and muscle function following infiltration or nerve block injections.

The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosae or soft palate when these structures are anesthetized. The ingestion of food should therefore be postponed until normal function returns. The patient should be advised to consult the dentist if anesthesia persists or if a rash develops.

**Clinically significant drug interactions:** The administration of local anesthetic solutions containing epinephrine or norepinephrine to patients receiving monoamine oxidase inhibitors, tricyclic antidepressants or phenothiazines may produce severe, prolonged hypotension or hypertension. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Concurrent administration of vasopressor drugs and ergot-type oxytocic drugs may cause severe, persistent hypertension or cerebrovascular accidents.

**Drug/Laboratory test interactions:** The intramuscular injection of lidocaine may result in an increase in creatine phosphokinase levels. Thus, the use of this enzyme determination, without isoenzyme separation, as a diagnostic test for the presence of acute myocardial infarction may be compromised by the intramuscular injection of lidocaine.

**Carcinogenesis, mutagenesis, impairment of fertility:** Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted.

**Pregnancy Teratogenic Effects.** Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place.

**Nursing mothers.** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when lidocaine is administered to a nursing woman.

**Pediatric use.** Dosages in children should be reduced, commensurate with age, body weight and physical condition. See DOSAGE AND ADMINISTRATION.

#### ADVERSE REACTIONS

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anesthetic agents. These adverse experiences are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption or unintended intravascular injection, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported:

**Central nervous system.** CNS manifestations are excitatory and/or depressant and may be characterized by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tremulousness, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Drowsiness following the administration of lidocaine is usually an early sign of a high blood level of the drug and may occur as a consequence of rapid absorption.

**Cardiovascular system.** Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest.

Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position. Less commonly, they may result from a direct effect of the drug. Failure to recognize the premonitory signs such as sweating, a feeling of faintness, changes in pulse or sensorium may result in progressive cerebral hypoxia and seizure or serious cardiovascular catastrophe. Management consists of placing the patient in the recumbent position and ventilation with oxygen. Supportive treatment of circulatory depression may require the administration of intravenous fluids and, when appropriate, a vasopressor (e.g., epinephrine) as directed by the clinical situation.

**Allergic.** Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

**Neurologic.** The incidences of adverse reactions (e.g., persistent neurologic deficit) associated with the use of local anesthetics may be related to the technique employed, the total dose of local anesthetic administered, the particular drug used, the route of administration, and the physical condition of the patient.

#### OVERDOSAGE

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics or to unintended subarachnoid injection of local anesthetic solution (see ADVERSE REACTIONS, WARNINGS, and PRECAUTIONS).

**Management of local anesthetic emergencies.** The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic injection. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., epinephrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

Endotracheal intubation, employing drugs and techniques familiar to the clinician, may be indicated, after initial administration of oxygen by mask, if difficulty is encountered in the maintenance of a patent airway or if prolonged ventilatory support (assisted or controlled) is indicated.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

The intravenous LD<sub>50</sub> of lidocaine HCl in female mice is 26 (21-31)mg/kg and the subcutaneous LD<sub>50</sub> is 264 (203-304)mg/kg.

#### DOSAGE AND ADMINISTRATION

When used for local anesthesia in dental procedures the dosage of Xylocaine (lidocaine HCl) Solution depends on the physical status of the patient, the area of the oral cavity to be anesthetized, the vascularity of the oral tissues, and the technique of anesthesia. The least volume of solution that results in effective local anesthesia should be administered; time should be allowed between injections to observe the patient for manifestations of an adverse reaction. For specific techniques and procedures of a local anesthesia in the oral cavity, refer to standard textbooks.

For most routine dental procedures, Xylocaine Solution 2% with epinephrine 1:100,000 is preferred. However, when greater depth and a more pronounced hemostasis are required, a 1:50,000 epinephrine concentration should be used.

Dosage requirements should be determined on an individual basis. In oral infiltration and/or mandibular block, initial dosages of 1.0-5.0ml (1½-2½ cartridges) of Xylocaine Solution 2% with epinephrine 1:50,000 or 1:100,000 are usually effective.

In children under 10 years of age it is rarely necessary to administer more than one-half cartridge (0.9-1.0ml or 18-20mg) of Xylocaine Solution per procedure to achieve local anesthesia for a procedure involving a single tooth. In maxillary infiltration, this amount will often suffice to the treatment of two or even three teeth. In the mandibular block, however, satisfactory anesthesia achieved with this amount of drug will allow treatment of the teeth in an entire quadrant.

Aspiration is recommended since it reduces the possibility of intravascular injection, thereby keeping the incidence of side effects and anesthetic failures to a minimum.

**NOTE:** Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit. Solutions that are discolored and/or contain particulate matter should not be used.

Any unused portion of a cartridge of Xylocaine Solution should be discarded.

#### Maximum recommended dosages:

##### Adult:

For normal healthy adults, the individual dose of lidocaine HCl with epinephrine should be kept below 500mg and in any case should not exceed 7mg/kg (3.2mg/lb) of body weight. When used without epinephrine, the amount of lidocaine HCl administered should be kept below 300mg and in any case should not exceed 4.5mg/kg (2mg/lb) of body weight.

##### Pediatric:

##### Children:

It is difficult to recommend a maximum dose of any drug for children since this varies as a function of age and weight. For children of less than ten years who have a normal lean body mass and normal body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50 lbs, the dose of lidocaine should not exceed 75-100mg when calculated according to Clark's rule. In any case, the maximum dose of Xylocaine Solution with epinephrine should not exceed 7mg/kg (3.2mg/lb) of body weight. When used without epinephrine, the amount of Xylocaine Solution administered should not exceed 4.5mg/kg (2.0mg/lb) of body weight.

#### HOW SUPPLIED

Xylocaine (lidocaine HCl) 2% Solution  
Cartridges, 1.8ml, 100 per carton (NDC 0186-0170-14)  
Multiple dose vials, 20ml (NDC 0186-0120-01)

Xylocaine (lidocaine HCl) 2% Solution with Epinephrine 1:100,000  
Cartridges, 1.8ml, 100 per carton (NDC 0186-0175-14)  
Multiple dose vials, 20ml (NDC 0186-0125-01)

Xylocaine (lidocaine HCl) 2% Solution with Epinephrine 1:50,000  
Cartridges, 1.8ml, 100 per carton (NDC 0186-0180-14)

#### Sterilization, Storage and Technical Procedures

- Cartridges should not be autoclaved, because the closures employed cannot withstand autoclaving temperatures and pressures. Vials containing lidocaine HCl solutions without epinephrine may be autoclaved repeatedly if necessary.
- If chemical disinfection of anesthetic cartridges is desired, either pure undiluted isopropyl alcohol (91%) or 70% ethyl alcohol U.S.P. is recommended. Many commercially available brands of rubbing alcohol, as well as solutions of ethyl alcohol not of U.S.P. grade, contain denaturants that are injurious to rubber and, therefore, are not to be used. It is recommended that chemical disinfection be accomplished just prior to use by wiping the cartridge cap thoroughly with a pledget of cotton that has been moistened with recommended alcohol.
- Certain metallic ions (mercury, zinc, copper etc.) have been related to swelling and edema after local anesthesia in dentistry. Therefore, chemical disinfectants containing or releasing these ions are not recommended. Antitrust tablets usually contain sodium nitrite or some similar agents that may be capable of releasing metal ions. Because of this, aluminum sealed cartridges should not be kept in such solutions.
- Quaternary ammonium salts, such as benzalkonium chloride, are electrolytically incompatible with aluminum. Cartridges of Xylocaine (lidocaine HCl) Solutions are sealed with aluminum caps and therefore should not be immersed in any solution containing these salts.
- To avoid leakage of solutions during injection, be sure to penetrate the center of the rubber diaphragm when loading the syringe. An off-center penetration produces an oval shaped puncture that allows leakage around the needle.
- Cracking of glass cartridges is most often the result of an attempt to use a cartridge with an extruded plunger. An extruded plunger loses its lubrication and can be forced back into the cartridge only with difficulty. Cartridges with extruded plungers should be discarded.
- Store at controlled room temperature: 15°-30°C (59°-86°F).



Astra Pharmaceutical Products, Inc.  
Westborough, MA 01581

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**NDA 006488/S-027**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

<b>NOTICE OF APPROVAL</b> <b>NEW DRUG APPLICATION OR SUPPLEMENT</b>		NDA NUMBER <b>N 6-488</b>
		DATE APPROVAL LETTER ISSUED <b>DEC 12 1984</b>
TO: <b>HFW-20</b> XXXXXXXXXXXXXXXXXXXX Press Relations Staff (HP140)	FROM: <input checked="" type="checkbox"/> Bureau of Drugs <input type="checkbox"/> Bureau of Veterinary Medicine	
<b>ATTENTION</b> Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.		
TYPE OF APPLICATION <input type="checkbox"/> ORIGINAL NDA <input checked="" type="checkbox"/> SUPPLEMENT TO NDA <input type="checkbox"/> ABBREVIATED ORIGINAL NDA <input type="checkbox"/> SUPPLEMENT TO ANDA		CATEGORY <input checked="" type="checkbox"/> HUMAN <input type="checkbox"/> VETERINARY
TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG <b>Xylocaine Solutions for Local Anesthesia in Dentistry</b>		
DOSAGE FORM <b>injectable</b>		HOW DISPENSED <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC
ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)  <b>lidocaine HCl - 2% plain</b> <b>2% w/ epinephrine 1:50,000</b> <b>2% w/ epinephrine 1:100,000</b>		
NAME OF APPLICANT (Include City and State) <b>Astra Pharmaceutical Products Inc.</b> <b>Otis Street</b> <b>Westborough, MA 01581</b>		
PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY <b>local anesthetic for use in dentistry</b>		
<b>COMPLETE FOR VETERINARY ONLY</b>		
ANIMAL SPECIES FOR WHICH APPROVED		
<b>COMPLETE FOR SUPPLEMENT ONLY</b>		
CHANGE APPROVED TO PROVIDE FOR  <b>revised final printed labeling in conformance with 21 CFR 201.56 and 201.57</b>		
FORM PREPARED BY NAME <b>James P. Hannan, R. Ph.</b>		DATE <b>5 Dec 1984</b>
FORM APPROVED BY NAME <b>Charles P. Hoiberg, Ph.D.</b>		DATE <b>12-7-84</b>

FPL

NDA NO. 6-488 REF. NO. S-027 FP

NDA SUPPL FOR Labeling

*OK 9/27/84*

**ANTRA** | Astra Pharmaceutical Products Inc.

*Satisfying Clinically  
Acceptable. Please  
issue approval  
letter*

NDA 6-488/S-027

Xylocaine (lidocaine HCl) Solutions for Local  
Anesthesia in Dentistry

*Dr. Seally  
1/20/84  
WAD 11-6-84*

FINAL PRINTED LABELING

September 21, 1984

Center for Drugs and Biologics, HFN-160  
Attention: Document Control Room, #18B-03  
5600 Fishers Lane  
Rockville, Maryland 20857

Gentlemen:

Reference is made to our Supplemental New Drug Application 6-488/S-027 submitted on April 30, 1981 and resubmitted on January 27, 1983 which provides for revised labeling to conform with 21 CFR 201.56 and 201.57 (Labeling Format Revision) and with the Local Anesthetic Human Prescription Drugs Class Labeling Guideline for Professional Labeling.

Please refer also to your letter of March 16, 1984 in which you requested that certain changes be included in the final printed package insert.

We have revised the package insert in accordance with your letter. We have also decided to include under Precautions, the subsection Use in the Head and Neck Area as previously requested by the Agency.

Enclosed are twelve (12) copies of printed labeling, eight (8) copies are unbound as required by regulation.

Thank you for your continuing review of our application.

Sincerely,

*David J. Pizzi*  
David J. Pizzi  
Drug Regulatory Affairs

DJP/jls

Enclosures

INTERNAL CONTROL  
REC'D  
SEP 25 1984  
HFN-160  
DRUGS AND BIOLOGICS