

These mailing pieces, identified as 118-67 and 119-67, should be discarded if still in your possession.

1. Intravenous regional anesthesia

Mailing piece 118-67 recommended the use of Citanest in intravenous regional anesthesia. The FDA regards use of this drug by that technique as experimental. The package insert for Citanest contains no information for its use in intravenous regional anesthesia and the drug has not been approved for use in that procedure.

2. Maximum single dosage

Mailing pieces 118-67 and 119-67 contained statements which implied that dosages of Citanest in excess of the maximum single dose (600 mg.) could be employed in clinical use. No such implication was intended by Astra, and Astra reaffirms that no more than 600 mg. of the drug should be used during any two-hour period.

Professional use information

Both booklets omitted essential and required professional use information. The attached page contains the warning, precautionary, and adverse reaction information which was omitted from the "full disclosure" sections of the booklets.

The safety and effectiveness of Citanest (prilocaine), when used in accordance with the conditions specified in the enclosed package insert, are not in question.

Sincerely yours,

ASTRA PHARMACEUTICAL PRODUCTS, INC.

ASTRA®

The following warning, precautionary, and adverse reaction information contained in the approved (November 18, 1965) Citanest labeling (identified "120" and "Issued October, 1965") is omitted from the product information text of Citanest® mailing pieces 118-67 and 119-67:

Warning: It should be remembered that all local anesthetics are potentially toxic drugs. Therefore, the minimum amount of local anesthetic agent necessary to produce adequate anesthesia and avoid toxic reactions should be used at all times. Moreover, as with other types of drugs, the use of local anesthetics such as Citanest (prilocaine) should be minimal during pregnancy. This, of course, does not exclude the use of local anesthetics at term for obstetrical analgesia. Citanest (prilocaine) has been used effectively for obstetrical analgesia with no adverse effects noted on the fetus, course of labor, or delivery.

Precautions: The peridural space can be approached from the thoracic, lumbar and sacral (caudal) regions. It must be kept in mind that these areas contain venous and arterial plexuses and lymph vessels. Further, the close proximity of these regions to the subarachnoid space constitutes an additional hazard of which the anesthesiologist must be constantly aware. Consequently, the technique of peridural anesthesia should be attempted only by skilled individuals. Close familiarity with, and readiness to make use of every known precautionary measure are mandatory. Further, in addition to the accepted procedure for locating the peridural space, a test dose of 5 cc should be administered at least 5 minutes prior to injecting the total required volume.

While desirable in most instances, the application of the test dose cannot be regarded as a completely effective safety measure. The judicious selection of needles of the proper length and bevel is also important; e.g., in the case of the sacral (caudal) approach, it is necessary that the sacral canal be penetrated for a distance of only 1½ to 2 inches. Since it is possible to puncture the dura by this approach, the use of excessively long needles is definitely precluded.

Local anesthetics react with certain metals and cause the release of their respective ions which, if injected, may cause severe local irritation. Adequate precaution should be taken to avoid this type of interaction.

Treatment:

1. Inadvertent subarachnoid injection:

- a) Resuscitate with oxygen and control blood pressure with vasopressor agents.
- b) Aspirate spinal fluid until 50 cc is removed.