DESCRIPTION:

Nesacaine and Nesacaine-MPF Injections are sterile non pyrogenic local anesthetics. The active ingredient in Nesacaine and Nesacaine-MPF Injections is chloroprocaine HCl (benzoic acid, 4-amino-2-chloro-2-diethylamino)ethyl monohydrochloride), which is represented by the following structural formula:

![Structural formula of chloroprocaine HCl](https://via.placeholder.com/150)

\[
\text{NH}_2\quad \text{COOCH}_2\text{CH}_2\text{N}-(\text{CH}_3)_2\cdot \text{HCl}
\]

The onset of action with chloroprocaine is rapid (usually within 6 to 12 minutes), and the duration of anesthesia, depending upon the amount used and the route of administration, may be up to 60 minutes.

Local anesthetics appear to cross the placenta by passive diffusion. However, the rate and degree of diffusion varies considerably among the different drugs as governed by: (1) the degree of plasma protein binding, (2) the degree of ionization, and (3) the degree of lipid solubility. Fetal/maternal ratios of local anesthetics appear to be inversely related to the degree of plasma protein binding, since only the free, unbound drug is available for placental transfer. Thus, drugs with the highest protein binding capacity may have the lowest fetal/maternal ratios. The extent of placental transfer is also determined by the degree of ionization and lipid solubility of the drug. Lipid soluble, nonionized drugs readily enter the fetal blood from the maternal circulation.

Depending upon the route of administration, local anesthetics are distributed to some extent to all body tissues, with high concentrations found in highly perfused organs such as the liver, lungs, heart, and brain.

Various pharmacokinetic parameters of the local anesthetics can be significantly altered by the presence of hepatic or renal disease, addition of epinephrine, factors affecting urinary pH, renal blood flow, the route of administration, and the age of the patient. The in vivo plasma half-life of chloroprocaine in adults is 21 ± 2 seconds for males and 25 ± 1 seconds for females. The in vitro plasma half-life in neonates is 43 ± 2 seconds.

Chloroprocaine is rapidly metabolized in plasma by hydrolysis of the ester linkage by pseudocholinesterase. The hydrolysis of chloroprocaine results in the production of 8-diettylamino ethanol and 2-chloro-4-aminobenzoic acid, which inhibits the action of the sulfonamides (see PRECAUTIONS).

The kidney is the main excretory organ for most local anesthetics and their metabolites. Urinary excretion is affected by urinary perfusion and factors affecting urinary pH.

INDICATIONS AND usage:

Nesacaine 1% and 2% Injections, in multidose vials with methylparaben as preservative, are indicated for the production of local anesthesia by infiltration and peripheral nerve block. They are not to be used for lumbar or caudal epidural anesthesia.

Nesacaine-MPF 2% and 3% Injections, in single dose vials without preservative and without EDTA, are indicated for the production of local anesthesia by infiltration, peripheral and central nerve block, including lumbar and caudal epidural blocks.

Nesacaine and Nesacaine-MPF Injections are not to be used for subarachnoid administration.

CONTRAINdications:

Nesacaine and Nesacaine-MPF Injections are contraindicated in patients hypersensitive (allergic) to drugs of the PABA ester group.

Lumbar and caudal epidural anesthesia should be used with extreme caution in persons with the following conditions: existing neurological disease, spinal deformities, septicemia, and severe hypertension.

WARNINGS:

LOCAL ANESTHETICS SHOULD ONLY BE EMPLOYED BY CLINICIANS WHO ARE WELL VERSED IN DIAGNOSIS AND MANAGEMENT OF DOSE RELATED TOXICITY AND OTHER ACUTE EMERGENCIES WHICH MIGHT ARISE FROM THE BLOCK TO BE EMPLOYED, AND THEN ONLY AFTER ENSURING THE IMMEDIATE AVAILABILITY OF OXYGEN, OTHER RESUSCITATIVE DRUGS, CARDIOPULMONARY RESUSCITATIVE EQUIPMENT, AND THE PERSONNEL RESOURCES NEEDED FOR PROPER MANAGEMENT OF TOXIC REACTIONS AND RELATED EMERGENCIES (see also ADVERSE REACTIONS and PRECAUTIONS).

The rate of systemic absorption of local anesthetic drugs is dependent upon the total dose and concentration of drug administered, the route of administration, the vascularity of the administration site, and the presence or absence of epinephrine in the anesthetic injection. Epinephrine usually reduces the rate of absorption and plasma concentration of local anesthetics and is sometimes added to local anesthetic injections in order to prolong the duration of action.
Local anesthetic injections containing a vasoconstrictor must be administered cautiously and in carefully circumscribed quantities in areas of the body supplied by end arteries or having otherwise poor blood supply. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated effects of the drug or decreased response. Ischemic injury or necrosis may result.

Since excitatory effects of local anesthetics are hydrolyzed by plasma cholinesterase produced by the liver, chloroprocaine should be used cautiously in patients with enzyme deficiencies. Local anesthetics should also be used with caution in patients with impaired cardiovascular function who may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these agents.

Use in Ophthalmic Surgery: When local anesthetic injections are employed for retrobulbar block, lack of corneal sensation should not be relied upon exclusively. Although it is possible the patient is not ready for surgery. This is because complete lack of corneal sensation usually precedes clinically acceptable external ocular muscle akinesia.

Information for Patients

When appropriate, patients should be informed in advance of surgery that they may experience temporary loss of sensation and motor activity, usually in the lower half of the body, following proper administration of local anesthetics. 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. Concurrent use of these agents should generally be avoided.

In situations when concurrent therapy is necessary, careful heart rate and blood pressure monitoring is essential. Concurrent administration of vasopressor drugs (for the treatment of hypotension related to obstetric blocks) and eutopic-type vasoconstrictor drugs may cause severe, persistent hypotension or cerebrovascular accidents. The par-ama-ni-bone-acid metabolite of chloroprocaine inhibits the action of sulfonamides. Therefore, chloroprocaine should not be used in any condition in which a sulfonamide drug is being employed.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic and reproduction studies to evaluate mutagenicity in the offspring of fertility have not been conducted with chloroprocaine.

Pregnancy: Category C

Animal reproduction studies have not been conducted with chloroprocaine. It is also not known whether chloroprocaine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Chloroprocaine should only be used in women who are pregnant only if clearly needed. This does not preclude the use of chloroprocaine at term for the production of obstetrical anesthesia.

Labor and Delivery

Local anesthetics rapidly cross the placenta, and when used for epidural, paracervical, pudendal, or spinal anesthesia, can cause varying degrees of maternal, fetal, and neonatal toxicity (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION). The incidence and degree of toxicity depend upon the procedure performed, the type and amount of drug, and the technique of drug administration. Adverse reactions in the parturient, fetal, and neonatal systems may involve alterations of the central nervous system, peripheral vascular tone and cardiac function.

Maternal hypotension has resulted from regional anesthesia. Local anesthetics produce vasodilation by blocking sympathetic nerve impulse transmission. Elevation of blood pressure and position of the head on her left side will help prevent decreases in blood pressure. The fetal heart rate also should be monitored during the administration of local anesthetic. Blurred vision, tremors, depression, or drowsiness may be early warning signs of central nervous system toxicity.
tion. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it may be useful to monitor renal function.

ADVERSE REACTIONS:

Systemic: The most commonly encountered acute adverse experiences that demand immediate countermeasures are related to the central nervous system and the cardiovascular system. These adverse experiences are generally dose-related and may result from rapid absorption from the injection site, diminished tolerance, or from unintentional intravascular injection of the local anesthetic solution. In addition to systemic dose-related toxicity, unintentional subarachnoid injection of drug during the intended performance of caudal or lumbar epidural block or nerve blocks near the vertebral column (especially in the head and neck region) may result in underventilation or apnea (“Total Spinal”). Factors influencing plasma protein binding, such as acidosis, systemic diseases that alter protein production, or competition of other drugs for protein binding sites, may diminish individual tolerance. Plasma cholinesterase deficiency may also account for diminished tolerance to ester-type local anesthetics.

Central Nervous System Reactions: These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors may occur, possibly preceding convulsions. However, excitement may be transient or absent, with depression being the first manifestation of an adverse reaction. This may quickly be followed by drowsiness merging into unconsciousness and respiratory arrest.

The incidence of convulsions associated with the use of local anesthetics varies with the procedure used and the total dose administered. In a survey of studies of epidural anesthesia, overt toxicity progressing to convulsions occurred in approximately 0.1 percent of local anesthetic administrations.

Cardiovascular System Reactions: High doses, or unintended intravascular injection, may lead to high plasma levels and related depression of the myocardium, hypotension, bradycardia, ventricular arrhythmias, and, possibly, cardiac arrest.

Allergic: Allergic type reactions are rare and may occur as a result of sensitivity to the local anesthetic or to other formulation ingredients, such as the antimicrobial preservative methylparaben, contained in multiple dose vials. These reactions are characterized by signs such as urticaria, pruritus, erythema, angioedema, edema (including laryngeal edema), tachycardia, sneezing, nausea, vomiting, dizziness, syncope, excessive sweating, elevated temperature, and possibly, anaphylactoid type symptomatology (including severe hypotension). Cross-reactivity among members of the ester-type local anesthetic group has been reported. The usefulness of screening for sensitivity has not been definitely established.

Neurologic: In the practice of caudal or lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter may occur (see PRECAUTIONS). Subsequent adverse observations may depend partially on the amount of drug administered systemically. These observations may include spinal block of varying magnitude (including total spinal block), hypotension secondary to spinal block, loss of bladder and bowel control, and loss of perineal sensation and sexual function. Arachnoiditis, persistent bowel control, and loss of perineal sensation may occur (see PRECAUTIONS). Subsequent adverse observations may be indicated, after initial administration of oxygen 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.

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, as well as underventilation or apnea due to unintentional subarachnoid injection of drug solution, 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 the use of anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor dictated by the clinical situation (such as ephedrine to enhance myocardial contractile force).

If not treated immediately, both convulsions and cardiovascular collapse may result in hypoxia, acidosis, bradycardia, arrhythmias, and cardiac arrest. Underventilation or apnea due to unintentional subarachnoid injection of local anesthetic solution may produce these same signs and also lead to cardiac arrest if ventilatory support is not instituted. If cardiac arrest should occur, standardcardiopulmonary resuscitative measures should be instituted. Recovery has been reported after prolonged resuscitative efforts.

Caudal and Lumbar Epidural Block:

Chloroprocaine may be administered as a single injection or continuously through an indwelling catheter. As with all local anesthetics, the dose administered varies with the anesthetic procedure, the vascularity of the tissues, the depth of anesthesia and degree of muscle relaxation required, the duration of anesthesia desired, and the physical condition of the patient. The smallest dose and concentration required to produce the desired result should be used. Dosage should be reduced for children, elderly and debilitated patients and patients with cardiac and/or liver disease. The maximum single recommended doses of chloroprocaine in adults are: without epinephrine, 11 mg/kg, not to exceed a maximum total dose of 800 mg; with epinephrine (1:200,000) 14 mg/kg, not to exceed a maximum total dose of 1000 mg. For specific techniques and procedures, refer to standard textbooks of the use of anesthetics. There have been adverse event reports of chondrolysis in patients receiving intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures. Nesacaine is not approved for this use (see ADVERSE REACTIONS AND DOSAGE AND ADMINISTRATION).

Caudal and Lumbar Epidural Block: In order to guard against adverse experiences sometimes noted following unintended penetration of the subarachnoid space, the following procedure modifications are recommended:

1. Use an adequate test dose (3 mL of Nesacaine-MPF 3% injection or 5 mL of Nesacaine-MPF 2% injection) prior to induction of complete block. This test dose should be repeated if the patient is moved in such a fashion as to have displaced the epidural catheter. Allow adequate time for onset of anesthesia following administration of each test dose.
2. Avoid the rapid injection of a large volume of local anesthetic injection through the catheter. Consider fractional doses, when feasible.
3. In the event of the known injection of a large volume of local anesthetic injection...
into the subarachnoid space, after suitable resuscitation and if the catheter is in place, consider attempting the recovery of drug by draining a moderate amount of cerebrospinal fluid (such as 10 mL) through the epidural catheter.

As a guide for some routine procedures, suggested doses are given below:

1. Infiltration and Peripheral Nerve Block: NESACAINE or NESACAINE-MPF (chloroprocaine HCl Injection, USP)

<table>
<thead>
<tr>
<th>Anesthetic Procedure</th>
<th>Solution Concentration %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandibular</td>
<td>2</td>
</tr>
<tr>
<td>Infraorbital</td>
<td>2</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>2</td>
</tr>
<tr>
<td>Digital (without epinephrine)</td>
<td>1</td>
</tr>
<tr>
<td>Pudendal</td>
<td>2</td>
</tr>
<tr>
<td>Paracervical (see also PRECAUTIONS)</td>
<td>1</td>
</tr>
</tbody>
</table>

(continues)

- Cardiovascular System Reactions:
  - The incidence of convulsions associated with the use of local anesthetics varies with the procedure used and the total dose administered.
  - Drowsiness merging into unconsciousness has not been definitely established.
  - Elevation of blood pressure with concomitant tachycardia, sneezing, nausea, vomiting, dizziness, and convulsions may occur.
  - Restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors may occur, possibly due to diminished tolerance to ester-type local anesthetics.

- Systemic:
  - Adverse experiences are generally related to high plasma levels and occur in patients with compromised cardiovascular or respiratory systems.
  - The most commonly encountered symptomatology (including severe hypotension, syncope, excessive sweating, elevated blood pressure, tachycardia, respiratory arrest, and cardiac arrest) should be immediately observed. If exposure to low temperaturesses, Nesacaine and Nesacaine-MPF Injections may deposit crystals of chloroprocaine HCl which will redissolve with shaking when returned to room temperature. The product should not be used if it contains undissolved (eg, particulate) material.

HOW SUPPLIED:
- NESACAINE (chloroprocaine HCl Injection, USP) with preservatives is supplied as follows:
  - Product No. NDC No. Strength Vial size
  - 470357 63323-475-37 1% 30 mL multiple dose vial packaged in trays of 25.
  - 470637 63323-476-37 2% 30 mL multiple dose vial packaged in trays of 25.

NESACAINE-MPF (chloroprocaine HCl Injection, USP) without preservatives and without EDTA is supplied as follows:

- Product No. NDC No. Strength Vial size
  - 470727 63323-477-27 1% 20 mL single dose vial packaged in trays of 25.
  - 470827 63323-478-27 2% 20 mL single dose vial packaged in trays of 25.

Keep from freezing. Protect from light. Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

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