IHEEZO- chloroprocaine hydrochloride ophthalmic gel gel
Harrow Eye, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use IHEEZO ™ safely and effectively. See full prescribing information for IHEEZO ™.

IHEEZO ™ (chloroprocaine hydrochloride ophthalmic gel) 3%, for topical ophthalmic use
Initial U.S. Approval: 1955

INDICATIONS AND USAGE

IHEEZO ™ is an ester anesthetic indicated for ocular surface anesthesia. (1)

DOSAGE AND ADMINISTRATION

- The recommended dose of IHEEZO ™ is 3 drops applied topically to the ocular surface in the area of the planned procedure. (2)
- IHEEZO ™ may be reapplied as needed to maintain anesthetic effect. (2)

DOSAGE FORMS AND STRENGTHS

IHEEZO ™ (chloroprocaine hydrochloride ophthalmic gel) 3% contains 24 mg of chloroprocaine hydrochloride per vial (800 mg). Clear, colorless to light yellow gel in single-patient-use vial. (3)

CONTRAINDICATIONS

IHEEZO ™ is contraindicated in patients with a history of hypersensitivity to any component of this preparation. (4)

WARNINGS AND PRECAUTIONS

- Not for Injection or Intraocular Administration (5.1).
- Corneal Injury Due to Insensitivity (5.2).
- Corneal Opacification (5.3)
- For Administration by Healthcare Provider: IHEEZO ™ is not intended for patient self-administration (5.5).

ADVERSE REACTIONS

Most common adverse reaction is mydriasis (approximately 25%) (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Harrow at 844.446.6979 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**.**

Revised: 10/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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2 DOSAGE AND ADMINISTRATION

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3 DOSAGE FORMS AND STRENGTHS

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4 CONTRAINDICATIONS

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5 WARNINGS AND PRECAUTIONS

5.1 Not for Injection or Intraocular Administration

IHEEZO ™ should not be injected or intraocularly administered.

5.2 Corneal Injury Due to Insensitivity

Patients should not touch the eye for at least 10 to 20 minutes after using anesthetic as accidental injuries can occur due to insensitivity of the eye.

5.3 Corneal Opacification

Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification and ulceration with accompanying visual loss.

5.4 Risk of Contamination

Do not touch the dropper tip to any surface as this may contaminate the gel.

5.5 For Administration by Healthcare Provider

IHEEZO ™ is indicated for administration under the direct supervision of a healthcare provider. IHEEZO ™ is not intended for patient self-administration.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect 201 patients undergoing various surgical ocular procedures in two placebo-controlled trials (Study 1 and Study 2). Patients in Study 1 were randomized to receive a single instillation of 3 drops of IHEEZO ™ or placebo. Patients in Study 2 were randomized to receive a single or multiple instillations of 1, 3 or 3+3 drops of IHEEZO ™ or placebo.

The most common adverse reactions in these studies, (incidence greater than or equal to 5%) following IHEEZO ™ administration were mydriasis, conjunctival hyperemia and eye irritation.

Adverse Reactions Reported in Controlled Trials

Table 1. Adverse Reactions in 5% or more of IHEEZO ™ Treated Patients in Studies 1 and 2

Preferred Term	IHEEZO ™ N=151 n (%)	Placebo N=50 n (%)
Mydriasis	39 (26%)	1 (2%)
Conjunctival hyperemia	16 (11%)	6 (12%)
Eye irritation	9 (6%)	2 (4%)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of IHEEZO ™ use in pregnant women to inform a drug associated risk. There are no animal reproduction studies for chloroprocaine.

8.2 Lactation

Risk Summary

There are no data on the presence of chloroprocaine in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IHEEZO ™ and any potential adverse effects on the breastfed infant from IHEEZO ™.

8.4 Pediatric Use

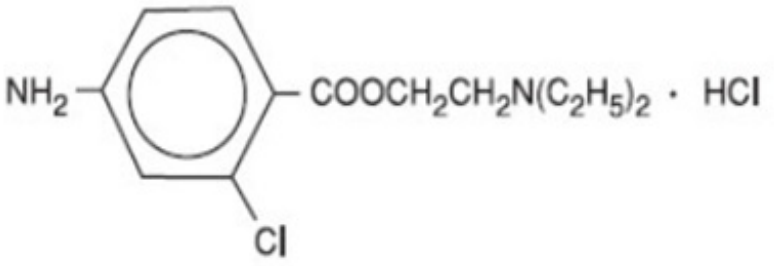
The safety and effectiveness of IHEEZO ™ have not been established in pediatric patients.

8.5 Geriatric Use

No overall differences in safety or effectiveness of IHEEZO ™ have been observed between elderly and younger patients.

11 DESCRIPTION

IHEEZO ™ is a sterile, single-patient-use ophthalmic gel preparation for topical ocular anesthesia containing chloroprocaine hydrochloride as the active pharmaceutical ingredient. Chloroprocaine hydrochloride is an ester anesthetic. It is a water-soluble white crystalline powder and its chemical name is 2-(Diethylamino)ethyl 4-amino-2-chlorobenzoate monohydrochloride. The molecular weight is 307.22 and the molecular formula is $C_{13}H_{19}ClN_2O_2 \cdot HCl$. It is represented by the following structural formula:



IHEEZO ™ contains:

Active: 30 mg of chloroprocaine hydrochloride (equivalent to 26 mg of chloroprocaine) per gram of gel.

Inactive ingredients: Hydroxyethyl Cellulose (HEC), and Water for Injection. The pH may be adjusted to 3.0 to 5.0 with Hydrochloric Acid. This product does not contain an antimicrobial preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.1 Mechanism of Action

Chloroprocaine, like other local anesthetics, blocks the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) skeletal muscle tone.

12.3 Pharmacokinetics

The systemic exposure to chloroprocaine following topical ocular administration of IHEEZO ™ has not been studied.

Elimination

Metabolism

Chloroprocaine is metabolized by plasma pseudocholinesterases and nonspecific esterases in ocular tissues. Chloroprocaine is rapidly metabolized in plasma by hydrolysis of the ester linkage by pseudocholinesterase. The hydrolysis of chloroprocaine results in the production of ß-diethylaminoethanol and 2-chloro-4-aminobenzoic acid, which inhibits the action of the sulfonamides.

Excretion

Chloroprocaine plasma half-life in vitro is approximately 25 seconds in adults and approximately 43 seconds in neonates. 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.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals to evaluate carcinogenic potential of chloroprocaine have not been conducted.

Mutagenesis

2-chloroprocaine and the main metabolite, ACBA, were negative in the in vitro bacterial reverse mutation test (Ames assay) and the in vitro chromosome aberrations assay.

Impairment of Fertility

Studies in animals to evaluate the impairment of fertility have not been conducted with chloroprocaine.

14 CLINICAL STUDIES

14.1 Study 1 and 2

Study 1 (NCT04779606) and **Study 2** (NCT04753710) were randomized, double-blinded placebo-controlled studies conducted to evaluate the efficacy, safety, and local tolerability of IHEEZO ™ in 145 healthy volunteers.

In **Study 1**, 85 healthy male and female were randomized in a 4:1 ratio to receive a single ocular instillation of IHEEZO ™ (N=68) or placebo (N=17). The double blinded treatment included a IHEEZO ™ or a placebo dose of 3 drops instilled at 1 minute ± 15 seconds intervals in the right eye of each volunteer. The median age was 39 years (range 19 to 55 years); 59% female and 41% male.

In **Study 2**, 60 healthy male and female were randomized (40:20) to receive single or multiple ocular instillations of IHEEZO ™ dose of 3 drops in the right eye. The median age was 25 years (range 18 to 59 years); 54% female ad 46% male.

The efficacy in Study 1 and 2 was determined by proportion of patients achieving full conjunctival anesthesia evaluated by conjunctival pinching, 5 minutes after administration.

Efficacy results of Study 1

The proportion of subjects with successful anesthesia was 90% in IHEEZO ™ group and 12% in the placebo group ($p<0.01$). The median time for the IHEEZO ™ group achieving anesthesia was 0.67 minutes. The median duration of anesthesia was 14.3 minutes.

Efficacy results of Study 2

The proportion of subjects with successful anesthesia was 95% in the IHEEZO ™ group and 20% in the placebo group ($p<0.01$). The median time for the IHEEZO ™ group achieving anesthesia was 0.67 minutes. The median duration of anesthesia was 19.3 minutes.

14.2 Study 3

Study 3 (NCT04685538) was a randomized, prospective, multi-center, active-controlled, observer-masked study conducted to evaluate the efficacy and safety of IHEEZO ™ (N=166) versus tetracaine ophthalmic solution 0.5% (N=172) in patients undergoing cataract surgery.

The primary endpoint was defined as the proportion of patients in each treatment group gaining successful anesthesia without any supplementation. On average, patients needed 1-1.5 minutes to obtain sufficient anesthesia to successfully perform the surgical procedure which lasted on average 22 minutes.

No patient treated with IHEEZO ™ required supplemental treatment to complete the intended surgical procedure.

16 HOW SUPPLIED/STORAGE AND HANDLING

IHEEZO ™ (chloroprocaine hydrochloride ophthalmic gel) 3% is supplied as a sterile, clear, colorless to light yellow gel in a single-patient-use vial. Each single-patient-use vial contains 24 mg chloroprocaine in 800 mg of gel.

Aluminum pouch containing 1 LDPE single-patient-use vial of IHEEZO ™.

The outer surface of the vial is not sterile.

NDC 82667-300-01 Package of 1 unit of 1.25 mL single-patient-use vial (800 mg filled)

NDC 82667-300-10 Package of 10 units of 1.25 mL single-patient-use vials (800 mg filled)

NDC 82667-300-00 Sample package of 1 unit of 1.25 mL single-patient-use vial (800 mg filled)

Storage

Store at 15°C to 25°C (59°F to 77°F).

Discard after use.

17 PATIENT COUNSELING INFORMATION

Eye Care Precaution

Do not touch the dropper tip to any surface as this may contaminate the gel.

Advise patients that their eyes will be insensitive for up to 20 minutes due to the effect of the anesthetic, and that care should be taken to avoid accidental injuries.

Manufactured by

Laboratoire Unither

1 Rue de l'Arquerie

50200 COUTANCES

France

Distributed by

Harrow Eye, LLC

102 Woodmont Blvd. Suite 610

Nashville, TN 37205

USA

PRINCIPAL DISPLAY PANEL - Carton

NDC 82667-300-01 Sterile Rx Only

Iheezo ™

(chloroprocaine hydrochloride ophthalmic gel) 3%

For topical ophthalmic use

Contains no preservatives. 1 Vial 800 mg each HARROW ®

PRINCIPAL DISPLAY PANEL - Pouch

NDC 82667-300-01

Iheezo ™

(chloroprocaine hydrochloride ophthalmic gel) 3%

To be administered by physician only.

Single-Patient-Use Vial

Discard unused portion.

For topical ophthalmic use.

Contains no preservatives.

Sterile (outer surface of the vial not sterile)

LOT: 1234

EXP: YYYY-MM

Rx Only

Vial 800 mg

PRINCIPAL DISPLAY PANEL - Sample Carton

NDC 82667-300-00

Professional sample - Not for sale Sterile Rx Only

Iheezo ™

(chloroprocaine hydrochloride ophthalmic gel) 3%

For topical ophthalmic use

Contains no preservatives. 1 Vial 800 mg each HARROW ®

IHEEZO

chloroprocaine hydrochloride ophthalmic gel gel

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:82667-300
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CHLOROPROCAINE HYDROCHLORIDE (UNII: LT7Z1YW11H) (CHLOROPROCAINE - UNII:5YVB0POT2H)	CHLOROPROCAINE HYDROCHLORIDE	24 mg in 800 mg

Inactive Ingredients	
Ingredient Name	**Strength**
HYDROXYETHYL CELLULOSE, UNSPECIFIED (UNII: T4V6TWG28D)	
WATER (UNII: 059QF0KO0R)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:82667-300-01	1 in 1 CARTON	09/27/2022	
1		1 in 1 POUCH		
1		800 mg in 1 VIAL; Type 0: Not a Combination Product		
2	NDC:82667-300-00	1 in 1 CARTON	03/15/2023	
2		1 in 1 POUCH		
2		800 mg in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA216227	09/27/2022	

Labeler - Harrow Eye, LLC (118526951)

Revised: 2/2023 Harrow Eye, LLC