IHEEZO™
(chloroprocaine HCl ophthalmic gel) 3%

Reimbursement Guide

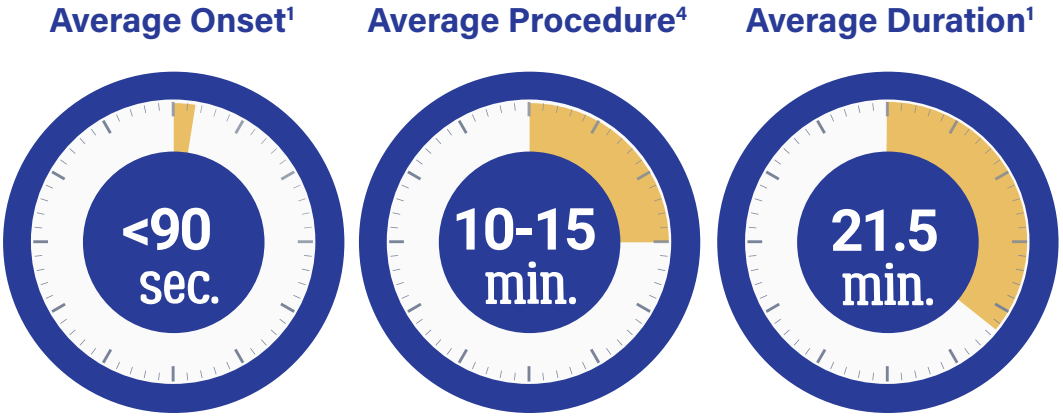
About IHEEZO™

A single dose of low-viscosity IHEEZO (chloroprocaine HCl ophthalmic gel) 3% has been proven to sustain sufficient ocular surface anesthesia throughout a routine ophthalmic procedure.[1]

SUFFICIENT ANESTHESIA WITH IHEEZO HAS FAST, RAPID ONSET

In the Phase III clinical trial:

- Rapid onset of less than 90 seconds to obtain sufficient anesthesia[1]
- Sufficient anesthesia with IHEEZO lasted an average of 21.5 minutes[1]
- No patient required supplemental treatment to maintain anesthesia*[1]



The Phase III clinical trial was a randomized, prospective, multicenter, active-controlled, observer-masked study in 338 patients undergoing routine cataract surgery.

APPROVED USE

IHEEZO is indicated for ocular surface anesthesia.

IMPORTANT SAFETY INFORMATION

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

IHEEZO HAS AN ESTABLISHED SAFETY PROFILE

IHEEZO (chloroprocaine HCl ophthalmic gel) 3% has an established safety profile comparable to other local anesthetics.[2]

IHEEZO is preservative-free and delivered in a sterile, single-use ampule for added patient safety. IHEEZO is meant for administration by a healthcare provider.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

IHEEZO should not be injected or intraocularly administered.

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.

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Coverage for IHEEZO

IHEEZO for ophthalmic procedures is generally covered by Medicare and other payers when medically necessary with the product-specific J-Code.

Medicare Fee for Service Billing and Reimbursement

- IHEEZO was granted Transitional Pass-Through status, which is embedded in the J-Code (J-2403).
- J-2403 allows for separate payment for Medicare Fee-for-Service patients in the ASC/HOPD setting AND in the physician office setting.
- Medicare reimburses 80% of the overall allowable payment amount (minus sequestration)
  - 20% is the responsibility of the beneficiary in the form of a co-pay.
  - Many patients with Fee-for-Service Medicare have a form of supplemental insurance that will cover some, if not all of the 20% co-insurance.

IMPORTANT SAFETY INFORMATION (cont'd)

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

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

IHEEZO is indicated for administration under the direct supervision of a healthcare provider.

Medicare Advantage Billing and Reimbursement

- Medicare Advantage plans follow Fee-for-Service Medicare coverage; however, reimbursement rates may differ.
- It is advised that you should always check with the Medicare Advantage plan in advance to determine coverage and reimbursement prior to use.

Commercial Billing and Reimbursement

- The amount that the commercial plan will reimburse, if at all, will vary depending on the contracts between the facility and the payer.
- It is advised that you should always check with the Commercial plan in advance to determine coverage and reimbursement prior to use.

Any Questions?

Contact the Harrow CONNECTS line to speak with a Reimbursement Specialist:

Phone: **(833) 742-0815** | Monday-Friday 9am-6pm EST

HARROW
CONNECTS

IMPORTANT SAFETY INFORMATION (cont'd)

IHEEZO is not intended for patient self-administration.

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

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Coding for IHEEZO

IHEEZO has a unique permanent J-code:

J-2403

- 1 billing unit = 1mg
- 1 standard 800mg ampule = 800 billing units

Your IHEEZO Reimbursement Business Manager will guide you and your staff step-by-step through the billing and reimbursement process to help facilitate questions.

CPT Codes	CPT Modifier	NDC
66984	RT (Right Eye)	82667-300-01*
66986	LT (Left Eye)	
67028 (Intravitreal Injection)	RT (Right Eye)	

*Some plans may require the 11-digit NDC #82667-0300-01

IMPORTANT SAFETY INFORMATION (cont'd)

You are encouraged to report suspected adverse reactions to the FDA. Visit **www.fda.gov/medwatch**, or call **1-800-FDA-1088**.

Please see the Full Prescribing Information for IHEEZO at **www.iheezo.com/prescribinginformation**.

Ordering Information

NDC#	Unit Size	Case Quantity
10-Digit: 82667-300-01	800mg	1 unit
11-Digit: 82667-0300-01	800mg	1 unit

Wholesaler/Distributor	Item Number	Contact Phone Number
AmerisourceBergen	#10278824	(800) 746-6273
Besse	#10280055	(800) 543-2111
Cardinal Specialty (SPD)	#5851738	(877) 453-3972
McKesson Medical Surgical	#1228615	(855) 571-2100
Metro Medical	#300101	(800) 768-2002

For more information about IHEEZO™, scan the QR code or visit iheezo.com/reimbursement

You can also call **(844) 446-6979** from 8am-8pm ET.

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Harrow CONNECTS Can Help!

HARROW CONNECTS

Call a dedicated
Reimbursement Specialist:

(833) 742-0815

Monday-Friday

9am-6pm EST

General Reimbursement Questions?

- Need help with denials and appeals
- Detailed information about pricing

Curious about IHEEZO coverage in your area?

Go to **iheezo.com/reimbursement** to utilize our policy lookup tool.

- Up to date policy coverages per plan
- Local Coverage Determinations
- Prior Authorizations forms at your fingertips

APPROVED USE

IHEEZO™ is indicated for ocular surface anesthesia.

IMPORTANT SAFETY INFORMATION

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

IHEEZO should not be injected or intraocularly administered.

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.

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

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

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

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

You are encouraged to report suspected adverse reactions to the FDA. Visit **www.fda.gov/medwatch**, or call **1-800-FDA-1088**.

Please see the accompanying Full Prescribing Information for IHEEZO.

References: 1. Iheezo. Prescribing information. Harrow IP, LLC; 2022. **2.** Data on file. Harrow IP, LLC; 2023. **3.** Kim JH, Kim EJ, Kim Y-H, et al. In vivo effects of preservative-free and preserved prostaglandin analogs: mouse ocular surface study. Korean J Ophthalmol. 2015;29(4):270-279. **4.** Intravitreal Injections. The Foundation of the American Society of Retina Specialists. Accessed October 30, 2022. https://www.asrs.org/content/documents/fact-sheet-30-intravitreal-injections.pdf.

HARROW®
Your patients. Our purpose.

Iheezo™

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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.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 9/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
IHEEZO™ is indicated for ocular surface anesthesia.

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

3 DOSAGE FORMS AND STRENGTHS
IHEEZO™ (chloroprocaine hydrochloride ophthalmic gel) 3% contains 24 mg of chloroprocaine hydrochloride per vial (800 mg of gel).

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

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

	IHEEZO™	Placebo
Preferred Term	**N=151 n (%)**	**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.

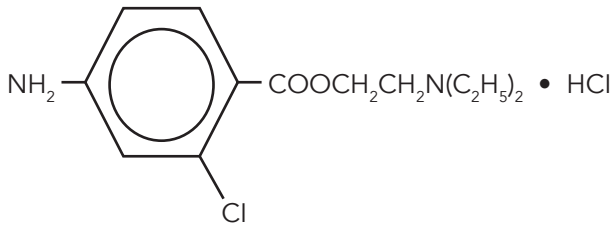
8.2 Lactation
Risk Summary

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 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
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 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)

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

HARROW®

Distributed by

Harrow Eye, LLC
102 Woodmont Blvd. Suite 610
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