IHEEZO™
(chloroprocaine HCl ophthalmic gel) 3%

Reimbursement Guide

IHEEZO™
(chloroprocaine HCl ophthalmic gel) 3%

Comfort & confidence made simple[1,2]

A modern take on ocular anesthesia, IHEEZO® is designed for efficiency and comfort—delivering reliable, lasting anesthesia without adding complexity.[1,2]

In a Phase III clinical trial evaluating IHEEZO for use in routine ophthalmic procedures, it was shown to deliver:*[,2]

90 second onset

Fast reliable onset

Achieves full anesthesia in under 90 seconds on average—potentially minimizing prep time.[2]

1 dose process

1 step, complete coverage

A single dose—just three drops—was shown to provide sufficient anesthesia.**[,1]

21.5 minute duration

Confidence that carries

Sustains anesthesia for an average of 21.5 minutes—outlasting most routine procedures.[1,3]

100% In this clinical trial, 100% of patients treated with IHEEZO maintained anesthesia without supplemental treatment.**[,1,2]

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

**In the clinical trial, no patient undergoing routine cataract surgery receiving IHEEZO required supplemental treatment to maintain anesthesia; this was not the case for patients receiving tetracaine. Supplemental treatment was defined as general anesthesia, intraoperative systemic analgesia, or local anesthesia. Though supplemental administration was not required by any patient in the clinical trial, IHEEZO may be reapplied as needed to maintain anesthesia.[1,2]

APPROVED USE

IHEEZO is indicated for ocular surface anesthesia.

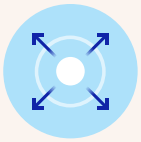
IMPORTANT SAFETY INFORMATION

- IHEEZO is contraindicated in patients with a history of hypersensitivity to any component of this preparation
- IHEEZO should not be injected or intraocularly administered.

Please see full Important Safety Information on page 12 and the Full Prescribing Information at **www.iheezo.com/prescribinginformation**.

VISCOSITY MATTERS

Novel low-viscosity gel for uniform coverage without acting as a barrier to povidone-iodine[4-6]



No excessive pooling or need for redistribution[4,5]

Reduces reliance on external applicators

Minimizes potential ocular surface irritation[4,5]

Supports antiseptic effectiveness[6]

Up to 75% less viscous than other FDA-approved topical ocular anesthetic gel.[1,2,5,6]

KEY SAFETY DATA

Sterile, single-use, and built for safety

IHEEZO is preservative-free and delivered in a sterile, single-use ampule for added patient safety.[2] Single-use packaging may decrease the risk of infection and medication errors.[7]

- Sterile
- Preservative-free
- Single-use ampule

TREATMENT-EMERGENT ADVERSE EVENTS BY ORGAN CLASS[1]

System organ class	Chloroprocaine 3% Gel N=167	Tetracaine 0.5% N=171 (%)
Treatment emergent adverse events (TEAEs)	**0**	**2** (1.2)
Eye disorders	**0**	**2** (1.2)
Corneal disorder	**0**	**1** (0.6)
Iridocele	**0**	**1** (0.6)

Two mild TEAEs were reported in the Tetracaine 0.5% group, while none were reported in the Chloroprocaine 3% Gel group.

IMPORTANT SAFETY INFORMATION

IHEEZO is indicated for administration under the direct supervision of a healthcare provider. Do not touch the dropper tip to any surface to avoid contamination. See full Important Safety Information on page 12.

CODING FOR IHEEZO®

J-Code and Billing Essentials

IHEEZO is assigned a permanent, product-specific J-code:

J2403

- **chloroprocaine HCl ophthalmic gel 3%**
- 1 billing unit = 1mg; 1 standard 800mg ampule = 800 billing units

Procedure	CPT Code	CPT Modifier
Intravitreal injection	**67028**	
Sub tenon injection	**67515**	
Panretinal Photocoagulation (PRP)	**67228**	
Selective laser trabeculoplasty (SLT)	**65855**	
Laser iridotomy	**66761**	
YAG laser capsulotomy	**66821**	**RT** (Right Eye)
Complex cataract surgery	**66982 / 66985**	**LT** (Left Eye)
Simple cataract surgery	**66984**	
Exchange of an intraocular lens	**66986**	
Cataract surgery with MIGS	**66991**	
Punctal plug insertion	**68761**	
Amniotic membrane placement	**65778**	
Gonioscopy	**92020**	

HCPCS code	HCPCS modifier	Long Descriptor	NDC number
J2403	**JZ***	chloroprocaine HCl ophthalmic gel 3%	**82667-0300-05** (11-digit)

*JZ modifier is used to indicate no wastage

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

Coverage for IHEEZO

IHEEZO (chloroprocaine HCl ophthalmic gel) 3% is generally covered by Medicare and other payers when medically necessary with the product-specific J-Code.

Billing and Reimbursement

- J2403 allows for separate reimbursement for Medicare Fee-for-Service patients in the physician office setting.†
- Medicare reimburses 80% of the overall allowable payment amount.
  - 20% is the responsibility of the secondary, supplemental insurance or beneficiary in the form of a co-pay or co-insurance.
  - 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 REMINDERS

- Questions related to insurance eligibility for IHEEZO can be addressed by contacting your IHEEZO Field Reimbursement Manager (FRM), emailing **reimbursement@harrowinc.com**, or working directly with your payer provider representative.
- Coverage and payment may vary by payer, contractual agreements, and site of service. 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.

Effective July 1, 2024, the NCCI Medically Unlikely Edits (MUE) list was updated to reflect 1600 units (2 vials) of IHEEZO per day, allowing for bilateral utilization.‡ Billing for bilateral procedures is payer specific.§ The following is a general guideline for billing on 1 or 2 lines:

- 1 Line: 1600 units, JZ modifier, 50 modifier.
- 2 Lines: 800 units (each line), JZ modifier.

†It is advised that you always check in advance to determine coverage and reimbursement prior to use.
‡Please refer to the CMS website at https://www.cms.gov/medicare/coding-billing/national-correct-coding-initiative-ncci-edits/medicare-ncci-medically-unlikely-edits
§Please refer to individual payer requirements

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

Billing and Reimbursement

May or may not use Medicare FFS payment rate as a benchmark

- Like traditional Medicare FFS, Medicare Advantage plans should cover IHEEZO®, but the payment rate may differ from traditional FFS or be subject to payer-specific practice contractual limitations.
- For a Medicare Advantage patient, the specific Medicare Advantage payer should be contacted in advance to determine its reimbursement process as well as the level of reimbursement for IHEEZO.

Best practices for dealing with Medicare Advantage plans

- Before a procedure, verify if patient has a Medicare Advantage plan.
- Check if your practice-specific payer contracts allow for separate payment of drugs, including IHEEZO.
- Individual plan coverage, payment, policies, and procedures vary and should be confirmed by the practice. Harrow does not guarantee reimbursement.

YOU CAN LOOK UP A PATIENT'S MEDICARE PLAN BY ENTERING THE PATIENT'S NAME AND DATE OF BIRTH IN ANY OF THE FOLLOWING DATABASES, AMONG OTHERS:

- Secure Provider Online Tool (SPOT), provided by First Coast MAC
- Palmetto e-services
- Noridian Medicare Portal
- Availity (for BCBS, Aetna, Humana)

You do not need to pay a subscription fee to access these databases.

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

Billing and Reimbursement

May or may not use Medicare FFS payment rate as a benchmark

- Like traditional Medicare FFS, commercial plans should cover IHEEZO, but the payment rate may differ from traditional FFS or be subject to payer-specific practice contractual limitations.
- For a commercial patient, the specific payer should be contacted in advance to determine its reimbursement process as well as the level of reimbursement for IHEEZO.

Best practices for dealing with Commercial Insurance plans

- Check if your practice-specific payer contracts allow for separate payment of drugs, new technologies, and pass-through drugs, including IHEEZO.
- Confirm if Prior Authorization (PA) is required for patient's specific commercial plan.
- Confirm and verify payer payment/fee schedules for IHEEZO.
- Verify payer-specific use of appropriate revenue code.
- Cultivate relationship with payer-provider network representative.
- Individual plan coverage, payment, policies, and procedures vary and should be confirmed by the practice. Harrow does not guarantee reimbursement.

QUESTIONS? CONTACT OUR DEDICATED REIMBURSEMENT TEAM.

Please email **reimbursement@harrowinc.com** and you will be connected directly with one of our reimbursement team members.

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

CMS-1500 CLAIM FORM (CLINIC)

Form locator 24B:
Place of service "11" indicates an office setting

Form locator 24-1D:
Enter the applicable procedure code (e.g. 68761 for punctal plug or 67028 for an intravitreal injection).Enter the Modifier for left (LT) or right (RT)

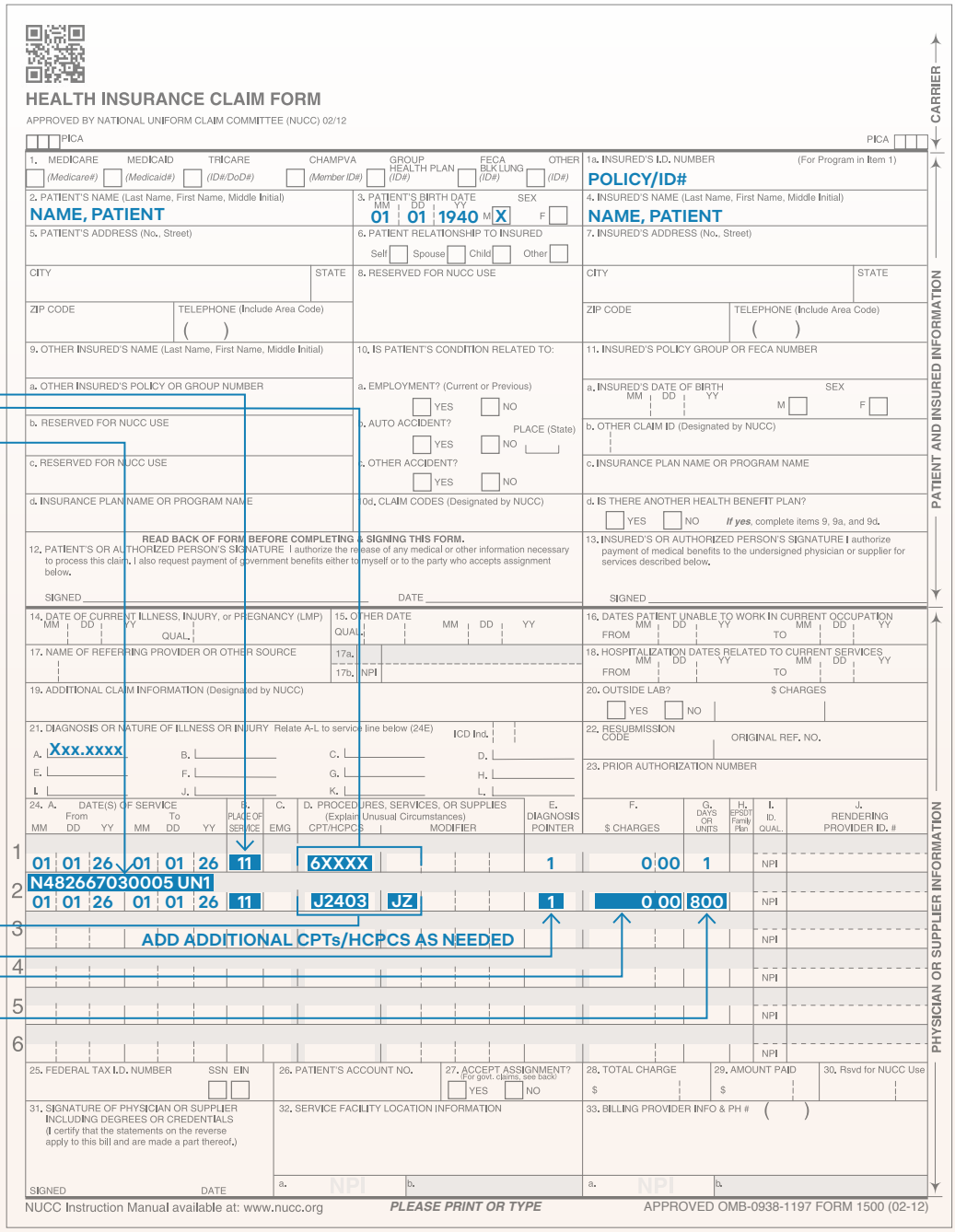
Form locator 24-2A:
Enter N4 qualifier 11-digit NDC Number.*

Form locator 24-2D:
Enter the unique Billing Code (J2403) and modifier (JZ) - indicating no wastage.

Form locator 24E:
Enter the diagnosis code pointer number from field 21 that related to the reason for service.

Form locator 24F:
Confirm charge for IHEEZO® reflects per unit cost x 800 units according to your set fee schedule.

Form locator 24G:
Enter the number of billable units. For **IHEEZO**, 1unit=800mg. Allowable billing for **IHEEZO** is 800 units for a single dose vial.



*Some plans may require the 10-digit NDC #82667-300-01

The information contained within this document is provided as a reference for obtaining appropriate reimbursement. This reference is for informational purposes only. Harrow does not guarantee submitting a completed CMS-1500 form will result in reimbursement. Providers should always contact their payers directly with any questions.

Understanding the acronyms

CPT=Current Procedural Terminology; **ICD-10-CM**=International Classification of Diseases, Tenth Revision, Clinical Modification; **NDC**=National Drug Code; **NPI**=National Provider Identifier; **HCPCS**=Healthcare Common Procedure Coding System

IMPORTANT SAFETY INFORMATION

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Appealing Denied Claims

Appealing claims

When a payer denies a claim for IHEEZO®, the first step in appealing the decision is to understand why the claim was denied.

Payers may deny claims for a number of reasons:

- Claim form contains missing or invalid information to adjudicate.
- Claim requires resubmission with invoice, operative report or injection documentation.
- Payer does not separately reimburse for use of IHEEZO.
- Missing/incomplete/invalid/deactivated/withdrawn National Drug Code (NDC).

Claims can typically be corrected through reopenings or new claim submissions depending on type of denial.

If the payer has denied the claim based on medical information:

- Utilize the payer-provider portal to review specific medical benefit coverage of IHEEZO.
- Reach out to your dedicated Field Reimbursement Manager (FRM)regarding the claims appeal process.

BEST PRACTICES FOR CLAIM SUBMISSIONS

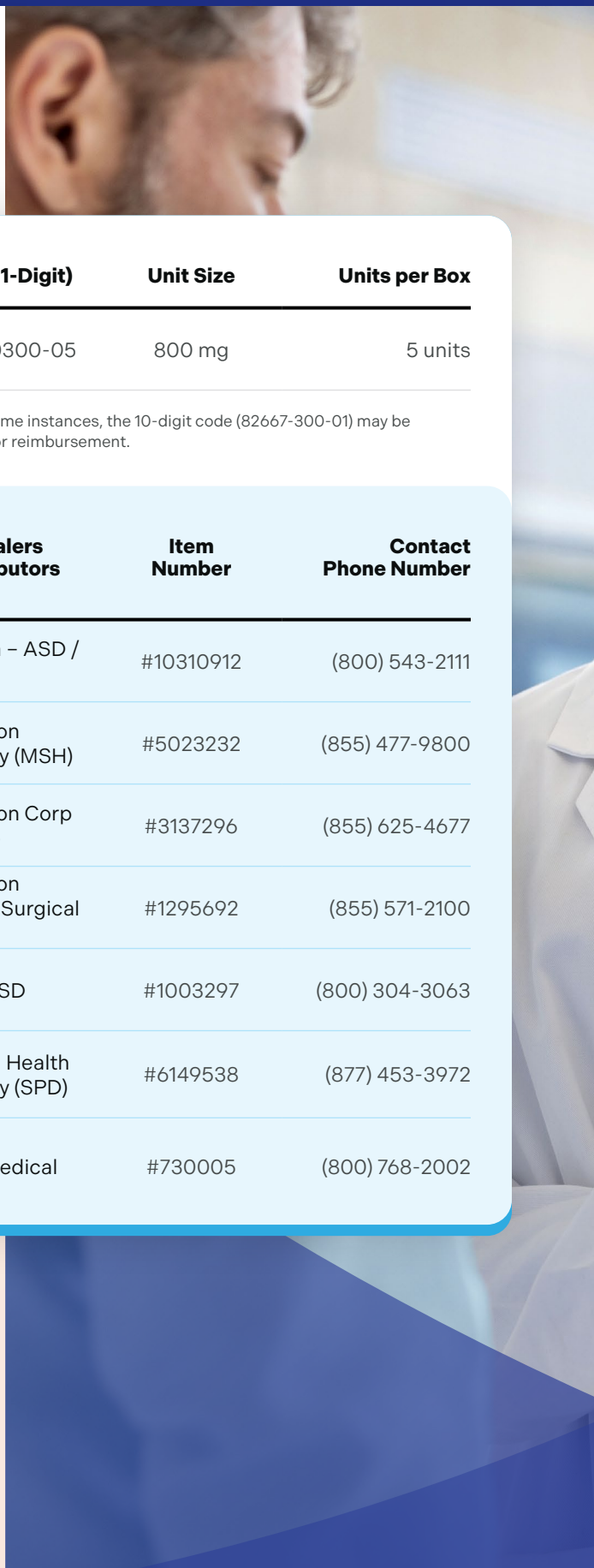
- Make sure submissions are timely and accurate.
- Double-check that codes and units match payer requirements.
- Check your payer contract.
- Verify
  - Diagnosis codes and procedure codes
  - CPT®, HCPCS, and revenue codes
  - NDC (depending on claim form)
- Stay up to date on payer coverage as well as billing and coding trends.

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

ORDERING INFORMATION

Order IHEEZO with Confidence



ORDERING

IHEEZO may be ordered from any of the following wholesalers/distributors.

IHEEZO is supplied in a sterile, single-use unit. IHEEZO contains 24mg of chloroprocaine hydrochloride per unit (800mg). IHEEZO is preservative-free and formulated with the inactive ingredient Hydroxyethyl Cellulose (HEC).

For any questions about ordering, reach out to your Harrow sales representative.

IHEEZO is available for GPO Contract Offerings based on qualified volume by tier.

Details can be discussed further with an IHEEZO team member.

NDC# (11-Digit)	Unit Size	Units per Box
82667-0300-05	800 mg	5 units

Note: In some instances, the 10-digit code (82667-300-01) may be required for reimbursement.

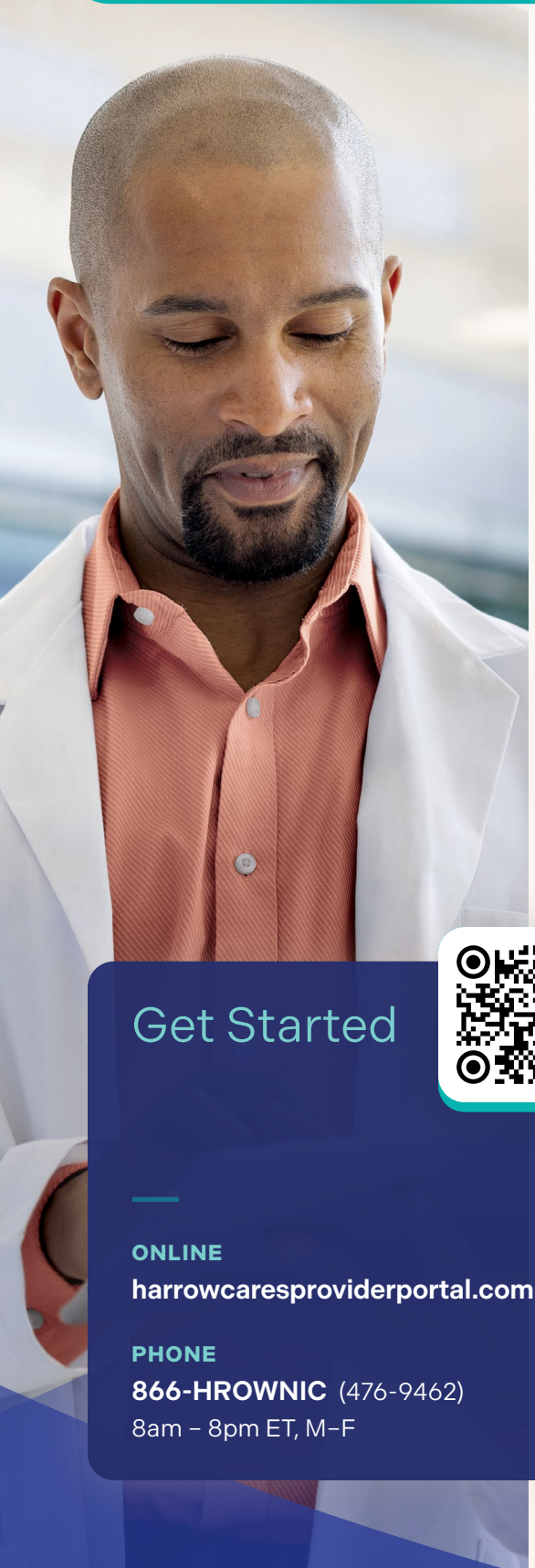
Wholesalers & Distributors	Item Number	Contact Phone Number
Cencora – ASD / Besse	#10310912	(800) 543-2111
McKesson Specialty (MSH)	#5023232	(855) 477-9800
McKesson Corp Full Line	#3137296	(855) 625-4677
McKesson Medical Surgical (MMS)	#1295692	(855) 571-2100
BioCareSD	#1003297	(800) 304-3063
Cardinal Health Specialty (SPD)	#6149538	(877) 453-3972
Metro Medical	#730005	(800) 768-2002

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

Need help with insurance and out-of-pocket costs?

HARROW CARES



Get Started

ONLINE
harrowcaresproviderportal.com

PHONE
866-HROWNIC (476-9462)
8am – 8pm ET, M–F

ACCESS MADE EASY

One-stop support for you, your staff, and your patients

Personalized Access Support

Connect with a specialist in under 30 seconds for access and cost support. Track patients' support updates in real-time via the Provider Portal.

Seamless Enrollment & Coverage

Offers simplified enrollment for benefit investigation and coverage verification. Get alerts when a PA* is required, or proceed directly—order, treat, and submit for reimbursement.

Copay & Product Assurance

Enroll in our commercial copay program or patient assistance based on need. Receive product replacement for breakage, spoilage, or loss—when you treat, you're covered.**

Reimbursement matters are supported by a dedicated Field Reimbursement Manager (FRM) through our Harrow Cares program.

*PA = Prior-Authorization

**It is advised that you always check in advance to determine coverage and reimbursement prior to use.

IMPORTANT SAFETY INFORMATION

IHEEZO is a prescription-only product. Reimbursement support does not guarantee payment. See full Important Safety Information on page 12.

Harrow can help!

IHEEZO™
(chloroprocaine HCl ophthalmic gel) 3%

CONTACT OUR DEDICATED REIMBURSEMENT TEAM

If you need any help with denials and appeals or need detailed information about pricing, please email **reimbursement@harrowinc.com** and you will be connected directly with one of our reimbursement team members.

NEED HELP UNDERSTANDING INSURANCE AND OUT-OF-POCKET COSTS?

Harrow Cares offers the highest quality access and affordability services to increase support to your patients and staff.

Visit **IHEEZO.com/access** today to learn more.

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 Full Prescribing Information for IHEEZO at www.iheezo.com/prescribinginformation.

References: 1. Data on file. Harrow IP, LLC; 2023. **2.** Iheezo. Prescribing information. Harrow IP, LLC; 2022. **3.** 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. **4.** Sintetica. Chloroprocaine hydrochloride ophthalmic gel 3%. Pharmaceutical Development. Sintetica; 2002. **5.** Akten. Material safety data sheet. Akorn Pharmaceuticals; 2010. **6.** Ilyas H, Costine R. The Effects of Low Viscosity Preservative-Free Chloroprocaine Ophthalmic Gel 3% versus BAK-Containing Tetracaine 0.5% on the Bactericidal Action of Povidone-Iodine. Clin Ophthalmol. 2024;18:825-831 https://doi.org/10.2147/OPTH.S454496. **7.** Rhinehart Siegel JD, Rhinehart E, Jackson M, Chiarello L. The Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings.

IZO-00256-2 06/26

HARROW®

IHEEZO®

(chloroprocaine HCl ophthalmic gel) 3%

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: 3/2025

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.

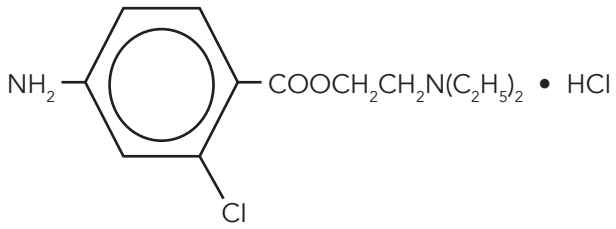
8.2 Lactation
Risk Summary

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

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HARROW®

Distributed by

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