- Nonsteroidal anti-inflammatory ophthalmic solution -  

NIFLAN® OPTHALMIC SOLUTION 0.1%  
< Pranoprofen ophthalmic solution >

<table>
<thead>
<tr>
<th>Storage</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. NIFLAN OPTHALMIC SOLUTION 0.1% should be stored at room temperature.</td>
<td></td>
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<tr>
<td>2. After unsealing outer box, NIFLAN OPTHALMIC SOLUTION 0.1% should be stored away from light.</td>
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<table>
<thead>
<tr>
<th>Expiration date</th>
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<tbody>
<tr>
<td>Three years from manufacturing date (even prior to the expiration date, use as soon as possible after first opening the bottle cap).</td>
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</table>

CONTRAINDICATIONS (NIFLAN OPTHALMIC SOLUTION 0.1% is contraindicated in the following patients.)  
Patients with a history of hypersensitivity to any of the ingredients of this product.

DESCRIPTION  
Product description  
Active ingredient/content (per 1 mL)  Pranoprofen 1 mg  
Inactive ingredients  Boric acid, Sodium borate, Polysorbate 80, Disodium edetate hydrate and Benzalkonium chloride  
Dosage form  Aqueous ophthalmic solution  
Clarity and color  Clear and colorless  
pH  7.0 to 8.0  
Others  Sterile preparation

INDICATIONS  
Symptomatic therapy of external or anterior ocular inflammatory diseases (blepharitis, conjunctivitis, keratitis, scleritis, episcleritis, anterior uveitis, and postoperative inflammation)

DOSAGE AND ADMINISTRATION  
Usually instill 1 to 2 drops in the eye 4 times daily. The frequency of instillation may be adjusted according to the patient’s condition.

PRECAUTIONS  
1. Important Precautions  
   (1) It should be noted that this drug is not for causal treatment but for symptomatic treatment.
   (2) Since this product may mask an ocular infection, this product should be administered cautiously for inflammations caused by infections, and patient should be carefully monitored.

2. Adverse Reactions  
Adverse reactions to this product were reported in 79 of 5,843 patients (1.35%) at approval and in drug-use results surveys.  
Major adverse reactions included irritation in 29 (0.50%), hyperemia of conjunctiva in 16 (0.27%), itching in 14 (0.24%), redness and swelling of eyelid in 11 (0.19%), blepharitis in 7 (0.12%), eye discharge in 6 (0.10%), lacrimation in 5 (0.09%), keratitis superficial diffuse in 4 (0.07%), foreign body sensation in eyes in 3 (0.05%), conjunctival edema in 3 (0.05%), and contact dermatitis in 1 (0.02%) (At the end of the reexamination).

The following adverse reactions have been shown in above surveys, spontaneous reports, and other sources.

<table>
<thead>
<tr>
<th>Incidence unknown</th>
<th>0.1% ≤ 5%</th>
<th>&lt;0.1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>Rash, urticaria</td>
<td>Contact dermatitis</td>
</tr>
<tr>
<td>Eye</td>
<td>Irritation, hyperemia of conjunctiva, itching, redness and swelling of eyelid, blepharitis, eye discharge</td>
<td>Lacrimation, keratitis superficial diffuse, foreign body sensation in eyes, conjunctival edema</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Airway stenosis</td>
<td></td>
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</tbody>
</table>

Note) If adverse reactions develop, administration should be discontinued.
3. Use during Pregnancy, Delivery or Lactation

This product should be administered to pregnant women, women who may possibly be pregnant, or nursing women only if the expected therapeutic benefits outweigh the potential risks associated with treatment. [The safety of this product has not been established in pregnant or nursing women. Delivery delay has been observed in rats.]

4. Pediatric Use

The safety of this product has not been established in low birth-weight infants, neonates, and nursing infants (limited number of clinical experiences).

5. Precautions concerning Use

(1) Administration route: Instillation into the eye only.
(2) Administration: Instill the product with care so that the tip of the container should not be directly touched the eye.
(3) Dispensing: When dispensing, instruct the patients to be certain to keep this product in the attached sachet.

PHARMACOKINETICS

(Rabbits)

Intraocular penetration

$^{14}$C-pranoprofen ophthalmic solution (0.01 mL, 0.1%) was instilled in both eyes of rabbits 4 times at 3-minute intervals and the radioactivity was measured after 30 minutes and 1, 2, 4, 6 and 8 hours, the transition of radioactivity concentration and distribution in various ocular tissues were graphically shown below. The radioactivity at 30 minutes after instillation is distributed, in the decreasing order of concentration, in the cornea, conjunctiva, anterior sclera, extraocular muscles, aqueous humor, iris, ciliary body, and posterior sclera. On the other hand, the distribution of radioactivity is low in the retina and choroid, lens, blood and liver, and scarce in the vitreous body.

CLINICAL STUDIES

The results of clinical studies in 596 cases including double-blind comparative controlled study are summarized in the following table. In most of the cases, the dosage and dosing duration was 1 to 2 drops 4 times daily for 1 to 4 weeks.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Efficacy rate (%)</th>
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<tbody>
<tr>
<td>Blepharitis</td>
<td>76.3 (29/38)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>82.3 (107/130)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>60.7 (51/84)</td>
</tr>
<tr>
<td>Scleritis</td>
<td>55.0 (11/20)</td>
</tr>
<tr>
<td>Episcleritis</td>
<td>100 (14/14)</td>
</tr>
<tr>
<td>Anterior uveitis</td>
<td>65.9 (87/132)</td>
</tr>
<tr>
<td>Postoperative inflammation</td>
<td>56.2 (100/178)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>66.9 (399/596)</td>
</tr>
</tbody>
</table>

Note) Consisting of the “Effective” and more categories

The usefulness of this product has been demonstrated in a double-blind comparative controlled study using 0.05% dexamethasone ophthalmic solution as control in subacute and chronic conjunctivitis and in a double-blind comparative controlled study using placebo as control in anterior uveitis.

PHARMACOLOGY

1. Pharmacological action

(1) Anti-inflammatory effects on experimental rabbit uveitis

NIFLAN OPHTHALMIC SOLUTION 0.1% shows anti-inflammatory effects on the experimental rabbit uveitis induced by injection of bovine serum albumin.

(2) Anti-inflammatory effects on experimental rat conjunctivitis

NIFLAN OPHTHALMIC SOLUTION 0.1% shows anti-inflammatory effects on experimental acute conjunctival edema due to carrageenin, arachidonic acid, and experimental persistent conjunctival edema due to nystatin or mustard in rats. It also shows anti-inflammatory effects on experimental allergic conjunctivitis due to reagin-like antiserum.

2. Mechanism of action

It has been demonstrated in the in vitro and in vivo experiments using rats, guinea pigs and rabbits that this product
has prostaglandin production inhibitory action and lysosome membrane stabilizing action.\(^{4-9}\)

**PHYSICOCHEMISTRY**

Nonproprietary name: Pranoprofen [JAN]

Chemical name: \((2RS)-2(10H-9-Oxa-1-azaanthracen-6-yl)-propanoic\) acid

Molecular formula: \(C_{15}H_{13}NO_3\)

Molecular weight: 255.27

Structural formula:

![Structural formula of Pranoprofen](image)

and enantiomer

**Description:**

Pranoprofen occurs as a white to pale yellowish white crystalline powder.

It is freely soluble in \(N,N\)-dimethylformamide, soluble in acetic acid (100), sparingly soluble in methanol, slightly soluble in acetonitrile, in ethanol (95) and in acetic anhydride, very slightly soluble in diethyl ether, and practically insoluble in water.

A solution of pranoprofen in \(N,N\)-dimethylformamide (1 in 30) shows no optical rotation.

**PACKAGING**

5 mL \(\times\) 10, 5 mL \(\times\) 50

**REFERENCES**


**REQUEST FOR LITERATURE SHOULD BE MADE TO:**

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