



PHYSICIANS' DESK REFERENCE FOR OPHTHALMOLOGY®

Editorial Consultants and Contributors

Clement A. Weisbecker, RPh, Director of Pharmacy, Wills Eye Hospital, Philadelphia, PA
F.T. Fraunfelder, MD, Director, National Registry of Drug-Induced Ocular Side Effects, Oregon Health Sciences University, Portland, OR

Michael Naidoff, MD, Cornea Service, Wills Eye Hospital, Philadelphia, PA
Douglas Rhee, MD, Wills Eye Hospital, Philadelphia, PA
Richard Tippermann, MD, Wills Eye Hospital, Philadelphia, PA

Vice President of Directory Services: Stephen B. Greenberg

Director of Product Management: David P. Reiss

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Associate Product Manager: Bill Shaughnessy

National Sales Manager: Dikran N. Barsamian

National Account Manager, Customized Projects:

Anthony Sorce

Senior Account Manager: Don Bruccoleri

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Jeffrey F. Pfohl, Christopher N. Schmidt,

Stephen M. Silverberg, Suzanne E. Yarrow, RN

National Sales Manager, Trade Group: Bill Gaffney

Director of Direct Marketing: Michael Bennett

Direct Marketing Manager: Lorraine M. Loening

Promotion Manager: Donna R. Lynn

Director, Professional Support Services:

Mukesh Mehta, RPh

Senior Drug Information Specialist:

Thomas Fleming, RPh

Drug Information Specialist: Maria Deutsch, MS, RPh, CDE

Editor, Special Projects: David W. Sifton

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Director of Print Purchasing: Marjorie A. Duffy

Director of Operations: Carrie Williams

Manager of Production: Kimberly H. Vivas

Senior Production Coordinators: Amy B. Brooks,

Dawn B. McCall

Production Coordinator: Mary Ellen R. Breun

Index/Format Manager: Jeffrey D. Schaefer

Senior Format Editor: Gregory J. Westley

Index Editors: Johanna M. Mazur, Robert N. Woerner

Art Associate: Joan K. Akerlind

Senior Digital Imaging Coordinator: Shawn W. Cahill

Digital Imaging Coordinator: Frank J. McElroy, III

Electronic Publishing Designer: Robert K. Grossman

Fulfillment Managers: Stephanie DeNardi, Kenneth Siebert



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SECTION 1 INDICE

This section offers f
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1. Manufacturers'
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PART I/MANUF**AKORN, INC.**

2500 Millbrook Driv
Buffalo Grove, IL 60
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Fort Worth, TX 761
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6. MEDICATIONS FOR DRY EYE

Dry eye refers to a deficiency in either the aqueous or mucin components of the precorneal tear film. The most commonly encountered aqueous-deficient dry eye in the United States is keratoconjunctivitis sicca, while mucin-deficient dry eyes may be seen in cases of hypovitaminosis A, Stevens-Johnson syndrome, ocular pemphigoid, extensive trachoma, and chemical burns.

Dry eye is treated with artificial tear preparations (see **Table 20**) and ophthalmic lubricants (see **Table 21**). The lubricants form an occlusive film over the ocular surface and protect the eye from drying. Administered as a nighttime medication, they are useful both for dry eye and in cases of recurrent corneal erosion.

TABLE 20

ARTIFICIAL TEAR PREPARATIONS

MAJOR COMPONENT(S)	CONCENTRATION (%)	TRADE NAME	PRESERVATIVE/EDTA*
Carboxymethyl cellulose	0.5%	Refresh Plus	None
	1%	Celluvisc	None
	0.25%	Theratears	None
Glycerin	3%	Dry Eye Therapy	None
Hydroxyethyl cellulose, polyvinyl alcohol		TearGard	Sorbic acid, EDTA
Hydroxypropyl cellulose		Lacrisert (biodegradable insert)	None
Hydroxypropyl methylcellulose	0.5%	Isopto Plain	Benzalkonium chloride
		Isopto Tears	Benzalkonium chloride
	1%	Tearisol	Benzalkonium chloride, EDTA
		Isopto Alkaline	Benzalkonium chloride
Hydroxypropyl methylcellulose, dextran 70		Bion Tears	None
		Ocucoat	Benzalkonium chloride, EDTA
		Ocucoat PF	None
		Tears Naturale II	Polyquad
		Tears Naturale Free	None
		Tears Renewed	Benzalkonium chloride, EDTA
Methylcellulose	1%	Murocel	Methyl-, propylparabens
Polycarbophil, PEG-400, dextran 70		AquaSite	EDTA
		AquaSite multi-dose	EDTA, Sorbic acid
Polysorbate 80		Viva Drops	EDTA
Polyvinyl alcohol	1.4%	AKWA Tears	Benzalkonium chloride, EDTA
	3%	Dry Eyes	Chlorobutanol
Polyvinyl alcohol, PEG-400, dextrose	1%	Liquifilm Tears	Chlorobutanol
		HypoTears	Benzalkonium chloride, EDTA
		HypoTears PF	EDTA
Polyvinyl alcohol, povidone	1.4% 0.6%	Puralube Tears	Benzalkonium chloride, EDTA
		Murine Tears	Benzalkonium chloride, EDTA
		Refresh	None
		Tears Plus	Chlorobutanol

*EDTA = ethylenediaminetetraacetic acid.

TABLE 21

OPHTHALMIC LUBRICANTS

TRADE NAME	COMPOSITION OF STERILE OINTMENT
AKWA Tears Ointment	White petrolatum, liquid lanolin, and mineral oil
Dry Eyes	White petrolatum, liquid lanolin, and mineral oil
Duolube	White petrolatum and mineral oil
Duratears Naturale	White petrolatum, liquid lanolin, and mineral oil
HypoTears	White petrolatum and light mineral oil
Lacri-Lube S.O.P., Lubritears	42.5% mineral oil, 55% white petrolatum, lanolin alcohol, and chlorobutanol
Puralube	White petrolatum, liquid lanolin, and mineral oil
Refresh P.M., Dry Eyes Lubricant	41.5% mineral oil, 55% white petrolatum, petrolatum, and lanolin alcohol

7. OCULAR DECONGESTANTS

These topically applied adrenergic medications are commonly used to whiten the eye. Three types are available. Those containing naphazoline and tetrahydrozoline are more stable than those with phenylephrine. Usual dosage is 1 or 2 drops no more than 4 times a day (see **Table 22**).

TABLE 22

OCULAR DECONGESTANTS

DRUG	TRADE NAME	ADDITIONAL COMPONENTS
Naphazoline hydrochloride	AK-Con*	Benzalkonium chloride, edetate disodium
	Albalon*	Benzalkonium chloride, edetate disodium
	Clear Eyes	Benzalkonium chloride, edetate disodium
	Naphcon	Benzalkonium chloride, edetate disodium
	Vasoclear	Benzalkonium chloride, edetate disodium
	Vasocon Regular*	Phenylmercuric acetate
Oxymetazoline hydrochloride	Visine L.R.	Benzalkonium chloride, edetate disodium
	Ocuclear	Benzalkonium chloride, edetate disodium
Phenylephrine hydrochloride	AK-Nefrin	Benzalkonium chloride, edetate disodium
	Eye Cool	Thimerosal, edetate disodium
	Prefrin Liquifilm	Benzalkonium chloride, edetate disodium
	Relief	—
Tetrahydrozoline hydrochloride	Collyrium Fresh	Benzalkonium chloride, edetate disodium
	Murine Plus	Benzalkonium chloride, edetate disodium
	Visine	Benzalkonium chloride, edetate disodium
DECONGESTANT/ASTRINGENT COMBINATIONS		
Naphazoline hydrochloride plus zinc sulfate	Clear Eyes ACR (allergy/cold relief)	Benzalkonium chloride, edetate disodium
Phenylephrine hydrochloride plus zinc sulfate	Zincfrin	Benzalkonium chloride
Tetrahydrozoline plus zinc sulfate	Visine Allergy Relief	Benzalkonium chloride, edetate disodium

*Prescription medication.

8. OPHTHA

Listed in **Table 23** general ophthalmic products. There are actions available for

TABLE 23

OPHTHALMIC II**TRADE NAME**

AK-Rinse

Collyrium Fresh Eyes

Dacriose

Eye-Stream

Irigate

Lavoptik Eye Wash

9. HYPER

Hyperosmolar (hy
They act through

TABLE 24

HYPEROSMO**GENERIC NAME**

A. Therapeutic prepa
Sodium chloride

B. Diagnostic prepa
Glycerin

8. OPHTHALMIC IRRIGATING SOLUTIONS

Listed in **Table 23** are sterile isotonic solutions for general ophthalmic use. They are all over-the-counter products. There are also intraocular irrigating solutions available for use during surgical procedures.

They include prescription medications such as Bausch & Lomb's Balanced Salt Solution, Alcon's BSS and BSS Plus, and Iolab's Iocare Balanced Salt Solution.

TABLE 23

OPHTHALMIC IRRIGATING SOLUTIONS

TRADE NAME	COMPONENTS	ADDITIONAL COMPONENTS
AK-Rinse	Sodium, potassium, calcium, and magnesium chlorides, sodium acetate, and sodium citrate	Benzalkonium chloride
Collyrium Fresh Eyes	Antipyrine, boric acid, and borax	Benzalkonium chloride
Dacriose	Sodium and potassium chlorides, and sodium phosphate	Benzalkonium chloride, edetate disodium
Eye-Stream	Sodium, potassium, magnesium and calcium chlorides, sodium acetate, and sodium citrate	Benzalkonium chloride
Irigate	Boric acid, potassium chloride, and sodium carbonate	Benzalkonium chloride, edetate disodium
Lavoptik Eye Wash	Sodium chloride, sodium biphosphate, and sodium phosphate	Benzalkonium chloride

9. HYPEROSMOLAR AGENTS

Hyperosmolar (hypertonic) agents are used to reduce corneal edema therapeutically or for diagnostic purposes. They act through osmotic attraction of water through the semipermeable corneal epithelium.

TABLE 24

HYPEROSMOLAR AGENTS

GENERIC NAME	TRADE NAME	CONCENTRATION (%)
A. Therapeutic preparations Sodium chloride	Adisorbonac Ophthalmic	2% or 5% (solution)
	AK-NaCl	5% (solution and ointment)
	Muro-128	2% or 5% (solution), 5% (ointment)
B. Diagnostic preparation Glycerin	Ophthalgan	

10. DIAGNOSTIC AGENTS

Some of the more common diagnostic agents and tests used in ophthalmologic practice are listed below.

A. Examination of the Conjunctiva, Cornea, and Lacrimal Apparatus

Fluorescein, applied primarily as a 2% alkaline solution, and with impregnated paper strips, is used to examine the integrity of the conjunctival and corneal epithelia. Defects in the corneal epithelium will appear bright green in ordinary light and bright yellow when a cobalt blue filter is used in the light path. Similar lesions of the conjunctiva appear bright orange-yellow in ordinary illumination.

Fluorescein has also come into wide use in the fitting of rigid contact lenses, though it cannot be used for soft lenses, which absorb the dye. Proper fit is determined by examining the pattern of fluorescein beneath the contact lens.

In addition, fluorescein is used in performing applanation tonometry and one test of lacrimal apparatus patency (Jones test) uses 1 drop of 1% fluorescein instilled into the conjunctival sac. If the dye appears in the nose, drainage is normal.¹

Rose bengal, as a 1% solution, is particularly useful for demonstrating abnormal conjunctival or corneal epithelium. Devitalized cells stain bright red, while normal cells show no change. The abnormal epithelial cells present in dry eye disorders are effectively revealed by this stain.

The Schirmer test is a valuable method of assessing tear production. It employs prepared strips of filter paper 5 by 30 mm in size. The strips are inserted into the topically anesthetized conjunctival sac at the junction of the middle and outer third of the lower lid, with approximately 25 mm of paper exposed. After 5 minutes, the strip is removed and the amount of moistening measured. The normal range is 10 to 25 mm. If inadequate production of tears is found on the initial test, a Schirmer II test can be performed by repeating the procedure while stimulating the nasal mucosa.² A number of variations of the Schirmer test can be found in textbooks and journals.

B. Examination of Acquired Ptosis or Extraocular Muscle Palsy

To confirm myasthenia gravis as the cause of ptosis or muscle palsy, an intravenous injection of 2 mg of *edrophonium chloride* is administered, followed 45 seconds later by an additional 8 mg if there is no response to the first dose. (In case of a severe reaction to the edrophonium, immediately give atropine sulfate, 0.6 mg intravenously.)

C. Examination of the Retina and Choroid

Sodium fluorescein solution, in concentrations of 5%, 10%, and 25%, is injected intravenously to study the

retinal and choroidal circulation. It has been used primarily in examination of lesions at the posterior pole of the eye, but anterior segment fluorescein angiography (wherein the vessels of the iris, sclera, and conjunctiva are studied) is also a useful clinical tool.

Intravascular fluorescein is normally prevented from entering the retina by the intact retinal vascular endothelium (blood-retinal barrier) and the intact retinal pigment epithelium. Defects in either the retinal vessels or the pigment epithelium will allow leakage of fluorescein, which can then be studied by either direct observation or photography. For good results, appropriate filters are needed to excite the fluorescein and exclude unwanted wavelengths. The peak frequencies for excitation lie between 485 and 500 nm and, for emission, between 520 and 530 nm.

Fluorescein has proved to be a safe diagnostic agent, the most common side effects being nausea and vomiting. However, occasional allergic and vagal reactions do occur, so oxygen and emergency equipment should be readily available when angiography is performed. Patients should also be warned that the dye will temporarily stain their skin and urine; in the average patient this lasts no more than a day.

Indocyanine green (IC-Green) has been used in recent years, either alone or with fluorescein, to obtain better frames of choroid neovascularization.

D. Examination of Abnormal Pupillary Responses

Methacholine, as a 2.5% solution instilled into the conjunctival sac, will cause the tonic pupil (Adie's pupil) to contract, but will leave a normal pupil unchanged. A similar pupillary response is seen following instillation of 2.5% methacholine in patients with familial dysautonomia (Riley-Day syndrome).

Table 25 shows the effects of several drugs on miosis due to interruption of the sympathetic system (Horner's syndrome). The effect depends on the location of the lesion in the sympathetic chain.

TABLE 25

HORNER'S SYNDROME

TOPICAL DROP (CENTRAL)	NEURON III (POST- GANGLIONIC)	NEURON II (PRE- GANGLIONIC)	NEURON I
Cocaine 2%–10%	–	–	+/-
Epinephrine (Adrenalin) 1:1000	+++	+	–
Phenylephrine 1%	+++	+	+/-

Pilocarpine may be used to dilate the pupil. Pupil dilation is due to rupture of the pupil's p an atropine-like drug react to pilocarpine. If of the parasympathetic aneurysm, Adie's tor carpine will cause the

11. VISCOELASTIC SUBSTANCES

Viscoelastic substances used in ophthalmologic surgery to maintain the dissection of tissues, act as a buffer, and prevent mechanically the corneal endothelium. The various characteristics of the various substances are the result of the chain length and molecular interactions of viscoelastic substance the potential to produce pressure if they are in the anterior chamber of the eye.

AMVISC (Chiron Vision) is a solution of sodium hyaluronate. The viscosity is 40,000 cP and molecular weight is estimated at 1.5 million.

AMVISC PLUS (Chiron) is composed of sodium hyaluronate. The viscosity (shear rate), and molecular weight (1,500,000 daltons). It is estimated that the total cP of hyaluronate of lower molecular weight is estimated at 1 year.

DUOVISC (Alcon) – is a solution of sodium hyaluronate. One syringe containing Viscoat. Please refer to the package insert for details of use.

HEALON (Pharmacia) is a solution of sodium hyaluronate 1% in pH 7.0. The viscosity is 200,000 cP (@ 0/sec) and molecular weight is approximately 1.5 million.

12. OFF-LABEL USES

B. Acetylcysteine

This agent is used to treat alkali burns, corneal ulcers, and sicca. It is thought to act by the action of collagenase healing. The drug is trade name Mucomin. Though none of the above are approved for use in the eye, they are administered as frequently as up to 4 times a day.

Pilocarpine may be used to determine whether a fixed dilated pupil is due to an atropine-like drug or interruption of the pupil's parasympathetic innervation.³ If an atropine-like drug is involved, the pupil will not react to pilocarpine. If dilation is due to interruption of the parasympathetic innervation (compression by aneurysm, Adie's tonic pupil) instillation of pilocarpine will cause the pupil to constrict.

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11. VISCOELASTIC MATERIALS USED IN OPHTHALMOLOGY

Viscoelastic substances are used in ophthalmic surgery to maintain the anterior chamber, hydraulically dissect tissues, act as a vitreous substitute/tamponade, and prevent mechanical damage to tissue, especially the corneal endothelium. The individual characteristics of the various viscoelastic materials are the result of the chain length and intra- and interchain molecular interactions of the compounds comprising the viscoelastic substance. All viscoelastic materials have the potential to produce a large postoperative increase in pressure if they are not adequately removed from the anterior chamber following surgery.

AMVISC (Chiron Vision - Bausch and Lomb) - Composed of sodium hyaluronate 1.2% in physiologic saline. The viscosity is 40,000 cSt (@25 C, 1/sec shear rate), and molecular weight is $\geq 2,000,000$ daltons. Its shelf life is estimated at 2 years.

AMVISC PLUS (Chiron Vision - Bausch and Lomb) - composed of sodium hyaluronate 1.6% in physiologic saline. The viscosity is 55,000 cSt (@25 C, 1/sec shear rate), and molecular weight is approximately 1,500,000 daltons. The greater viscosity is obtained by increasing total concentration and using sodium hyaluronate of lower molecular weight. Its shelf life is estimated at 1 year.

DUOVISC (Alcon) - Package contains two separate syringes. One syringe containing Provisc; the other containing Viscoat. Please see individual descriptions below for details of each.

HEALON (Pharmacia - UpJohn) - Composed of sodium hyaluronate 1% in physiologic saline. The viscosity is 200,000 (@ 0/sec shear rate), and the molecular weight is approximately 4,000,000 daltons.

HEALON GV (Pharmacia - UpJohn) - Composed of sodium hyaluronate 1.4% in physiologic saline. The viscosity is 2,000,000 (@ 0/sec shear rate), and the molecular weight is approximately 5,000,000 daltons. In the presence of high positive vitreous pressure, Healon GV has three times more resistance to pressure than does Healon.

OCCUCOAT (Storz - Bausch and Lomb) - Composed of hydroxypropylmethylcellulose 2% in balance salt solution (BSS). The viscosity is 4,000 cSt (@ 37 C measured on Cannon-Fenske Viscometer), and the molecular weight is approximately 80,000 daltons. Occucoat is termed a viscoadherent rather than a viscoelastic because of its coating ability, which is related to its contact angle and low surface tension.

PROVISC (Alcon) - Composed of sodium hyaluronate 1% in physiologic saline. The viscosity is 39,000 cps (@ 25 C, 2/sec shear rate) and the molecular weight is approximately 1,900,000 daltons. Clinical studies demonstrate that ProVisc functions in a similar fashion to Healon.

VISCOAT (Alcon) - Composed of a 1:3 mixture of chondroitin sulfate 4% (CS) and sodium hyaluronate 3% (SH) in physiologic saline. The viscosity is 40,000 cps (@ 25 C, 2/sec shear rate), and the molecular weight is 22,500 daltons for CS and 500,000 daltons for SH.

VITRAX (Allergan) - Composed of sodium hyaluronate 3% in balanced salt solution (BSS). The viscosity is 30,000 cps (@ 2/sec shear rate) and the molecular weight is 500,000 daltons. It is highly concentrated to produce a significantly viscous material. It does not require refrigeration and has a shelf life of 18 months.

12. OFF-LABEL DRUG APPLICATIONS IN OPHTHALMOLOGY

B. Acetylcysteine

This agent is used to treat corneal conditions such as alkali burns, corneal melts, and keratoconjunctivitis sicca. It is thought to improve healing by inhibiting the action of collagenase, which may contribute to delay in healing. The drug is available generically or under the trade name Mucomyst in 10% and 20% solutions. Though none of the commercially available solutions are approved for use in ophthalmology, they have been administered as frequently as hourly in acute cases, and up to 4 times a day in maintenance therapy.

B. Alteplase (tissue plasminogen activator)

This thrombolytic agent, trade-named Activase, is used to treat fibrin formation in postvitrectomy patients. Though initial studies were based on intraocular injections of 25 μ g, more recent work has shown the drug to be effective in doses of as little as 3 to 6 μ g. Because by-products of alteplase activity may mediate endothelial cell toxicity, the lower doses are preferred. This agent has also been used for submacular hemorrhage, but this use is controversial.

been used prior to posterior pole rescein angiography, sclera, and conical tool.

prevented from retinal vascular and the intact retina. Whether the retinal allow leakage studied by either or good results, cite the fluoresceins. The peak 485 and 500 nm 530 nm.

diagnostic agent, ing nausea and and vagal reactivity equipment. Angiography is performed that the dye remains in the average day.

is used in recent, to obtain better.

Adverse Responses

instilled into the dilated pupil (Adie's tonic pupil). A normal pupil response is seen following instillation in patients with Adie's syndrome.

Other drugs on the parasympathetic system may also be used on the location of the lesion.

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C. Antimetabolites

5-Fluorouracil (5-FU). This drug inhibits fibroblasts and therefore diminishes scarring after glaucoma filtering surgery. Initial recommendations called for subconjunctival injection of 5 mg twice daily for 7 days postoperatively and once daily for the succeeding 7 days. However, many physicians today are achieving positive results with as little as 4 mg administered 4 to 6 times during a 10-day period. Use of this drug is associated with a number of complications, including conjunctival wound leak, corneal epithelial defects, hypotony associated with permanently reduced vision acuity, serious corneal infections in eyes with preexistent corneal epithelial edema, and increased susceptibility to late-onset bleb infections. The drug should be considered only when there is a high risk of surgical failure.

Mitomycin. This potent chemotherapeutic agent, trade-named Mutamycin, is being used in filtering surgery for the same purpose and on the same type of patients as 5-FU. It is applied once during surgery on a small piece of Gelfilm or Weck Cell in a concentration of 0.2 to 0.4 mg/mL. Reported side effects are similar to those of 5-FU. However, some serious side effects may go unreported, since there is a possibility of delayed reactions 6 to 24 months after surgery. Mitomycin has also been administered in a 0.02% to 0.04% solution 2 to 4 times a day to prevent recurrence after pterygium surgery. Serious side effects associated with this therapy include corneal melts and scleral ulceration and calcification.

Physicians should bear in mind the possibility of major side effects from all antineoplastic agents and carefully weigh the risks and benefits of the use. Remember, too, that these agents should always be handled and discarded in accordance with OSHA, AMA, ASHP, and/or hospital policies regarding the safe use of antineoplastics.

D. Cyclosporine

This potent immunosuppressant has a high degree of selectivity for T lymphocytes. Available under the trade name Sandimmune, it has been used in a 2% topical solution as prophylaxis against rejection in high-risk, penetrating keratoplasty and for treatment of severe vernal conjunctivitis resistant to more conventional therapy, ligneous conjunctivitis unresponsive to other topical therapy, and noninfectious peripheral ulcerative keratitis associated with systemic autoimmune disorders. All contraindications for systemic use also apply to topical administration, since blood levels of up to 64 ng/mL have been observed after topical application. All patients receiving this medication should have blood work that includes cyclosporine levels, blood urea nitrogen, creatinine, lactate dehydrogenase, alkaline phosphatase, and total bilirubin.

E. Doxycycline

This derivative of tetracycline is used for the treatment of ocular rosacea and meibomianitis. The usual dose is 100 mg PO daily for a 6 to 12 week course of treatment. It has the same side effects, contraindications, and interactions as tetracycline.

F. Edetate disodium

This chelating agent plays a role in the treatment of band keratopathy. After removal of the corneal epithelium, it is used to remove calcium from Bowman's membrane.

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13. OCULA

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