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

NAVSTEL® Intraocular Irrigating Solution (balanced salt ophthalmic solution with hypromellose, dextrose and glutathione) Sterile
Initial U.S. Approval: 2008

----------INDICATIONS AND USAGE----------
NAVSTEL® Solution is indicated for use as an intraocular irrigating solution during surgical procedures involving perfusion of the eye (1).

----------DOSAGE AND ADMINISTRATION----------
The solution should be used according to the standard technique employed by the operating surgeon. (2)

----------DOSAGE FORMS AND STRENGTHS----------
- 250 mL: 250 mL bottle filled with 240 mL Part I and 10 mL vial filled with 10 mL Part II of sterile intraocular irrigating solution
- 500 mL: 500 mL bottle filled with 480 mL Part I and 20 mL vial filled with 20 mL Part II of sterile intraocular irrigating solution (3)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
Do not use this container for more than one patient since NAVSTEL® Solution does not contain a preservative. (5.1)

----------ADVERSE REACTIONS----------
The most frequently reported adverse reaction in patients exposed to NAVSTEL® Solution was increased intraocular pressure, occurring in 12% of patients.

To report SUSPECTED ADVERSE REACTIONS, contact Alcon Laboratories, Inc. at 1-800-757-9195 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 7/2008

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

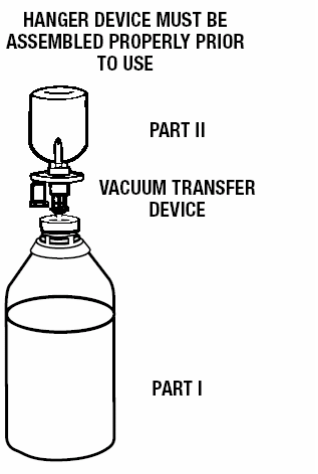
NAVSTEL® Solution is indicated for use as an intraocular irrigating solution during surgical procedures involving perfusion of the eye.

2 DOSAGE AND ADMINISTRATION

General Instructions
- The solution should be used according to the standard technique employed by the operating surgeon.
- Follow strict aseptic procedures in the reconstitution of NAVSTEL® Solution.
- Not for injection or intravenous infusion.
- Do not use if product is discolored or contains a precipitate.
- Do not use NAVSTEL® until Part I is fully reconstituted with Part II. Reconstitute just prior to surgery.
- Do not use unless product is clear, seal is intact, vacuum is present and container is undamaged.

Reconstitution Instructions
1. Remove the blue flip-off seals from the NAVSTEL® Part I bottle and NAVSTEL® Part II vial. Prepare the stoppers on both parts by using sterile alcohol wipes.
2. Peel open a NAVSTEL® Vacuum Transfer Device package (supplied) and remove the sterile transfer spike. NOTE: This device is vented permitting air to enter vial during solution transfer, thereby preventing the creation of a vacuum inside the vial. An air-inlet filter is provided to protect the system. Do not remove the air-inlet filter.
3. Remove protector from the white plastic piercing pin.
4. Firmly grasp device from behind the flange and insert the white plastic piercing pin into the upright rubber stopper of the NAVSTEL® Part II vial.

5. Remove guard from filter needle. Firmly grasp vial in the palm of one hand and with thumb and index finger, hold plastic flange against top of vial.
6. Invert vial and immediately insert filter needle into the outer target of the rubber stopper of the NAVSTEL® Part I bottle.
   (See illustration.)
7. Fluid will automatically transfer from the vial into the large vacuum bottle unless the filter becomes occluded or loss of vacuum occurs. NOTE: An excess amount of NAVSTEL® Part II is provided in each vial. A small amount of residual solution can be expected to remain in the vial.
8. Immediately remove needle from the NAVSTEL® Part I container and discard it after solution transfer has been completed.
9. Place a sterile safety cap over the rubber stopper of Part I if the solution is not going to be used immediately. Mix the solution gently until uniform. Peel off the right-hand side of Part I bottle label (fully reconstituted NAVSTEL®). Record the date and time of reconstitution. NAVSTEL® is now ready for use.
10. Reconstituted NAVSTEL® should be used within 6 hours of mixing.



Alternative Transfer Method
If preferred, the contents of the NAVSTEL® Part II component may be aspirated with an 18-gauge cannula attached to a 20 mL syringe and then transferred into the Part I bottle.

After Reconstitution

After reconstitution, use a single patient administration set with an air-inlet in the plastic spike since the bottle does not contain a separate airway tube. Follow the directions for the particular administration set to be used. Insert the spike aseptically into the bottle through the center target area of the rubber stopper. Allow the fluid to flow to remove air from the tubing before intraocular irrigation begins. If a second bottle is necessary to complete the surgical procedure, insure that the vacuum is vented from the second bottle BEFORE attachment to the administration set.

3 DOSAGE FORMS AND STRENGTHS

- 250 mL: 250 mL bottle filled with 240 mL Part I and 10 mL vial filled with 10 mL Part II of sterile intraocular irrigating solution
- 500 mL: 500 mL bottle filled with 480 mL Part I and 20 mL vial filled with 20 mL Part II of sterile intraocular irrigating solution

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Single Patient Use Only

Do not use this container for more than one patient since NAVSTEL® Solution does not contain a preservative.

5.2 Diabetes

Studies suggest that intraocular irrigating solutions which are iso-osmotic with normal aqueous fluids should be used with caution in diabetic patients undergoing vitrectomy since intraoperative lens changes have been observed.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Increased intraocular pressure was the most frequently reported adverse reaction which occurred in 12% of the 391 patients exposed to NAVSTEL® Solution and 11% of the 431 patients exposed to BSS PLUS® Solution.

The following table presents the incidence of patients with IOP ≥ 25 mmHg**.** IOP lowering medication was not administered until after the first IOP assessment at hour 6 (anterior segment studies) or Day 1 (posterior segment study).

Table 1
Anterior Segment Studies

Treatment	**NAVSTEL® N=223**	**BSS PLUS® n=220**
IOP ≥ 25 mmHg	%	%
Hour 6	38	35
Day 1	17	15
Day 3	6	4
Day 7	0.5	0

Posterior Segment Study

Treatment	**NAVSTEL® N=168**	**BSS PLUS® n=176**
IOP ≥ 25 mmHg	%	%
Day 1	7	5
Day 7	8	8
Day 14	10	4
Day 30	4	4

Table 2 presents the most common adverse reactions reported with NAVSTEL® and BSS PLUS.

Table 2

Treatment	**NAVSTEL® N=391**	**BSS PLUS® n=431**
Coded Adverse Reactions	**%**	**%**
Nervous system disorders		
Headache	3	3
Eye disorders		
Ocular Discomfort	5	3
Macular Edema	4	4
Conjunctival Hyperemia	4	3
Dry Eye	3	5
Iritis	3	1
Retinal Hemorrhage	3	1
Vision Blurred	2	1
Posterior Capsule Opacification	2	3

In the posterior segment surgical study, cataract was reported in 11% of patients exposed to NAVSTEL®, compared to 7% of patients exposed to BSS PLUS®.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. NAVSTEL® Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

There have been no controlled studies addressing the safety of NAVSTEL® in lactating women. Caution should be exercised when NAVSTEL® is administered to a nursing woman.

8.4 Pediatric Use

Safety and efficacy of NAVSTEL® have been demonstrated in pediatric patients.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and other patients.

11 DESCRIPTION

NAVSTEL® Solution is a sterile intraocular irrigating solution for use during ophthalmic surgical procedures, including those requiring a relatively long intraocular perfusion time (e.g. vitrectomy and anterior segment reconstruction). The solution does not contain a preservative and should be prepared just prior to use in surgery.
Contains:
Part I: Part I is a sterile 240 mL or 480 mL solution in a 250 mL or 500 mL single-dose glass bottle to which the Part II concentrate is added. Each mL of Part I contains: hypromellose, sodium chloride, potassium chloride, dibasic sodium phosphate, sodium bicarbonate, hydrochloric acid and/or sodium hydroxide (to adjust pH) in water for injection USP.

Part II: Part II is a sterile concentrate in a 10 mL or 20 mL single-dose vial for addition to Part I. Each mL of Part II contains: calcium chloride, magnesium chloride, dextrose, gluthathione disulfide (oxidized glutathione), in water for injection USP.
After addition of NAVSTEL® Part II to the Part I bottle, each mL of the reconstituted product contains: hypromellose 1.25 to 1.73 mg, sodium chloride 7.14 mg, potassium chloride 0.38 mg, calcium chloride 0.154 mg, magnesium chloride 0.2 mg, dibasic sodium phosphate 0.42 mg, sodium bicarbonate 2.1 mg, dextrose 0.92 mg, glutathione disulfide (oxidized glutathione) 0.184 mg, hydrochloric acid and/or sodium hydroxide (to adjust pH) in water for injection.

The reconstituted product has a pH of approximately 7.4, osmolality of approximately 305 mOsm/kg, and viscosity of approximately 3 centipoise.

12 CLINICAL PHARMACOLOGY

12.3 Pharmacokinetics

The components of NAVSTEL® Solution are normally found in aqueous humor with the exception of hypromellose. Hypromellose is a high molecular weight polymer and is not expected to be absorbed into ocular tissues.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of NAVSTEL® Solution has not been investigated. The hypromellose in NAVSTEL® has been demonstrated to be non-mutagenic in the *in vitro* Ames assay and the bacterial reverse mutation assay. A similar modified cellulose polymer (methylcellulose) was also non-mutagenic at concentrations up to 5,000 mg/kg in the rat bone marrow cytogenic assay. Fertility studies have not been conducted with hypromellose; however, rats fed a diet of up to 5% methylcellulose had no significant adverse effects relative to reproductive function.

14 CLINICAL STUDIES

Results from clinical studies in patients undergoing cataract surgery demonstrated that NAVSTEL® Solution was an effective irrigating solution for anterior segment surgical procedures and significantly reduced turbulent flow during phacoemulsification. Results from an additional clinical study demonstrated that NAVSTEL® was an effective irrigating solution for posterior segment surgical procedures.

16 HOW SUPPIED/STORAGE AND HANDLING

NAVSTEL® Solution is supplied in two sizes, 250 mL and 500 mL. Each size consists of two packages for reconstitution prior to use: 250 mL size consists of a 250 mL glass bottle containing 240 mL (Part I) and a 10 mL glass vial (Part II); both using grey butyl stoppers and aluminum seals with polypropylene flip-off caps; 500 mL size consists of a 500 mL glass bottle containing 480 mL (Part I) and a 20 mL glass vial (Part II); both using grey butyl stoppers and aluminum seals with polypropylene flip-off caps. Each of the two packages also contains a Vacuum Transfer Device.

Product must be reconstituted prior to use *[see Dosage and Administration (2)*].

- 250 mL fill **NDC** 0065-0810-24
- 500 mL fill **NDC** 0065-0810-48

Storage

Store between 2° and 25°C (36° and 77°F). DO NOT FREEZE.

Handling

Solution should be used when between 15° and 25°C (59° and 77°F). Discard prepared solution after 6 hours.

17 PATIENT COUNSELING INFORMATION

Patients should be advised to seek immediate care from an ophthalmologist if the eye becomes red, sensitive to light, pain increases or a decrease in vision develops in the days following NAVSTEL® Solution administration.

Rx Only

U.S. Patent Nos. 5,409,904; 5,578,578; and 7,084,130

ALCON®
ALCON LABORATORIES, INC.
Fort Worth, Texas 76134 USA