



U.S. Food and Drug Administration

Final Administrative Order (OTC000023)

Over-the-Counter Monograph M018: Ophthalmic Drug Products for Over-the-Counter Human Use (Posted April 4, 2022)

I. Summary

Over-the-Counter Monograph M018: Ophthalmic Drug Products for Over-the-Counter Human Use, as set forth in this document, is a final administrative order (final order) deemed by section 505G(b)(8) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355h(b)(8)), and effective upon enactment of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), Public Law 116-136, on March 27, 2020.

II. Background

The CARES Act added section 505G of the FD&C Act, which revised the framework for the regulation of over-the-counter (OTC) monograph drug products. Among other things, section 505G of the FD&C Act provides as a baseline status that, as of the date of enactment of the CARES Act, drugs that satisfy certain requirements described in section 505G(a)(1) or (2) are deemed to be generally recognized as safe and effective under section 201(p)(1) of the FD&C Act (21 U.S.C. 321(p)(1)), not a new drug under section 201(p), and not subject to section 503(b)(1) of the FD&C Act (21 U.S.C. 353(b)(1)). To obtain this status, among other things, a drug either must be one that is in conformity with the requirements for nonprescription use of a final monograph issued under part 330 (21 CFR part 330) (except as provided in section 505G(a)(2)),¹ as well as other requirements,² or must be one that is (i) classified in category I for safety and effectiveness under a tentative final monograph that is the most recently applicable proposal or determination issued under part 330, and (ii) in conformity with the proposed requirements for nonprescription use of such tentative final monograph and any applicable subsequent determination by the Secretary, as well as other requirements.³ Other applicable requirements in section 505G(a)(1) of the FD&C Act include conditions or requirements under section 505G(b) of the FD&C Act.

Complementary to the requirements for conformity to tentative final or final monographs described in section 505G(a)(1) and (2) of the FD&C Act, Congress provided that, under section

¹ Section 505G(a)(2) of the FD&C Act is inapplicable here. It establishes the applicable requirements in terms of conformity with a final monograph, for purposes of section 505G(a)(1)(A)(i) of the FD&C Act, for sunscreen drugs subject to section 505G of the FD&C Act.

² Section 505G(a)(1)(A) of the FD&C Act.

³ Section 505G(a)(1)(B) of the FD&C Act.

505G(b)(8) of the FD&C Act, a final monograph or tentative final monograph that establishes conditions of use for a drug described in section 505G(a)(1) or (2) and that represents the most recently promulgated version of the conditions of use, including as modified, in whole or in part, by any proposed or final rule, is deemed to be a final order. The final order may be amended, revoked, or otherwise modified in accordance with the procedures under section 505G of the FD&C Act. Under section 505G(b)(8)(C) of the FD&C Act, the deemed establishment of a final order is construed to include technical amendments necessary to ensure that the order is appropriately harmonized, in terms of terminology or cross-references, with the applicable provisions of the FD&C Act (and regulations) and any other final orders issued under section 505G of the FD&C Act.

In the *Federal Register* of March 4, 1988 (53 FR 7076 at 7090), FDA issued a final OTC monograph under the procedure in part 330, establishing conditions under which OTC ophthalmic drug products are generally recognized as safe and effective (GRASE). This final OTC monograph was codified in 21 CFR part 349 and subsequently amended by final rules issued on June 21, 2000 (65 FR 38426 at 38428), February 19, 2003 (68 FR 7919 at 7921), and June 3, 2003 (68 FR 32981 at 32982).

In the *Federal Register* of February 19, 2003 (68 FR 7951 at 7955), FDA issued a proposed rule to amend the OTC monograph for OTC ophthalmic drug products to include OTC emergency first aid eye wash drug products.

Accordingly, this final order for OTC ophthalmic drug products incorporates the requirements of the final monograph for OTC ophthalmic drug products issued under part 330, as codified in part 349 as of March 27, 2020 and the proposed rule issued in the *Federal Register* on February 19, 2003 (68 FR 7951), with technical amendments including consolidating a professional use provision into its own part.

III. Final Administrative Order

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SOURCE: 53 FR 7090, Mar. 4, 1988, unless otherwise noted.

Part A—General Provisions

§ M018.1 Scope

An over-the-counter (OTC) ophthalmic drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this OTC monograph and each of the general conditions established in 21 CFR 330.1.

§ M018.3 Definitions

As used in this OTC monograph:

- (a) Ophthalmic drug product. A drug product, which should be sterile in accordance with 21 CFR 200.50, to be applied to the eyelid or instilled in the eye.
- (b) Astringent. A locally acting pharmacologic agent that, by precipitating protein, helps to clear mucus from the outer surface of the eye.
- (c) Buffering agent. A substance that stabilizes the pH of solutions against changes produced by introduction of acids or bases from such sources as drugs, body fluids, tears, etc.
- (d) Demulcent. An agent, usually a water-soluble polymer, that is applied topically to the eye to protect and lubricate mucous membrane surfaces and relieve dryness and irritation.

(e) Emollient. An agent, usually a fat or oil, that is applied locally to eyelids to protect or soften tissues and to prevent drying and cracking.

(f) Eyewash, eye lotion, irrigating solution. A sterile aqueous solution intended for washing, bathing, or flushing the eye.

(g) Hypertonicity agent. An agent that exerts an osmotic gradient greater than that present in body tissues and fluids, so that water is drawn from the body tissues and fluids across semipermeable membranes. Applied topically to the eye, a hypertonicity agent creates an osmotic gradient that draws water out of the cornea.

(h) Isotonicity. A state or quality in which the osmotic pressure in two fluids is equal.

(i) Vasoconstrictor. A pharmacologic agent that, when applied topically to the mucous membranes of the eye, causes transient constriction of conjunctival blood vessels.

Part B—Active Ingredients

§ M018.10 Ophthalmic astringent

The active ingredient and its concentration in the product are as follows: Zinc sulfate, 0.25 percent.

§ M018.12 Ophthalmic demulcents

The active ingredients of the product consist of any of the following, within the established concentrations for each ingredient:

(a) Cellulose derivatives:

(1) Carboxymethylcellulose sodium, 0.2 to 2.5 percent.

(2) Hydroxyethyl cellulose, 0.2 to 2.5 percent.

(3) Hypromellose, 0.2 to 2.5 percent.

(4) Methylcellulose, 0.2 to 2.5 percent.

(b) Dextran 70, 0.1 percent when used with another polymeric demulcent agent in § M018.12.

(c) Gelatin, 0.01 percent.

(d) Polyols, liquid:

(1) Glycerin, 0.2 to 1 percent.

- (2) Polyethylene glycol 300, 0.2 to 1 percent.
 - (3) Polyethylene glycol 400, 0.2 to 1 percent.
 - (4) Polysorbate 80, 0.2 to 1 percent.
 - (5) Propylene glycol, 0.2 to 1 percent.
- (e) Polyvinyl alcohol, 0.1 to 4 percent.
- (f) Povidone, 0.1 to 2 percent.

[53 FR 7090, Mar. 4, 1988, as amended at 68 FR 32982, June 3, 2003]

§ M018.14 Ophthalmic emollients

The active ingredients of the product consist of any of the following:

(a) Lanolin preparations:

- (1) Anhydrous lanolin, 1 to 10 percent in combination with one or more oleaginous emollient agents included in the OTC monograph.
- (2) Lanolin, 1 to 10 percent in combination with one or more oleaginous emollient agents included in the OTC monograph.

(b) Oleaginous ingredients:

- (1) Light mineral oil, up to 50 percent, in combination with one or more other emollient agents included in the OTC monograph.
- (2) Mineral oil, up to 50 percent, in combination with one or more other emollient agents included in the OTC monograph.
- (3) Paraffin, up to 5 percent, in combination with one or more other emollient agents included in the OTC monograph.
- (4) Petrolatum, up to 100 percent.
- (5) White ointment, up to 100 percent.
- (6) White petrolatum, up to 100 percent.
- (7) White wax, up to 5 percent, in combination with one or more other emollient agents included in the OTC monograph.

(8) Yellow wax, up to 5 percent, in combination with one or more other emollient agents included in the OTC monograph.

§ M018.16 Ophthalmic hypertonicity agent

The active ingredient and its concentration in the product is as follows: Sodium chloride, 2 to 5 percent.

§ M018.18 Ophthalmic vasoconstrictors

The active ingredient of the product consists of one of the following, within the established concentration for each ingredient:

- (a) Ephedrine hydrochloride, 0.123 percent.
- (b) Naphazoline hydrochloride, 0.01 to 0.03 percent.
- (c) Phenylephrine hydrochloride, 0.08 to 0.2 percent.
- (d) Tetrahydrozoline hydrochloride, 0.01 to 0.05 percent.

§ M018.20 Eyewashes

The active ingredient of the product is purified water. The product also contains suitable tonicity agents to establish isotonicity with tears, suitable agents for establishing pH and buffering to achieve the same pH as tears, and a suitable preservative agent.

[68 FR 7921, Feb. 19, 2003]

§ M018.22 Emergency first aid eyewashes

These products contain water, agents to achieve the pH within a range of 6.6 and 7.4, and a suitable antimicrobial preservative agent. Additionally, they may contain tonicity agents to establish isotonicity with tears and agents for buffering the pH.

[68 FR 7955, Feb. 19, 2003]

§ M018.30 Permitted combinations of active ingredients

The following combinations are permitted provided each active ingredient is present within the established concentration, and the product is labeled in accordance with § M018.79.

- (a) Any single ophthalmic astringent active ingredient identified in § M018.10 may be combined with any single ophthalmic vasoconstrictor active ingredient identified in § M018.18.

- (b) Any two or three ophthalmic demulcent active ingredients identified in § M018.12 may be combined.
- (c) Any single ophthalmic demulcent active ingredient identified in § M018.12 or any ophthalmic demulcent combination identified in § M018.30(b) may be combined with any single ophthalmic vasoconstrictor identified in § M018.18.
- (d) Any single ophthalmic astringent active ingredient identified in § M018.10 may be combined with any single ophthalmic vasoconstrictor active ingredient identified in § M018.18 and any single ophthalmic demulcent identified in § M018.12 or ophthalmic demulcent combination identified in § M018.30(b).
- (e) Any two or more emollient active ingredients identified in § M018.14 may be combined as necessary to give the product proper consistency for application to the eye.

Part C—Labeling

§ M018.50 Labeling of ophthalmic drug products

- (a) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this OTC monograph.
- (b) Where applicable, indications in this OTC monograph applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in § M018.50(b) may also be used, as provided in 21 CFR 330.1(c)(2), subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 352) relating to misbranding and the prohibition in section 301(d) of the FD&C Act (21 U.S.C. 331(d)) against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the FD&C Act (21 U.S.C. 355(a)).
- (c) The labeling of the product contains the following warnings, under the heading "Warnings":
- (1) For ophthalmic drug products packaged in multi-use containers. "To avoid contamination, do not touch tip of container to any surface. Replace cap after using."
 - (2) For ophthalmic drug products packaged in single-use containers. "To avoid contamination, do not touch tip of container to any surface. Do not reuse. Once opened, discard."
 - (3) For ophthalmic drug products containing mercury compounds used as a preservative. "This product contains (name and quantity of mercury-containing ingredient) as a preservative. Do not use this product if you are sensitive to" (select one of the following: "mercury" or "(insert name of mercury-containing ingredient) or any other ingredient containing mercury)."

§ M018.55 Labeling of ophthalmic astringent drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug, if any, and identifies the product as an "astringent" (select one of the following: "eye" or "ophthalmic") "(insert dosage form, e.g., drops)."

(b) Indications. The labeling of the product states, under the heading "Uses," the following phrase: "For the temporary relief of discomfort from minor eye irritations."

(c) Warnings. In addition to the warnings in § M018.50, the labeling of the product contains the following warnings under the heading "Warnings" for products containing any ingredient identified in § M018.10:

(1) "If you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 72 hours, discontinue use and consult a doctor."

(2) "If solution changes color or becomes cloudy, do not use."

(d) Directions. The labeling of the product contains the following information under the heading "Directions": Instill 1 to 2 drops in the affected eye(s) up to four times daily.

§ M018.60 Labeling of ophthalmic demulcent drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug(s), if any, and identifies the product as a "lubricant" or "demulcent (lubricant)" (select one of the following: "eye" or "ophthalmic") "(insert dosage form, e.g., drops)."

(b) Indications. The labeling of the product states, under the heading "Uses," one or more of the following phrases:

(1) "For the temporary relief of burning and irritation due to dryness of the eye."

(2) "For the temporary relief of discomfort due to minor irritations of the eye or to exposure to wind or sun."

(3) "For use as a protectant against further irritation or to relieve dryness of the eye."

(4) "For use as a lubricant to prevent further irritation or to relieve dryness of the eye."

(c) Warnings. In addition to the warnings in § M018.50, the labeling of the product contains the following warnings under the heading "Warnings" for products containing any ingredient identified in § M018.12:

(1) "If you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 72 hours, discontinue use and consult a doctor."

(2) "If solution changes color or becomes cloudy, do not use."

(d) Directions. The labeling of the product contains the following information under the heading "Directions": Instill 1 or 2 drops in the affected eye(s) as needed.

§ M018.65 Labeling of ophthalmic emollient drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug(s), if any, and identifies the product as a "lubricant" or "emollient (lubricant)" (select one of the following: "eye" or "ophthalmic") "(insert dosage form, e.g., ointment)."

(b) Indications. The labeling of the product states, under the heading "Uses," one or more of the following phrases:

(1) "For the temporary relief of burning and irritation due to dryness of the eye."

(2) "For the temporary relief of discomfort due to minor irritations of the eye or to exposure to wind or sun."

(3) "For use as a protectant against further irritation or to relieve dryness of the eye."

(4) "For use as a lubricant to prevent further irritation or to relieve dryness of the eye."

(c) Warnings. In addition to the warnings in § M018.50, the labeling of the product contains the following warnings under the heading "Warnings" for products containing any ingredient identified in § M018.14: "If you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 72 hours, discontinue use and consult a doctor."

(d) Directions. The labeling of the product contains the following information under the heading "Directions": Pull down the lower lid of the affected eye and apply a small amount (one-fourth inch) of ointment to the inside of the eyelid.

§ M018.70 Labeling of ophthalmic hypertonicity drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug, if any, and identifies the product as a "hypertonicity" (select one of the following: "eye" or "ophthalmic") "(insert dosage form, e.g., drops)."

(b) Indications. The labeling of the product states, under the heading "Uses," the following phrase: "For the temporary relief of corneal edema."

(c) Warnings. In addition to the warnings in § M018.50, the labeling of the product contains the following warnings under the heading "Warnings" for products containing any ingredient identified in § M018.16:

(1) "Do not use this product except under the advice and supervision of a doctor. If you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists, consult a doctor."

(2) "This product may cause temporary burning and irritation on being instilled into the eye."

(3) "If solution changes color or becomes cloudy, do not use."

(d) Directions. The labeling of the product contains the following information under the heading "Directions": Instill 1 or 2 drops in the affected eye(s) every 3 or 4 hours, or as directed by a doctor.

§ M018.75 Labeling of ophthalmic vasoconstrictor drug products

(a) Statement of identity. The labeling of the product contains the established name of the drug(s), if any, and identifies the product as a "redness reliever" or "vasoconstrictor (redness reliever)" (select one of the following: "eye" or "ophthalmic") "(insert dosage form, e.g., drops)."

(b) Indications. The labeling of the product states, under the heading "Uses," the following phrase: "Relieves redness of the eye due to minor eye irritations."

(c) Warnings. In addition to the warnings in § M018.50, the labeling of the product contains the following warnings under the heading "Warnings" for products containing any ingredient identified in § M018.18:

(1) "If you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 72 hours, discontinue use and consult a doctor."

(2) "Ask a doctor before use if you have [in bold type] narrow angle glaucoma."

(3) "Overuse of this product may produce increased redness of the eye."

(4) "If solution changes color or becomes cloudy, do not use."

(5) "When using this product [in bold type] pupils may become enlarged temporarily."

(d) Directions. The labeling of the product contains the following information under the heading "Directions": Instill 1 to 2 drops in the affected eye(s) up to four times daily.

[53 FR 7090, Mar. 4, 1988, as amended at 65 FR 38428, June 21, 2000]

§ M018.78 Labeling of eyewash drug products

(a) Statement of identity. The labeling of the product identifies the product with one or more of the following terms: "eyewash," "eye irrigation," or "eye irrigating solution."

(b) Indications. The labeling of the product states, under the heading "Uses," one of the following phrases:

(1) "For" (select one of the following: "flushing," "irrigating," "cleansing," "washing," or "bathing") "the eye to remove" (select one or more of the following: "loose foreign material," "air pollutants (smog or pollen)," or "chlorinated water").

(2) "For" (select one of the following: "flushing," "irrigating," "cleansing," "washing," or "bathing") "the eye to help relieve" (select one or more of the following: "irritation," "discomfort," "burning," "stinging," "smarting," or "itching") "by removing" (select one or more of the following: "loose foreign material," "air pollutants (smog or pollen)," or "chlorinated water").

(c) Warnings. In addition to the warnings in § M018.50, the labeling of the product contains the following warnings under the heading "Warnings" for all eyewash products:

(1) "If you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists, consult a doctor."

(2) "Obtain immediate medical treatment for all open wounds in or near the eyes."

(3) "If solution changes color or becomes cloudy, do not use."

(d) Directions. The labeling of the product contains the following information under the heading "Directions":

(1) For eyewash products intended for use with an eyecup. Rinse cup with clean water immediately before each use. Avoid contamination of rim and inside surfaces of cup. Fill cup half full and apply the cup to the affected eye, pressing tightly to prevent the escape of the liquid, and tilt the head backward. Open eyelids wide and rotate eyeball to ensure thorough bathing with the wash or lotion. Rinse cup with clean water after each use.

(2) For eyewash products intended for use with a nozzle applicator. Flush the affected eye as needed, controlling the rate of flow of solution by pressure on the bottle.

[53 FR 7090, Mar. 4, 1988, as amended at 68 FR 7921, Feb. 19, 2003]

§ M018.79 Labeling of permitted combinations of active ingredients

Statements of identity, indications, warnings, and directions for use, respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) Statement of identity. For a combination drug product that has an established name, the labeling of the product states the established name of the combination drug product, followed by the statement of identity for each ingredient in the combination, as established in the statement of identity sections of this OTC monograph. For a combination drug product that does not have an established name, the labeling of the product states the statement of identity for each ingredient in the combination, as established in the statement of identity sections of this OTC monograph.

(b) Indications. The labeling of the product states, under the heading "Uses," the indication(s) for each ingredient in the combination, as established in the indications sections of this OTC monograph.

(c) Warnings. The labeling of the product states, under the heading "Warnings," the warning(s) for each ingredient in the combination, as established in the warnings sections of this OTC monograph.

(d) Directions. The labeling of the product states, under the heading "Directions," directions that conform to the directions established for each ingredient in the directions sections of this OTC monograph. When the time intervals or age limitations for administration of the individual ingredients differ, the directions for the combination product may not exceed any maximum dosage limits established for the individual ingredients in the applicable OTC monograph.

§ M018.82 Labeling of emergency first aid eyewash drug products

(a) Statement of identity. The labeling of the product identifies the product with one of the following: "Emergency first aid eyewash," "First aid eye rinse," or "Emergency eyewash."

(b) Indications. The labeling of the product states, under the heading "Uses," "for" (select one of the following: "flushing," or "irrigating") "the eye to reduce chances of severe injury caused by acid, alkali, or particulate contamination."

(c) Warnings. In addition to the warnings in § M018.50 (the "Replace cap after using," warning in § M018.50(c)(1) should only be used if applicable), the labeling of the product contains the following warnings under the heading "Warnings" for all emergency eyewash products:

(1) "Do not use [in bold type] [bullet]⁴ for injection [bullet] in intraocular surgery [bullet] internally [bullet] if solution changes color or becomes cloudy."

⁴ See 21 CFR 201.66(b)(4) for definition of bullet symbol.

(2) “Ask a doctor if you have [in bold type] [bullet] eye pain [bullet] changes in vision [bullet] redness or irritation of the eye after use [bullet] an injury caused by an alkali.”

(d) Directions. The labeling of the product states, as appropriate, under the heading “Directions,” “[bullet] do not dilute solution or reuse bottle [in bold type] [bullet] hold container a few inches above the eye [bullet] control rate of flow by pressure on bottle [bullet] flush affected area for a minimum of 20 minutes [bullet] continue flushing with water if necessary [bullet] obtain medical treatment.”

(1) For products packaged in a container that also serves as an eyecup. The labeling states “[bullet] use only unopened bottle [bullet] remove safety seal and cap [bullet] avoid contamination of rim of bottle [bullet] place rim over affected eye [bullet] tilt head backward [bullet] open eyelids wide [bullet] thoroughly bathe eye with solution [bullet] allow solution to flow away from eye.” The directions in § M018.82(d) shall be placed in sequence with the directions provided in § M018.82(d), as appropriate.

(2) For products intended for use with a nozzle applicator. The labeling states “[bullet] flush affected eye as needed [bullet] control flow of solution by pressure on bottle.”

(3) For products that use a concentrate with potable water. The word “concentrate” shall be in bold type. Labeling must provide adequate directions for adding the concentrate to potable water to obtain a solution that meets the requirements of § M018.22. The directions shall also state that the concentrate should be added to potable water to have a fully constituted solution available in advance of an emergency.

[68 FR 7955, Feb. 19, 2003]

Part D—Professional Use

§ M018.83 Professional labeling

The labeling of any OTC ophthalmic demulcent drug product provided to health professionals (but not to the general public) may contain instructions for the use of these products in professional eye examinations (i.e., gonioscopy, electroretinography).