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R_U and R_S are the peak response ratios of warfarin to propylparaben obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Warfarin Sodium Tablets

» Warfarin Sodium Tablets contain not less than 90.0 percent and not more than 105.0 percent of the labeled amount of $C_{19}H_{15}NaO_4$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—*USP Warfarin RS.*

Identification—

A: The retention time of the major peak obtained from the *Assay preparation* corresponds to that obtained from the *Standard preparation*, both relative to the internal standard, obtained as directed in the *Assay*.

B: Triturate a quantity of finely powdered Tablets, equivalent to about 200 mg of warfarin sodium, with 50 mL of water, centrifuge, and filter the supernatant liquid. Extract with 50 mL of ether, transfer the aqueous layer to a second separator, and discard the ether. Adjust with hydrochloric acid to a pH of less than 3, using short-range pH indicator paper, and extract with 25 mL of chloroform. Transfer the chloroform layer to another separator, extract with 50 mL of sodium hydroxide solution (1 in 250), and discard the chloroform. Transfer the aqueous layer to a beaker, and adjust with hydrochloric acid to a pH of less than 3 (using the pH indicator paper) to precipitate the warfarin. Stir the mixture and allow the precipitate to coagulate. Filter, and wash the precipitate with four 5-mL portions of water. If the precipitate is not white or practically white, dissolve it in a minimum volume of sodium hydroxide solution (1 in 250), dilute with water to 50 mL, and repeat the foregoing procedure, beginning with "Extract with 50 mL of ether." Dry the precipitate in a vacuum over phosphorus pentoxide for 4 hours: the infrared absorption spectrum of the warfarin so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of *USP Warfarin RS*.

C: Dissolve a quantity of finely powdered Tablets, equivalent to about 100 mg of warfarin sodium, in 25 mL of water, and filter, if necessary: a 5-mL portion of the filtrate responds to the tests for *Sodium* ⟨191⟩.

Dissolution ⟨711⟩—

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay*.

Internal standard solution—Prepare a solution of propylparaben in water containing, in each mL, an amount of propylparaben equivalent to 0.0025 times the labeled amount, in mg, of warfarin sodium in each Tablet. [NOTE—A small amount of methanol may be used, if necessary, to dissolve the propylparaben.]

Standard stock solution—Dissolve an accurately weighed quantity of USP Warfarin RS in water to obtain a solution having a known concentration of about $0.0011L$ mg per mL, L being the labeled amount, in mg, of warfarin sodium in the Tablets. [NOTE—Use a small amount of 0.1 *N* sodium hydroxide to aid the dissolution.]

Standard solution—To 3.0 mL of *Standard stock solution*, add 1.0 mL of *Internal standard solution*, and mix.

Test solution—To a filtered 3.0-mL aliquot of the solution under test, add 1.0 mL of *Internal standard solution*, and mix.

Procedure—Separately inject equal volumes (about 40 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of warfarin sodium dissolved by the formula:

$$(330.32/308.34)(900C)(R_U/R_S),$$

in which C is the concentration, in mg per mL, of USP Warfarin RS in the *Standard stock solution*, 330.32 and 308.34 are the molecular weights of warfarin sodium and warfarin, respectively, and R_U and R_S are the ratios of the peak responses of warfarin to those of propylparaben obtained from the *Test solution* and the *Standard solution*, respectively.

Tolerances—Not less than 80% (Q) of the labeled amount of $C_{19}H_{15}NaO_4$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

pH 7.4 buffer and *Chromatographic system*—Proceed as directed in the *Assay* under *Warfarin Sodium*.

Solvent mixture—Prepare a mixture of *pH 7.4 buffer* and acetonitrile (85:15).

Mobile phase—Prepare a filtered and degassed mixture of methanol, water, and glacial acetic acid (68:32:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution of propylparaben in acetonitrile having a concentration of 1 mg per mL.

Diluted internal standard solution—Dilute a volume of *Internal standard solution* with *Solvent mixture* to obtain a solution having a concentration of 0.1 mg of propylparaben per mL.

Standard preparation—Transfer about 62.5 mg of USP Warfarin RS, accurately weighed, to a 200-mL volumetric flask, and dissolve in 78 mL of 0.1 *N* sodium hydroxide. Add 50 mL of 0.2 *M* monobasic potassium phosphate, dilute with water to volume, and mix. Transfer 15.0 mL of this solution to a 50-mL volumetric flask. Add 5.0 mL of *Internal standard solution*, and dilute with *Solvent mixture* to volume.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 5 mg of warfarin sodium, to a 50-mL volumetric flask, and add 5 mL of *Internal standard solution* and about 30 mL of *Solvent mixture*. Sonicate for 10 minutes, and then shake by mechanical means for 60 minutes. Dilute with solvent mixture to volume, and filter.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{19}H_{15}NaO_4$ in the portion of Tablets taken by the formula:

$$(330.32/308.34)C(R_U/R_S),$$

in which 330.32 and 308.34 are the molecular weights of warfarin sodium and warfarin, respectively, C is the concentration, in mg per mL, of USP Warfarin RS in the *Standard preparation*, and R_U and R_S are the ratios of the peak responses of warfarin to those of propylparaben obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Water for Injection

» Water for Injection is water purified by distillation or by reverse osmosis. It contains no added substance.

NOTE—Water for Injection is intended for use as a solvent for the preparation of parenteral solutions. Where used for the preparation of parenteral solutions subject to final sterilization, use suitable means to minimize microbial growth, or first render the Water for Injection sterile and thereafter protect it from microbial contamination. For parenteral solutions that are prepared under aseptic conditions and are not sterilized by appropriate filtration or in the final container, first render the Water for Injection sterile and, thereafter, protect it from microbial contamination.

Packaging and storage—Where packaged, preserve in tight containers. Where packaged, it may be stored at a temperature below or above the range in which microbial growth occurs.

USP Reference standards ⟨11⟩—*USP Endotoxin RS*.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.25 USP Endotoxin Unit per mL.

Bacteriostatic Water for Injection

» Bacteriostatic Water for Injection is Sterile Water for Injection containing one or more suitable antimicrobial agents.

NOTE—Use Bacteriostatic Water for Injection with due regard for the compatibility of the antimicrobial agent or agents it contains with the particular medicinal substance that is to be dissolved or diluted.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type II glass, of not larger than 30-mL size.

Labeling—Label it to indicate the name(s) and proportion(s) of the added antimicrobial agent(s). Label it also to include the statement "NOT FOR USE IN NEWBORNS" in boldface capital letters on the label immediately under the official name, printed in a contrasting color, preferably red. Alternatively, the statement may be placed prominently elsewhere on the label if the statement is enclosed within a box.

USP Reference standards ⟨11⟩—*USP Endotoxin RS*.

Antimicrobial agent(s)—It meets the requirements under *Antimicrobial Preservatives—Effectiveness* ⟨51⟩, and meets the labeled claim for content of the antimicrobial agent(s), as determined by the method set forth under *Antimicrobial Agents—Content* ⟨341⟩.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.5 USP Endotoxin Unit per mL.

Sterility—It meets the requirements under *Sterility Tests* ⟨71⟩.

pH ⟨791⟩: between 4.5 and 7.0, determined potentiometrically in a solution prepared by the addition of 0.30 mL of saturated potassium chloride solution to 100 mL of test specimen.

Particulate matter ⟨788⟩: meets the requirements under *Small-volume Injections*.

Other requirements—It meets the requirements of the tests for *Sulfate*, *Calcium*, *Carbon dioxide*, and *Heavy metals* under *Sterile Water for Injection*.

Sterile Water for Inhalation

» Sterile Water for Inhalation is water purified by distillation or by reverse osmosis and rendered sterile. It contains no antimicrobial agents, except where used in humidifiers or other similar devices and where liable to contamination over a period of time, or other added substances.

NOTE—Do not use Sterile Water for Inhalation for parenteral administration or for other sterile compendial dosage forms.

Packaging and storage—Preserve in single-dose containers.

Labeling—Label it to indicate that it is for inhalation therapy only and that it is not for parenteral administration.

USP Reference standards ⟨11⟩—*USP Endotoxin RS*.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.5 USP Endotoxin Unit per mL.

Sterility—It meets the requirements under *Sterility Tests* ⟨71⟩.

pH ⟨791⟩: between 4.5 and 7.5, in a solution containing 0.30 mL of saturated potassium chloride solution per 100 mL of test specimen.

Chloride—To 20 mL in a color-comparison tube add 5 drops of nitric acid and 1 mL of silver nitrate TS, and gently mix: any turbidity formed within 10 minutes is not greater than that produced in a similarly treated control consisting of 20 mL of *High-purity Water* (see under *Chemical Resistance—Glass Containers* ⟨661⟩), containing 10 µg of Cl, viewed downward over a dark surface with light entering the tubes from the sides (0.5 ppm).

Other requirements—It meets the requirements of the tests for *Sulfate*, *Calcium*, *Carbon dioxide*, and *Heavy metals* under *Purified Water* and of the tests for *Ammonia*, *Oxidizable substances*, and *Total solids* under *Sterile Water for Injection*.

Sterile Water for Injection

» Sterile Water for Injection is Water for Injection sterilized and suitably packaged. It contains no antimicrobial agent or other added substance.

Packaging and storage—Preserve in single-dose glass or plastic containers, of not larger than 1-liter size. Glass containers are preferably of Type I or Type II glass.

Labeling—Label it to indicate that no antimicrobial or other substance has been added, and that it is not suitable for intravascular injection without its first having been made approximately isotonic by the addition of a suitable solute.

USP Reference standards ⟨11⟩—*USP Endotoxin RS*.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.25 USP Endotoxin Unit per mL.

Sterility—It meets the requirements under *Sterility Tests* ⟨71⟩.

Particulate matter ⟨788⟩: meets the requirements under *Small-volume Injections*.

Ammonia—For Sterile Water for Injection in containers having a fill volume of less than 50 mL, dilute 50 mL with 50 mL of *High-purity Water* (see *Reagents* under *Containers* ⟨661⟩), and use this dilution as the test solution; where the fill volume is 50 mL or more, use 100 mL of Sterile Water for Injection as the test solution. To 100 mL of the test solution add 2 mL of alkaline mercuric-potassium iodide TS: any yellow color produced immediately is not darker than that of a control containing 30 µg of added NH_3 in *High-purity Water* (see *Reagents* under *Containers* ⟨661⟩) (0.6 ppm for Sterile Water for Injection in containers having a fill volume of less than 50 mL; 0.3 ppm where the fill volume is 50 mL or more).

Chloride—To 20 mL in a color-comparison tube add 5 drops of nitric acid and 1 mL of silver nitrate TS, and gently mix: any turbidity formed within 10 minutes is not greater than that produced in a similarly treated control consisting of 20 mL of *High-purity Water* (see under *Reagents* in *Containers* ⟨661⟩) containing 10 µg of Cl (0.5 ppm), viewed downward over a dark surface with light entering the tubes from the sides.

Oxidizable substances—To 100 mL add 10 mL of 2 *N* sulfuric acid, and heat to boiling. For Sterile Water for Injection in containers having a fill volume of less than 50 mL, add 0.4 mL of 0.1 *N* potassium permanganate, and boil for 5 minutes; where the fill volume is 50 mL or more, add 0.2 mL of 0.1 *N* potassium permanganate, and boil for 5 minutes. If a precipitate forms, cool in an ice bath to room temperature, and filter through a sintered-glass filter: the pink color does not completely disappear.

Total solids—Proceed as directed in the test for *Total solids* under *Purified Water*. The following limits apply for Sterile Water for Injection in containers having a fill volume of less than 30 mL, 0.004%; where the fill volume is 30 mL or more, but less than 100 mL, 0.003%; and for a fill volume of 100 mL or more, 0.002%.

Other requirements—It meets the requirements of the tests for *pH*, *Sulfate*, *Calcium*, *Carbon dioxide*, and *Heavy metals* under *Purified Water*.

Sterile Water for Irrigation

» Sterile Water for Irrigation is Water for Injection sterilized and suitably packaged. It contains no antimicrobial agent or other added substance.

Packaging and storage—Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I or Type II glass. The container may contain a volume of more than 1 liter, and may be designed to empty rapidly.

Labeling—Label it to indicate that no antimicrobial or other substance has been added. The designations "For irrigation only" and "Not for injection" appear prominently on the label.

USP Reference standards ⟨11⟩—*USP Endotoxin RS*.

Other requirements—It meets the requirements of all of the tests under *Sterile Water for Injection* except the test for *Particulate matter* ⟨788⟩.

Purified Water

H_2O 18.02

» Purified Water is water obtained by distillation, ion-exchange treatment, reverse osmosis, or other suitable process. It is prepared from water complying with the regulations of the federal Environmental Protection Agency with respect to drinking water. It contains no added substance.

NOTE—Purified Water is intended for use as an ingredient in the preparation of compendial dosage forms. Where used for sterile dosage forms, other than for parenteral administration, process the article to meet the requirements under Sterility Tests ⟨71⟩, or first render the Purified Water sterile and thereafter protect it from microbial contamination. Do not use Purified Water in preparations intended for parenteral administration. For such purposes use Water for Injection, Bacteriostatic Water for Injection, or Sterile Water for Injection.

Packaging and storage—Where packaged, preserve in tight containers.

Labeling—Where packaged, label it to indicate the method of preparation.

pH ⟨791⟩: between 5.0 and 7.0, determined potentiometrically in a solution prepared by the addition of 0.30 mL of saturated potassium chloride solution to 100 mL of test specimen.

Chloride—To 100 mL add 5 drops of nitric acid and 1 mL of silver nitrate TS: no opalescence is produced.

Sulfate—To 100 mL add 1 mL of barium chloride TS: no turbidity is produced.

Limit of ammonia—To 100 mL add 2 mL of alkaline mercuric-potassium iodide TS: any yellow color produced immediately is not darker than that of a control containing 30 µg of added NH_3 in *High-purity Water* (see under *Reagents* in *Containers* ⟨661⟩) [0.3 ppm].

Calcium—To 100 mL add 2 mL of ammonium oxalate TS: no turbidity is produced.

Carbon dioxide—To 25 mL add 25 mL of calcium hydroxide TS: the mixture remains clear.

Heavy metals—Adjust 40 mL of Purified Water with 1 *N* acetic acid to a pH of 3.0 to 4.0 (using short-range pH indicator paper), add 10 mL of freshly prepared hydrogen sulfide TS, and allow the liquid to stand for 10 minutes: the color of the liquid, when viewed downward over a white surface, is not darker than the color of a mixture of 50 mL of the same Purified Water with the same amount of 1 *N* acetic acid as was added to the test specimen, matched color-comparison tubes being used for the comparison.

Oxidizable substances—To 100 mL add 10 mL of 2 *N* sulfuric acid, and heat to boiling. Add 0.1 mL of 0.1 *N* potassium permanganate, and boil for 10 minutes: the pink color does not completely disappear.

Total solids—Evaporate 100 mL on a steam bath to dryness, and dry the residue at 105° for 1 hour: not more than 1 mg of residue remains (0.001%).

Wax, Carnauba—*see* Wax, Carnauba NF
Wax, Cetyl Esters—*see* Cetyl Esters Wax NF
Wax, Emulsifying—*see* Wax, Emulsifying NF
Wax, Microcrystalline—*see* Wax, Microcrystalline NF
Wax, White—*see* Wax, White NF
Wax, Yellow—*see* Wax, Yellow NF

White Lotion

» Prepare White Lotion as follows:

Zinc Sulfate	40 g
Sulfurated Potash	40 g
Purified Water, a sufficient quantity, to make	1000 mL

Dissolve the Zinc Sulfate and the Sulfurated Potash separately, each in 450 mL of Purified Water, and filter each solution. Add the sulfurated potash solution slowly to the zinc sulfate solution with constant stirring. Then add the required amount of purified water, and mix.

NOTE—Prepare the Lotion fresh, and shake it thoroughly before dispensing.

Packaging and storage—Dispense in tight containers.

Witch Hazel

» Witch Hazel is a clear, colorless distillate prepared from recently cut and partially dried dormant twigs of *Hamamelis virginiana* Linné.

Prepare Witch Hazel as follows. Macerate a weighed amount of the twigs for about 24 hours in about twice their weight of water, then distil until not less than 800 mL and not more than 850 mL of clear, colorless distillate is obtained from each 1000 g of the twigs taken. Add 150 mL of Alcohol to each 850 mL of distillate, and mix thoroughly.

Packaging and storage—Preserve in tight containers, and avoid exposure to excessive heat.

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