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Mupirocin Cream

» Mupirocin Cream contains a quantity of Mupirocin Calcium equivalent to not less than 90.0 percent and not more than 120.0 percent of the labeled amount of mupirocin ($C_{26}H_{44}O_9$). It may contain one or more suitable buffers, dispersants, and preservatives.

Packaging and storage—Preserve in collapsible tubes or well-closed containers. Store at 25°, excursions permitted between 15° and 30°.

Labeling—Label it to indicate that it contains Mupirocin Calcium and its equivalent content of mupirocin.

USP Reference standards ⟨11⟩—
USP Mupirocin Lithium RS

Identification—The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Minimum fill ⟨755⟩: meets the requirements.

pH ⟨791⟩: between 6.0 and 8.0.

Microbial enumeration tests ⟨61⟩ and Tests for specified microorganisms ⟨62⟩—It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa.* The total aerobic microbial count does not exceed 100 cfu per g.

Related compounds—

0.1 M Ammonium acetate, Solution A, Solution B, Mobile phase, and *pH 6.3 Phosphate buffer*— Proceed as directed in the *Assay*.

Sodium acetate solution—Add 5.8 mL of glacial acetic acid to 900 mL of water, adjust with sodium hydroxide TS to a pH of 4.0, dilute with water to 1000 mL, and mix.

Tetrahydrofuran solution—Mix 750 mL of tetrahydrofuran and 250 mL of water.

Sodium acetate and tetrahydrofuran solution—Prepare a mixture of *Sodium acetate solution* and *Tetrahydrofuran solution* (50:50).

System suitability solution—Use the *Standard preparation,* prepared as directed in the *Assay*.

Test stock solution—Transfer an accurately weighed quantity of Cream, equivalent to about 50 mg of mupirocin, to a screw-capped centrifuge tube. Add 5.0 mL of *Tetrahydrofuran solution,* cap, and disperse the Cream by mixing on a vortex mixer and shaking. Add 5.0 mL of *Sodium acetate solution,* cap, and mix. Centrifuge for about 15 minutes. Withdraw the lower layer from the tube, pass it through a filter having a 0.5-µm or finer porosity, and use the filtrate.

Test solution—Transfer 1.0 mL of the *Test stock solution* to a 50-mL volumetric flask, dilute with *Sodium acetate and tetrahydrofuran solution* to volume, mix, and pass through a filter having a 0.5-µm or finer porosity.

Chromatographic system (see *Chromatography ⟨621⟩*)—Prepare as directed in the *Assay*. Chromatograph the *Test stock solution,* and record the responses as directed for *Procedure.* Identify the peaks based on the relative retention times for mupirocin and related substances shown in *Table 1:* the resolution, *R,* between pseudomonic acid D and mupirocin is not less than 3. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the column efficiency for the mupirocin peak is not less than 7000 theoretical plates; the tailing factor for the mupirocin peak is not more than 1.75; and the relative standard deviation of the mupirocin peak for replicate injections is not more than 2%.

Change to read:

Procedure—[Note—Ensure that buffers, dispersants, or preservatives in the formulation do not interfere with quantification of either impurities or degradation products.] Separately inject equal volumes (about 20 µL) of the *Test stock solution* and the *Test solution* into the chromatograph, and measure the peak responses for all of the peaks that do not correspond to buffers, dispersants, or preservatives. Calculate the percentage of each related compound and degradation product relative to mupirocin in the portion of Cream taken by the formula:

$$(r_i/r_M)(100/50)$$

in which r_i is the peak response for each related compound or degradation product obtained from the *Test stock solution;* r_M is the peak response of the mupirocin peak obtained from the *Test solution;* and 50 is the dilution factor for the *Test solution*.

Table 1

Name	Relative Retention Time	Limit (%)
Pseudomonic acid F[1]	0.36	NMT 1.2

Name	Relative Retention Time	Limit (%)
Mupirocin impurity 1[2]	0.6	NMT 8.5
Mupirocin impurity 2[3]	0.63	NMT 16
Pseudomonic acid D[4]	0.75	NMT 3.0
Pseudomonic acid B[5]	0.9	NMT 1.2
Mupirocin	1.0	—
Mupirocin impurity 3[6]	1.15	NMT 1.2
Mupirocin impurity 4[6]	1.23	NMT 1.2
Pseudomonic acid C[7]	2.03	NMT 1.2
Pseudomonic acid E[8]	2.24	NMT 1.2
Any other unspecified impurity	—	NMT 1.2
Total impurities	—	NMT 30

[1] 7-{(*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-Dihydroxy-5-({(2*S*,3*S*)-3-[(2*S*,3*S*)-3-hydroxybutan-2-yl]oxiran-2-yl}methyl)tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl
oxy}heptanoic acid.

▲[2] 9-{(*E*)-4-[(2*R*,3*aS*,6*S*,7*S*)-2-{(1*RS*,2*S*,3*S*)-1,3-Dihydroxy-2-methylbutyl}-7-hydroxyhexahydro-2*H*-furo[3,2-*c*]pyran-6-yl]-3-methylbut-2-enoyloxy}nonanoic acid. ▲ (ERR 1-May-2022)

[3] 9-{(*E*)-4-[(2*R*,3*RS*,4*aS*,7*S*,8*S*,8*aR*)-3,8-Dihydroxy-2-{(2*S*,3*S*)-3-hydroxybutan-2-yl}octahydropyrano[3,2-*c*]pyran-7-yl]-3-methylbut-2-enoyloxy}nonanoic acid.

[4] (*E*)-9-{(*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-Dihydroxy-5-({(2*S*,3*S*)-3-[(2*S*,3*S*)-3-hydroxy
butan-2-yl]oxiran-2-yl}methyl)tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyloxy}non-4-enoic acid.

[5] 9-{(*E*)-3-Methyl-4-[(2*S*,3*R*,4*S*,5*R*)-3,4,5-trihydroxy-5-({(2*S*,3*S*)-3-[(2*S*,3*S*)-3-hydroxybutan-2-yl]oxiran-2-yl}methyl)tetrahydro-2*H*-pyran-2-yl]but-2-enoyl
oxy}nonanoic acid.

[6] 9-((*E*)-4-{(2*S*,3*R*,4*R*,5*S*)-3,4-Dihydroxy-5-[(3-hydroxy-4,5-dimethyltet
rahydrofuran-2-yl)methyl]tetrahydro-2*H*-pyran-2-yl}-3-methylbut-2-enoyl
oxy)nonanoic acid.

[7] 9-((*E*)-4-{(2*S*,3*R*,4*R*,5*S*)-3,4-Dihydroxy-5-[(4*R*,5*S*,*E*)-5-hydroxy-4-methylhex-2-enyl]tetrahydro-2*H*-pyran-2-yl}-3-methylbut-2-enoyloxy)nonanoic acid.

[8] 11-{(*E*)-4-[(2*S*,3*R*,4*R*,5*S*)-3,4-Dihydroxy-5-({(2*S*,3*S*)-3-[(2*S*,3*S*)-3-hydroxybutan-2-yl]oxiran-2-yl}methyl)tetrahydro-2*H*-pyran-2-yl]-3-methylbut-2-enoyl
oxy}undecanoic acid.

Assay—

0.1 M Ammonium acetate—Dissolve about 7.7 g of ammonium acetate in about 900 mL of water in a 1000-mL volumetric flask, adjust with glacial acetic acid to a pH of 5.7, and dilute with water to volume.

Solution A—Prepare a filtered and degassed mixture of *0.1 M Ammonium acetate* and tetrahydrofuran (75:25).

Solution B—Prepare a filtered and degassed mixture of *0.1 M Ammonium acetate* and tetrahydrofuran (70:30).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

pH 6.3 Phosphate buffer—Dissolve 69 g of monobasic sodium phosphate in 800 mL of water, adjust with sodium hydroxide TS to a pH of 6.3, dilute with water to 1000 mL, and mix.

Standard preparation—Dissolve an accurately weighed portion of USP Mupirocin Lithium RS in *pH 6.3 Phosphate buffer*. Dilute an accurately measured volume of this solution quantitatively with the same solvent to obtain a solution having a known concentration of about 0.1 mg of mupirocin per mL.

Assay preparation—Transfer an accurately weighed quantity of Cream, equivalent to about 10 mg of mupirocin, to a 100-mL volumetric flask. Add 50 mL of *pH 6.3 Phosphate buffer* and 25 mL of tetrahydrofuran. Insert the stopper into the flask, mix on a vortex mixer, and shake for 1 to 3 minutes. Dilute with *pH 6.3 Phosphate buffer* to volume. Allow to stand until the oil layer separates out, then dilute the aqueous layer with *pH 6.3 Phosphate buffer* to volume. Repeat 2 to 3 times until as much of the oil layer has separated out as possible. After the final dilution, pass the final solution (bottom layer) through a filter having a 0.5-µm or finer porosity. This solution will have a nominal concentration of 0.1 mg per mL of mupirocin based on label claim.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 240-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L7. The flow rate is about 1 mL per minute. Maintain the column at a constant temperature up to 35°. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	100	0	equilibration
0–6	100	0	isocratic
6–35	100→0	0→100	linear gradient
35–55	0	100	isocratic
55–55.01	0→100	100→0	immediate
55.01–65	100	0	isocratic

Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure.* [Note—Pseudomonic acid D is a minor component that is always present in mupirocin calcium.] Identify the peaks by their retention times which are about 0.75 for pseudomonic acid D and 1.0 for mupirocin: the resolution, *R,* between pseudomonic acid D and mupirocin is not less than 3; the column efficiency for the mupirocin peak is not less than 7000 theoretical plates; the tailing factor for the mupirocin peak is not more than 1.75; and the relative standard deviation of the mupirocin peak for replicate injections is not more than 2%.

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 peak area responses for the major peaks. Calculate the percent label claim of mupirocin in the portion of Cream taken by the formula:

$$(P/1000)(C_S/C_U)(r_U/r_S)(100)$$

in which $P/1000$ is the potency of mupirocin, converted from µg per mg to mg per mg, in USP Mupirocin Lithium RS; C_S is the concentration, in mg per mL, of USP Mupirocin Lithium RS in the *Standard preparation;* C_U is the nominal concentration, in mg per mL, of Cream in the *Assay preparation;* and r_U and r_S are the mupirocin peak area responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MUPIROCIN CREAM	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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