Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Aug-2022
Document Type: USP Monographs
DocId: GUID-394AAB0C-38E6-4F4F-9609-30F9738AB56B_2_en-US
DOI: https://doi.org/10.31003/USPNF_M15595_02_01
DOI Ref: x5adp

Add the following:

▲Diltiazem Hydrochloride Compounded Cream

DEFINITION

Diltiazem Hydrochloride Compounded Cream contains NLT 90.0% and NMT 110.0% of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$). Prepare Diltiazem Hydrochloride Compounded Cream 20 mg/g[1] as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Diltiazem Hydrochloride	2 g
Glycerin	4 g
VersaBase Cream,[a] a sufficient quantity to make	100 g

[a] PCCA, Houston, TX.

In an appropriately sized electronic mortar and pestle container, add 50 g of *VersaBase Cream*, place the *Diltiazem Hydrochloride* and *Glycerin* on top, and add sufficient *VersaBase Cream* to bring to final weight. Mix the mixture with an electronic mortar and pestle for 2 min at a speed of about 1500 rpm. Process through an ointment mill once at the middle setting and once at the finest setting to reduce the particle size of the active ingredient and to reduce air content of the preparation. Return the mixture to the electronic mortar and pestle container and mix again for 1 min at a speed of about 1100 rpm.

ASSAY

• **Procedure**

Solution A: 5.44 g/L of potassium phosphate dibasic in water, adjusted with phosphoric acid to a pH of 7.5. Pass through a polyvinyl difluoride filter of 0.22-µm pore size.

Diluent: Methanol and water (80:20)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Acetonitrile (%)
0	60	40
3	60	40
13	40	60
18	40	60
20	60	40
26	60	40

Standard solution: 0.1 mg/mL of USP Diltiazem Hydrochloride RS, prepared as follows. Transfer about 20 mg of USP Diltiazem Hydrochloride RS to a 200-mL volumetric flask and add about 150 mL of *Diluent*. Sonicate for 2 min until completely dissolved. Dilute with *Diluent* to volume and shake or vortex until well mixed.

Sample solution: Transfer approximately 2 mL of Cream to a 3-mL syringe, taking care to minimize air bubbles. Transfer this Cream to a 1-mL syringe with the piston removed until the syringe is fully filled. Insert the piston and move the piston to about 5 mm above the 1-mL mark. Wipe the outside of the 1-mL syringe, using a delicate task wipe to remove any excess cream. Weigh the 1-mL syringe, recording the weight to 0.01 mg (initial). Precharge a 200-mL volumetric flask with approximately 10 mL of 2-propanol, ensuring the neck of the flask is wetted. Transfer the Cream from the 1-mL syringe to the volumetric flask. Keep the syringe at the center of the flask to try to minimize the Cream sticking to the neck. Weigh the empty syringe again, recording the weight to 0.01 mg (final). The difference between the initial and final

weight should be between 900 and 1100 mg. Vortex the volumetric flask for at least 3 min to break the Cream. Sonicate for 5 min. Vortex for an additional 2 min. Add sufficient *Diluent* to bring the flask to volume and vortex or shake for 2 min. The resultant solution should be partially cloudy. Pass through a polyvinyl difluoride filter of 0.22-µm pore size, discarding the first 3 mL, and then transfer to HPLC vials.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Columns

Guard: 4.0-mm × 3-mm; 5-µm packing L1

Analytical: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 15°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for diltiazem hydrochloride is about 11.4 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) in the portion of Cream taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of diltiazem hydrochloride from the *Sample solution*

r_S = peak response of diltiazem hydrochloride from the *Standard solution*

C_S = concentration of USP Diltiazem Hydrochloride RS in the *Standard solution* (mg/g)

C_U = nominal concentration of diltiazem hydrochloride in the *Sample solution* (mg/g)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **pH ⟨791⟩:** 4.1–5.1
- **APPEARANCE:** White opaque cream

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Package in a tight, light-resistant plastic tube. Store at controlled room temperature.
- **BEYOND-USE DATE:** NMT 90 days after the date on which it was compounded when stored at controlled room temperature.
- **LABELING:** Label it to indicate that it is for external use only and to state the *Beyond-Use Date*.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Diltiazem Hydrochloride RS▲ (USP 1-Aug-2022)

[1] This formulation meets the requirements in Antimicrobial Effectiveness Testing ⟨51⟩.

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

Topic/Question	Contact	Expert Committee
DILTIAZEM HYDROCHLORIDE COMPOUNDED CREAM	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(5)
Current DocID: GUID-394AAB0C-38E6-4F4F-9609-30F9738AB56B_2_en-US
DOI: https://doi.org/10.31003/USPNF_M15595_02_01
DOI ref: x5adp