Diltiazem Hydrochloride Extended-Release Capsules

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Expert Committee	Chemical Medicines Monographs 2

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Chemical Medicines Monographs 2 Expert Committee intends to revise the Diltiazem Hydrochloride Extended-Release Capsules monograph.

Based on the supporting documents received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add *Test 17* in *Dissolution* section of the monograph.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.[1]

In addition, the term of “desacetyl diltiazem” is corrected to “desacetyl diltiazem hydrochloride” in the calculation section in the test of *Organic Impurities*.

Should you have any questions, please contact Edith Chang**,** Ph.D., Scientific Liaison to the Chemical Medicines Monographs 2 Expert Committee (301–816–8392 or yec@usp.org).

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[1] This text is not the official version of a USP–NF monograph and may not reflect the full and accurate contents of the monograph in effect today. Please refer to the current edition of the USP–NF for official text.

USP provides this text as a courtesy to indicate changes that we anticipate will be made official once the product subject to this pending monograph receives FDA approval. Once FDA approval is granted, the official monograph will include the changes indicated herein and any changes indicated in the product’s final approval, combined with the text of the monograph as effective on the date of approval.

Diltiazem Hydrochloride Extended-Release Capsules

DEFINITION

Diltiazem Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$).

IDENTIFICATION

- **A.** The UV-Vis spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Solution A: 0.79 g/L of ammonium bicarbonate in water. Adjust with diluted ammonia solution or acetic acid to a pH of 8.0.
Solution B: Acetonitrile
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2.0	95	5
5.0	60	40
13.0	60	40
16.0	30	70
20.0	30	70
20.1	95	5
25.0	95	5

Diluent: Acetonitrile and water (40:60)
Standard solution: 0.05 mg/mL of USP Diltiazem Hydrochloride RS in *Diluent*
Sample stock solution: Nominally 0.5 mg/mL of diltiazem hydrochloride from the Capsules in *Diluent* prepared as follows. Transfer a portion of finely powdered contents of NLT 20 Capsules to a suitable volumetric flask. Add *Diluent* equivalent to 80% of the flask volume, mechanically shake for 30 min, and sonicate for 60 min. Dilute with the *Diluent* to volume. Centrifuge and use the supernatant.
Sample solution: Nominally 0.05 mg/mL of diltiazem hydrochloride prepared in *Diluent* from *Sample stock solution*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 240 nm. For *Identification A*, use a diode array detector in the range of 190–400 nm.
Column: 2.1-mm × 15-cm; 1.7-µm packing L1
Flow rate: 0.3 mL/min
Injection volume: 2.0 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 1.0%
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 Capsules taken:

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

r_U = peak response of diltiazem from the *Sample solution*
r_S = peak response of diltiazem from the *Standard solution*
C_S = concentration of USP Diltiazem Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of diltiazem hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **DISSOLUTION** ⟨711⟩

For products labeled for dosing every 12 h
Test 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*.
Medium: Water; 900 mL
Apparatus 2: 100 rpm
Times: 3, 9, and 12 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 2*.

Table 2

Time (h)	Amount Dissolved (%)
3	10–25
9	45–85
12	NLT 70

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.
Medium: Water; 900 mL
Apparatus 2: 100 rpm
Times: 4, 8, 12, and 24 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 3*.

Table 3

Time (h)	Amount Dissolved (%)
4	10–25
8	35–60
12	55–80
24	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.
Medium: 0.05 M phosphate buffer, pH 7.2; 900 mL
Apparatus 2: 50 rpm
Times: 1, 3, and 8 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 4*.

Table 4

Time (h)	Amount Dissolved (%)
1	NMT 15
3	45–70
8	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 10: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 10*.
Buffer: Dissolve 7.1 g of anhydrous dibasic sodium phosphate in 1000 mL of water, and adjust with phosphoric acid to a pH of 6.5.
Medium: *Buffer*; 900 mL
Apparatus 1: 100 rpm
Times: 1, 6, 9, and 24 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 5*.

Table 5

Time (h)	Amount Dissolved (%)
1	NMT 10
6	10–30
9	34–60
24	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

For products labeled for dosing every 24 h

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
Medium: Water; 900 mL
Apparatus 2: 100 rpm
Times: 1, 4, 10, and 15 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 6*.

Table 6

Time (h)	Amount Dissolved (%)
1	5–20
4	30–50
10	70–90
15	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Times: 6, 12, 18, 24, and 30 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 7*.

Table 7

Time (h)	Amount Dissolved (%)
6	20–45
12	25–50
18	35–70
24	NLT 70
30	NLT 85

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.
Medium: Water; 900 mL
Apparatus 1: 100 rpm
Times: 2, 4, 8, 12, and 16 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 8*.

Table 8

Time (h)	Amount Dissolved (%)
2	NMT 25
4	25–50

Table 8 *(Continued)*

Time (h)	Amount Dissolved (%)
8	60–85
12	NLT 70
16	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 7: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.
Buffer: Transfer 115 mL of acetic acid to a 10-L volumetric flask, dilute with water to volume, and mix (*Solution A*). Transfer 165.4 g of anhydrous sodium acetate to a 10-L volumetric flask, dilute with water to volume, and mix (*Solution B*). Mix 4410 mL of *Solution A* with 1590 mL of *Solution B*. Adjust, if necessary, with the addition of *Solution A* or *Solution B* to a pH of 4.2 ± 0.05.
Medium: *Buffer*; 900 mL
Apparatus 2: 100 rpm
Times: 1, 4, 10, and 15 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 9*.

Table 9

Time (h)	Amount Dissolved (%)
1	NMT 10
4	15–35
10	65–85
15	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 8: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 8*.
Medium: Water; 900 mL
Apparatus 2: 100 rpm
Times: 1, 4, 10, and 15 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 10*.

Table 10

Time (h)	Amount Dissolved (%)
1	5–20
4	30–50
10	60–90
15	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 9: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 9*.
[NOTE—Perform the test separately in each of the two media.]
Medium 1: 0.1 N hydrochloric acid; 900 mL
Medium 2: Simulated intestinal fluid TS, prepared without enzyme and adjusted to a pH of 7.5 ± 0.1; 900 mL
Apparatus 2: 75 rpm
Time for Medium 1: 2 h
Times for Medium 2: 2, 12, 18, and 24 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 11*.

Table 11

Time (h)	Amount Dissolved, Medium 1 (%)	Amount Dissolved, Medium 2 (%)
2	0–5	20–45
12	—	35–55
18	—	NLT 60
24	—	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 11: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 11*.
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Times: 1, 6, 12, and 18 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 12*.

Table 12

Time (h)	Amount Dissolved (%)
1	NMT 10
6	30–40
12	36–58
18	NLT 85

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 12: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 12*. Proceed as directed for *Extended-Release Dosage Forms* in *Procedure, Apparatus 1 and Apparatus 2*.

Medium: Water; 900 mL
Apparatus 1: 100 rpm
Times: 2, 8, 14, and 24 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 13*.

Table 13

Time (h)	Amount Dissolved (%)
2	NMT 20
8	30–55
14	NLT 65
24	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 13: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 13*. Proceed as directed for *Extended-Release Dosage Forms* in *Procedure, Apparatus 1 and Apparatus 2*.
Medium: Water; 900 mL
Apparatus 1: 100 rpm
Times: 2, 8, 14, and 24 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 14*.

Table 14

Time (h)	Amount Dissolved (%)
2	NMT 20
8	30–55
14	60–80
24	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 14: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 14*. Proceed as directed for *Extended-Release Dosage Forms* in *Procedure, Apparatus 1 and Apparatus 2*.
Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Times: 6, 12, 18, 24, and 30 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 15*.

Table 15

Time (h)	Amount Dissolved (%)
6	20–45
12	25–50
18	35–70
24	NLT 70
30	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 15: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 15*. Proceed as directed for *Extended-Release Dosage Forms* in *Procedure, Apparatus 1 and Apparatus 2*.
Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL
Apparatus 2: 75 rpm
Times: 2, 4, 8, 12, and 16 h
Detector: UV 237 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.
Tolerances: See *Table 16*.

Table 16

Time (h)	Amount Dissolved (%)
2	NMT 25
4	20–40
8	60–85
12	NLT 70
16	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 16: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 16*.
Medium, Apparatus 2, Times, Standard solution, and **Sample solution:** Proceed as directed for *Test 3*.
Detector: UV 238 nm
Tolerances: See *Table 17*.

Table 17

Time (h)	Amount Dissolved (%)
6	20–45
12	30–55
18	40–75
24	NLT 70
30	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

►**Test 17:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 17*.

Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm, with wire helix sinkers
Times: 6, 12, and 30 h
Detector: UV 238 nm
Standard solution: USP Diltiazem Hydrochloride RS in *Medium*
Sample solution: Dilute with *Medium*, if necessary, to a concentration that is similar to that of the *Standard solution*.
Blank: *Medium*
Tolerances: See *Table 18*.

Table 18

Time (h)	Amount Dissolved (%)
6	20–40
12	35–55
30	NLT 80

The percentages of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.◄ (TBD)

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 2.5 µg/mL each of USP Desacetyl Diltiazem Hydrochloride RS and USP Diltiazem Hydrochloride RS in *Diluent*
Sample solution: Nominally 0.5 mg/mL of diltiazem hydrochloride from the Capsules in *Diluent* prepared as follows. Transfer a portion of the finely powdered contents of NLT 20 Capsules to a suitable volumetric flask. Add *Diluent* equivalent to 80% of the flask volume, mechanically shake for 30 min, and sonicate for 60 min. Dilute with *Diluent* to volume. Centrifuge and use the supernatant.
System suitability
Sample: *Standard solution*
[NOTE—For relative retention times see *Table 19*.◄ (TBD)]
Suitability requirements
Resolution: NLT 2.0 between desacetyl diltiazem and diltiazem
Relative standard deviation: NMT 3.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of desacetyl diltiazem ►hydrochloride◄ (TBD) in the portion of Capsules taken:

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

r_U = peak response of desacetyl diltiazem from the *Sample solution*
r_S = peak response of desacetyl diltiazem from the *Standard solution*
C_S = concentration of USP Desacetyl Diltiazem Hydrochloride RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of diltiazem hydrochloride in the *Sample solution* (µg/mL)

Calculate the percentage of any individual unspecified impurity in the portion of Capsules taken:

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

r_U = peak response of each unspecified impurity from the *Sample solution*
r_S = peak response of diltiazem from the *Standard solution*
C_S = concentration of USP Diltiazem Hydrochloride RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of diltiazem hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: See ►*Table 19*.◄ (TBD) Disregard limit: 0.05%.

Table ►19◄ (TBD)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Diltiazem related compound H[a,b]	0.44	—
Diltiazem related compound G[b,c]	0.52	—
Diltiazem related compound C[b,d]	0.58	—
Diltiazem related compound D[b,e]	0.61	—
Diltiazem related compound E[b,f]	0.66	—
Desacetyl diltiazem	0.75	1.5
Diltiazem related compound A[b,g]	0.83	—
Diltiazem related compound B[b,h]	0.89	—
Diltiazem	1.0	—
Any individual unspecified impurity	—	0.2
Total impurities	—	2.0

[a] (2*S*,3*S*)-5-(2-Aminoethyl)-3-hydroxy-2-(4-hydroxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5*H*)-one.
[b] These are impurities related to the drug substance. They are not to be reported for the drug product and should not be included in the total impurities.
[c] (2*S*,3*S*)-3-Hydroxy-2-(3-methoxyphenyl)-5-(2-(methylamino)ethyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4(5*H*)-one.
[d] (2*S*,3*S*)-5-[2-(Dimethylamino)ethyl]-2-(4-hydroxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepin-3-yl acetate.
[e] (2*S*,3*S*)-2-(4-Methoxyphenyl)-5-[2-(methylamino)ethyl]-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate.
[f] (2*S*,3*S*)-3-Hydroxy-2-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5*H*)-one.
[g] (2*R*,3*S*)-5-[2-(Dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate.
[h] (2*S*,3*S*)-2-(4-Methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.
- **LABELING:** The labeling indicates the *Dissolution* test with which the product complies.
- **USP REFERENCE STANDARDS ⟨11⟩**
USP Desacetyl Diltiazem Hydrochloride RS
$C_{20}H_{24}N_2O_3S \cdot HCl$ 408.95
USP Diltiazem Hydrochloride RS