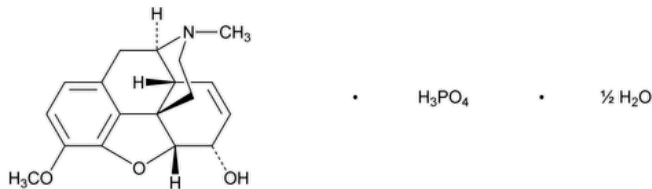


Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-1702BF9E-4213-4BF4-909F-AC0C01260E42_4_en-US
DOI: https://doi.org/10.31003/USPNF_M19590_04_01
DOI Ref: bc7f3

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Codeine Phosphate

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click <https://www.uspnf.com/rb-codeine-phosphate-notice-20210430>.



$\text{C}_{18}\text{H}_{21}\text{NO}_3 \cdot \text{H}_3\text{PO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$ 406.37
Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-, (5 α ,6 α)-, phosphate (1:1) (salt), hemihydrate;
7,8-Didehydro-4,5 α -epoxy-3-methoxy-17-methylmorphinan-6 α -ol phosphate (1:1) (salt) hemihydrate CAS RN[®]: 41444-62-6.
Anhydrous CAS RN[®]: 52-28-8.

DEFINITION

Change to read:

Codeine Phosphate contains $\blacktriangle$ NLT 98.0% and NMT 102.0% $\blacktriangle$ (USP 1-May-2021) of codeine phosphate ($\text{C}_{18}\text{H}_{21}\text{NO}_3 \cdot \text{H}_3\text{PO}_4$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K or $\blacktriangle$ 197A $\blacktriangle$ (USP 1-May-2021)

Add the following:

- $\blacktriangle$ • **B.** The retention time of the codeine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay. $\blacktriangle$
(USP 1-May-2021)

Change to read:

- $\blacktriangle$ **C.** $\blacktriangle$ (USP 1-MAY-2021)

Analysis: Neutralize 20 mg/mL of Codeine Phosphate in [water](#) with [6 N ammonium hydroxide](#) and add [silver nitrate TS](#).
Acceptance criteria: A yellow precipitate of silver phosphate is formed, and it is soluble in 2 N [nitric acid](#) and [6 N ammonium hydroxide](#).

ASSAY

Change to read:

- **PROCEDURE**

$\blacktriangle$ **Solution A:** 2% [acetic acid](#) in [water](#). Adjust with 50% (w/v) [sodium hydroxide](#) solution to a pH of 4.5.
Solution B: [Acetonitrile](#)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	96	

Time (min)	Solution A (%)	Solution B (%)
15	96	4
22	89	11
31	63	37
31.1	96	4
36	96	4

Diluent: 0.5% (v/v) [phosphoric acid](#) in [water](#)

Standard solution: 4 mg/mL of [USP Codeine Phosphate RS](#) in *Diluent*

Sample solution: 4 mg/mL of Codeine Phosphate in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 15-cm; 3.0-μm packing [L1](#)

Column temperature: 37°

Flow rate: 1.88 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–3.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4$) in the portion of Codeine Phosphate taken:

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

r_U = peak response of codeine from the *Sample solution*

r_S = peak response of codeine from the *Standard solution*

C_S = concentration of [USP Codeine Phosphate RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Codeine Phosphate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis ▲ (USP 1-May-2021)

IMPURITIES

Delete the following:

▲ • LIMIT OF MORPHINE

Analysis: Dissolve about 50 mg of [potassium ferricyanide](#) in 10 mL of [water](#), add 1 drop of [ferric chloride](#) TS, and 1 mL of 10 mg/mL Codeine Phosphate solution.

Acceptance criteria: No blue color is produced immediately. ▲ (USP 1-May-2021)

Change to read:

• ORGANIC IMPURITIES

▲ **Solution A, Solution B, Mobile phase, Diluent, Standard solution, Sample solution, and Chromatographic system:** Proceed as directed in the Assay.

Sensitivity solution: 0.002 mg/mL of [USP Codeine Phosphate RS](#) in *Diluent*

System suitability solution: 4 mg/mL of [USP Codeine System Suitability Mixture RS](#) in *Diluent*