Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Aug-2017
Document Type: USP Monographs
DocId: GUID-7D97C3D4-B52A-4353-8B70-1AAD6893D405_1_en-US
DOI: https://doi.org/10.31003/USPNF_M33373_01_01
DOI Ref: dau30



# Flumazenil Injection

**DEFINITION**

Flumazenil Injection is a sterile solution of Flumazenil. It contains NLT 90.0% and NMT 110.0% of the labeled amount of flumazenil ($C_{15}H_{14}FN_3O_3$).

**IDENTIFICATION**

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

**ASSAY**

- **Procedure**

**Buffer:** 0.02 M monobasic potassium phosphate TS, adjusted with 0.02 M phosphoric acid to a pH of 2.7 ± 0.05

**Mobile phase:** Tetrahydrofuran, methanol, and *Buffer* (20:5:75)

**Diluent:** Tetrahydrofuran, methanol, and water (20:5:75)

**System suitability solution:** 0.01 mg/mL each of USP Flumazenil RS, USP Flumazenil Related Compound A RS, and USP Flumazenil Related Compound B RS in *Diluent*

**Standard solution:** 0.1 mg/mL of USP Flumazenil RS in *Mobile phase*

**Sample solution:** Nominally 0.1 mg/mL of flumazenil from Injection prepared as follows. Dilute a portion of Injection with *Diluent*, if necessary.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 230 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

**Column:** 4.6-mm × 25-cm; 5-µm packing L10

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**Run time:** NLT 2 times the retention time of flumazenil

**System suitability**

**Samples:** *System suitability solution* and *Standard solution*

[Note—See *Table 1* for the relative retention times.]

**Suitability requirements**

**Resolution:** NLT 1.8 between flumazenil related compound B and flumazenil, *System suitability solution*

**Tailing factor:** NMT 2.0 for flumazenil related compound A, *System suitability solution*

**Relative standard deviation:** NMT 2.0%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of flumazenil ($C_{15}H_{14}FN_3O_3$) in the portion of Injection taken:

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

$r_U$ = peak response from the *Sample solution*

$r_S$ = peak response from the *Standard solution*

$C_S$ = concentration of USP Flumazenil RS in the *Standard solution* (mg/mL)

$C_U$ = nominal concentration of flumazenil in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

## IMPURITIES

• **Organic Impurities**

**Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*.

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

$r_U$ = peak response from the *Sample solution*

$r_S$ = peak response from the *Standard solution*

$C_S$ = concentration of USP Flumazenil RS in the *Standard solution* (mg/mL)

$C_U$ = nominal concentration of flumazenil in the *Sample solution* (mg/mL)

$F$ = relative response factor (see *Table 1*)

**Acceptance criteria:** See *Table 1*.

**Table 1**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Flumazenil related compound A | 0.71 | 1.1 | 1.0 |
| Flumazenil related compound B | 0.85 | 1.0 | 0.5 |
| Flumazenil | 1.0 | — | — |
| Any individual unspecified impurity | — | 1.0 | 0.5 |
| Total impurities | — | — | 2.0 |

## SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 100 USP Endotoxin Units/mg of flumazenil

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

• **pH ⟨791⟩:** 3.4–4.6

• **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in multiple-dose containers, preferably of Type I glass, and store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Endotoxin RS

USP Flumazenil RS

USP Flumazenil Related Compound A RS

8-Fluoro-5-methyl-6-oxo-5,6-dihydro-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylic acid;
Also known as 8-Fluoro-5,6-dihydro-5-methyl-6-oxo-4*H*-imidazol-[1,5-*a*][1,4]benzodiazepine-3-carboxylic acid.

$C_{13}H_{10}FN_3O_3$ 275.24

USP Flumazenil Related Compound B RS

Ethyl 8-hydroxy-5-methyl-6-oxo-5,6-dihydro-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate;
Also known as Ethyl 8-hydroxy-5,6-dihydro-5-methyl-6-oxo-4*H*-imidazol-[1,5-*a*][1,4]benzodiazepine-3-carboxylate.

$C_{15}H_{15}N_3O_4$ 301.30

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| FLUMAZENIL INJECTION | Documentary Standards Support | SM42020 Small Molecules 4 |

**Chromatographic Database Information:** Chromatographic Database

**Most Recently Appeared In:**
Pharmacopeial Forum: Volume No. PF 42(3)

**Current DocID: GUID-7D97C3D4-B52A-4353-8B70-1AAD6893D405_1_en-US**

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