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Dacarbazine for Injection

DEFINITION

Dacarbazine for Injection is a sterile, freeze-dried mixture of dacarbazine and suitable buffers or diluents. It contains NLT 90.0% and NMT 110.0% of the labeled amount of dacarbazine ($C_6H_{10}N_6O$). [**Caution—**Great care should be taken to prevent inhaling particles of Dacarbazine for Injection and exposing the skin to it.]

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**

Protect solutions containing dacarbazine from light and store at 2°–8°.

Solution A: 4.1 g/L of sodium acetate in water. Adjust with phosphoric acid to a pH of 7.0.

Solution B: 4.1 g/L of sodium acetate in water. Adjust with phosphoric acid to a pH of 5.5. Mix this solution with acetonitrile (75:25).

Mobile phase: See *Table 1*. Return to original conditions, and equilibrate the system for 10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
20	5	95
23	5	95
25	100	0
35	100	0

Diluent: 0.1 mg/mL of citric acid in water

Standard solution: 0.1 mg/mL of USP Dacarbazine RS in *Diluent*

Sample solution: Nominally equivalent to 0.1 mg/mL of dacarbazine in water, from Dacarbazine for Injection

Chromatographic system

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

Mode: LC

Detector: UV 250 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 L1

Autosampler temperature: 2°–8°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dacarbazine ($C_6H_{10}N_6O$) in the portion of Dacarbazine for 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 Dacarbazine RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

Protect solutions containing dacarbazine and its related compounds from light and store at 2°–8°.

Solution A, Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 8.0 µg/mL of USP Dacarbazine RS in water, from the *Standard solution* in the *Assay*

Dacarbazine related compound A standard solution: 0.04 mg/mL of USP Dacarbazine Related Compound A RS in water. Sonicate to ensure complete dissolution.

Dacarbazine related compound B standard solution: 0.04 mg/mL of USP Dacarbazine Related Compound B RS in water. Sonicate to ensure complete dissolution.

Sensitivity solution: 2.0 µg/mL of USP Dacarbazine RS in water from *Standard solution*

Sample solution: Nominally equivalent to 4.0 mg/mL of dacarbazine in water prepared as follows. Transfer the contents of 1 vial into a suitable volumetric flask, rinse the vial with several portions of water, add the rinsings into the same volumetric flask and dilute with water to volume.

System suitability

Samples: *Dacarbazine related compound A standard solution*, *Dacarbazine related compound B standard solution*, and *Sensitivity solution*

Suitability requirements

Relative standard deviation 1: NMT 5.0%, *Dacarbazine related compound A standard solution*

Relative standard deviation 2: NMT 5.0%, *Dacarbazine related compound B standard solution*

Signal-to-noise ratio: ▲NLT▲ (ERR 1-Sep-2022) 10, *Sensitivity solution*

Analysis

Samples: *Standard solution*, *Dacarbazine related compound A standard solution*, *Dacarbazine related compound B standard solution*, and *Sample solution*

Calculate the percentage of 5-aminoimidazole-4-carboxamide (free base of USP Dacarbazine Related Compound A RS) in the portion of Dacarbazine for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of 5-aminoimidazole-4-carboxamide from the *Sample solution*

r_S = peak response of dacarbazine related compound A from the *Dacarbazine related compound A standard solution*

C_S = concentration of USP Dacarbazine Related Compound A RS in the *Dacarbazine related compound A standard solution* (mg/mL)

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

M_{r1} = molecular weight of 5-aminoimidazole-4-carboxamide, 126.12

M_{r2} = molecular weight of USP Dacarbazine Related Compound A RS, 162.58

Calculate the percentage of 2-azahypoxanthine (anhydrous) (anhydrous form of USP Dacarbazine Related Compound B RS) in the portion of Dacarbazine for Injection taken:

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

r_U = peak response of 2-azahypoxanthine (anhydrous) from the *Sample solution*

r_S = peak response of dacarbazine related compound B from the *Dacarbazine related compound B standard solution*

C_S = concentration of USP Dacarbazine Related Compound B RS in the *Dacarbazine related compound B standard solution* (mg/mL)

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

Calculate the percentage of each individual unspecified impurity in the portion of Dacarbazine for Injection 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 dacarbazine from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
5-Aminoimidazole-4-carboxamide[a]	0.28	1.0
2-Azahypoxanthine (anhydrous)[b]	0.45	1.0
Dacarbazine	1.0	—
Any individual unspecified impurity	—	0.2
Total impurities	—	2.0

[a] It is the free base of USP Dacarbazine Related Compound A RS ($C_4H_6N_4O$).

[b] It is the anhydrous form of USP Dacarbazine Related Compound B RS ($C_4H_3N_5O$).

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: Nominally equivalent to 10 mg/mL of dacarbazine in water, from Dacarbazine for Injection

  Acceptance criteria: 3.0–4.0

- **Water Determination** ⟨921⟩, *Method I*: NMT 1.5%
- **Bacterial Endotoxins Test** ⟨85⟩: It contains NMT 0.52 USP Endotoxin Units/mg of dacarbazine.
- **Sterility Tests** ⟨71⟩: Meets the requirements
- **Completeness of Solution:** When dissolved as directed in the labeling, it yields a clear, pale yellow to yellow solution.
- **Constituted Solution:** At the time of use, it meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩, *Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and clarity of solutions*.
- **Particulate Matter in Injections** ⟨788⟩: Meets the requirements for small-volume injections

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*, preferably of Type I glass, protected from light.

• **Labeling:** Meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*

• **USP Reference Standards ⟨11⟩**

USP Dacarbazine RS

USP Dacarbazine Related Compound A RS

5-Aminoimidazole-4-carboxamide hydrochloride.

$C_4H_6N_4O \cdot HCl$ 162.58

USP Dacarbazine Related Compound B RS

2-Azahypoxanthine monohydrate.

$C_4H_3N_5O \cdot H_2O$ 155.12

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

Topic/Question	Contact	Expert Committee
DACARBAZINE FOR INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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