**Mode:** LC
**Detector:** UV 230 nm
**Column:** 4.6-mm × 15-cm; 5-µm packing L7
**Column temperature:** 30°
**Flow rate:** 1.5 mL/min
**Injection size:** 200 µL

**System suitability**
**Sample:** *Standard solution*
**Suitability requirements**
**Column efficiency:** NLT 5000
**Tailing factor:** 0.8–2.0
**Relative standard deviation:** NMT 2%

**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Determine the percentage of $C_{23}H_{28}ClN_3O_5S$ dissolved:

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

$r_U$ = peak response from the *Sample solution*
$r_S$ = peak response from the *Standard solution*
$C_S$ = concentration of the *Standard solution* (mg/mL)
$C_U$ = nominal concentration of glyburide in the *Sample solution* (mg/mL)

**Tolerances:** NLT 85% (Q) of the labeled amount of glyburide is dissolved.

**Metformin hydrochloride**
**Medium:** 0.05 M phosphate buffer, pH 6.8. Prepare by dissolving 6.8 g of monobasic potassium phosphate in 1000 mL of water, and adjust with 0.2 N sodium hydroxide to a pH of 6.8 ± 0.1; 1000 mL.
**Apparatus 2:** 50 rpm
**Time:** 30 min
**Standard solution:** Dissolve a quantity of USP Metformin Hydrochloride RS in *Medium*. Dilute further, if necessary, with *Medium* to obtain a solution having a metformin hydrochloride concentration, in mg/mL, of L/1000 where L is the label claim, in mg, of metformin hydrochloride.
**Sample solution:** Sample per *Dissolution* ⟨711⟩. Pass a portion of the solution under test through a 0.45- µm polypropylene filter or a 1- µm glass fiber filter. Dilute with *Medium*, if necessary.
**Spectrometric conditions**
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
**Mode:** UV-Vis
**Analytical wavelength:** 232 nm
**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Calculate the percentage of $C_4H_{11}N_5 \cdot HCl$ dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

$A_U$ = absorbance of the *Sample solution*
$A_S$ = absorbance of the *Standard solution*
$C_S$ = concentration of USP Metformin Hydrochloride RS in the *Standard solution* (mg/mL)
$C_U$ = nominal concentration of metformin hydrochloride in the *Sample solution* (mg/mL)

**Tolerances:** NLT 85% (Q) of the labeled amount of metformin hydrochloride is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements for *Weight Variation* for metformin hydrochloride and for *Content Uniformity* for glyburide

## IMPURITIES

### Organic Impurities

- **Procedure 1: Glyburide**

**Solution A, Mobile phase, Diluent, Sample solution, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay* for *Glyburide*.
**Standard solution:** Dilute 1.0 mL of the *Standard solution* from the *Assay* for *Glyburide* with *Diluent* to 100 mL.

**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Calculate the percentage of each glyburide impurity in the Tablets:

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

$r_U$ = peak response from the *Sample solution*
$r_S$ = peak response from the *Standard solution*
$C_S$ = concentration of USP Glyburide RS in the *Standard solution* (mg/mL)
$C_U$ = nominal concentration of glyburide in the *Sample solution* (mg/mL)
F = relative response factor, use 0.8 for glyburide related compound A, and use 1.0 for all other impurities

**Acceptance criteria**
[NOTE—Disregard any peak less than 0.05%, and disregard any peak observed in the blank.]
**Glyburide related compound A:** NMT 1.0%
**Any other individual impurities:** NMT 0.2%
**Total impurities:** NMT 0.50%, excluding glyburide related compound A

- **Procedure 2: Metformin Hydrochloride**

**Solution A, Mobile phase, Sample solution, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay* for *Metformin Hydrochloride*.
**Analysis**
**Sample:** *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times 100$$

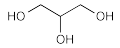
$r_U$ = peak response for each impurity from the *Sample solution*
$r_T$ = sum of the responses of all peaks from the *Sample solution*

**Acceptance criteria**
[NOTE—Disregard any peak less than 0.05%, and disregard any peak observed in the blank.]
**Individual impurities:** NMT 0.1%
**Total impurities:** NMT 0.5 %

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**
USP Glyburide RS
USP Glyburide Related Compound A RS
(4-[2-(5-Chloro-2-methoxybenzamido)ethyl] benzenesulfonamide.
USP Metformin Hydrochloride RS
USP Metformin Related Compound B RS
1-Methylbiguanide.
$C_3H_9N_5$ 115.14
USP Metformin Related Compound C RS
Dimethylmelamine, or *N,N*-dimethyl-[1,3,5]triazine-2,4,6-triamine.
$C_5H_{10}N_6$ 154.17

# Glycerin




$C_3H_8O_3$ 92.10
1,2,3-Propanetriol;
Glycerol [56-81-5].

## DEFINITION

Glycerin contains NLT 99.0% and NMT 101.0% of $C_3H_8O_3$, calculated on the anhydrous basis.

## IDENTIFICATION

[NOTE—Compliance is determined by meeting the requirements for *Identification* tests *A, B,* and *C.*]

- **A. INFRARED ABSORPTION ⟨197F⟩**
- **B. LIMIT OF DIETHYLENE GLYCOL AND ETHYLENE GLYCOL**

**Standard solution:** 2.0 mg/mL of USP Glycerin RS, 0.050 mg/mL of USP Ethylene Glycol RS, 0.050 mg/mL of USP Diethylene Glycol RS, and 0.10 mg/mL of 2,2,2-trichloroethanol (internal standard) in methanol

**Sample solution:** 50 mg/mL of Glycerin and 0.10 mg/mL of 2,2,2-trichloroethanol (internal standard) in methanol

**Chromatographic system**

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

**Mode:** GC

**Detector:** Flame ionization

**Column:** 0.53-mm × 30-m fused-silica analytical column coated with 3.0-µm G43 stationary phase, and a deactivated split liner with glass wool

**Temperature**

**Injector:** 220°

**Detector:** 250°

**Column:** See the temperature program table.

| Initial Temperature (°) | Temperature Ramp (°/min) | Final Temperature (°) | Hold Time at Final Temperature (min) |
|---|---|---|---|
| 100 | — | 100 | 4 |
| 100 | 50 | 120 | 10 |
| 120 | 50 | 220 | 6 |

**Carrier gas:** Helium

**Injection size:** 1.0 µL

**Flow rate:** 4.5 mL/min

**Injection type:** Split ratio, about 10:1

**System suitability**

**Sample:** *Standard solution*

[NOTE—The relative retention times for ethylene glycol, 2,2,2-trichloroethanol, diethylene glycol, and glycerin are about 0.3, 0.6, 0.8 and 1.0, respectively.]

**Suitability requirements**

**Resolution:** NLT 1.5 between diethylene glycol and glycerin

**Analysis**

**Sample:** *Sample solution*

**Acceptance criteria:** If a peak at the retention times for the diethylene glycol or ethylene glycol is present in the *Sample solution,* the peak response ratio relative to 2,2,2-trichloroethanol is NMT the peak response ratio for diethylene glycol or ethylene glycol relative to 2,2,2-trichloroethanol in the *Standard solution;* NMT 0.10% each for diethylene glycol and ethylene glycol is found.

- **C.** Examine the chromatograms obtained in *Identification* test *B.* The retention time of the glycerin peak of the *Sample solution* corresponds to that obtained in the *Standard solution*.

## ASSAY

- **PROCEDURE**

**Sodium periodate solution:** Dissolve 60 g of sodium metaperiodate in sufficient water containing 120 mL of 0.1 N sulfuric acid to make 1000 mL. Do not heat to dissolve the periodate. If the solution is not clear, pass through a sintered-glass filter. Store the solution in a glass-stoppered, light-resistant container. Test the suitability of this solution as follows. Pipet 10 mL into a 250-mL volumetric flask, and dilute with water to volume. T o 550 mg of Glycerin dissolved in 50 mL of water, add 50 mL of the diluted periodate solution with a pipet. For a blank, pipet 50 mL of the solution into a flask containing 50 mL of water. Allow the solutions to stand for 30 min, then to each add 5 mL of hydrochloric acid and 10 mL of potassium iodide TS, and rotate to mix. Allow to stand for 5 min, add 100 mL of water, and titrate with 0.1 N sodium thiosulfate, shaking continuously and adding 3 mL of star ch TS as the endpoint is approached. The ratio of the volume of 0.1 N sodium thiosulfate required for the glycerin–periodate mixture to that required for the blank should be between 0.750 and 0.765.

**Analysis:** Transfer 400 mg of Glycerin to a 600-mL beaker, dilute with 50 mL of water, add bromothymol blue TS, and acidify with 0.2 N sulfuric acid to a definite green or greenish yellow color. Neutralize with 0.05 N sodium hydroxide to a definite blue endpoint, free from green color. Prepare a blank containing 50 mL of water, and neutralize in the same manner. Pipet 50 mL of the *Sodium periodate solution* into each beaker, mix by swirling gently, cover with a watch glass, and allow to stand for 30 min at room temperature (not exceeding 35 °) in the dark or in subdued light. Add 10 mL of a mixture of equal volumes of ethylene glycol and water, and allow to stand for 20 min. Dilute each solution with water to 300 mL, and titrate with 0.1 N sodium hydroxide VS to a pH of 8.1 ± 0.1 for the specimen under assay and 6.5 ± 0.1 for the blank, using a pH meter. Each mL of 0.1 N sodium hydroxide, after correction for the blank, is equivalent to 9.210 mg of $C_3H_8O_3$.

**Acceptance criteria:** 99.0%–101.0% on the anhydrous basis

## IMPURITIES

### Inorganic Impurities

- **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩**:** A 7.0-g portion shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (NMT 10 ppm).
- **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩**:** A 10-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (NMT 20 ppm).
- **HEAVY METALS** ⟨**231**⟩

**Analysis:** Mix 4.0 g with 2 mL of 0.1 N hydrochloric acid, and dilute with water to 25 mL.

**Acceptance criteria:** NMT 5 ppm

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** Heat 50 g in an open, shallow 100-mL porcelain dish until it ignites, and allow it to burn without further application of heat in a place free from drafts. Cool, moisten the residue with 0.5 mL of sulfuric acid, and ignite to constant weight: the weight of the residue does not exceed 5 mg (0.01%).

### Organic Impurities

- **PROCEDURE 1: RELATED COMPOUNDS**

**System suitability solution:** 0.5 mg/mL each of USP Diethylene Glycol RS and USP Glycerin RS

**Sample solution:** 50 mg/mL of Glycerin

**Chromatographic system**

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

**Mode:** GC

**Detector:** Flame ionization

**Column:** 0.53-mm × 30-m fused-silica analytical column coated with 3.0-µm G43 stationary phase, and an inlet liner having an inverted cup or spiral structure

**Temperature**

**Injector:** 220°

**Detector:** 250°

**Column:** See the temperature program table below.

| Initial Temperature (°) | Temperature Ramp (°/min) | Final Temperature (°) | Hold Time at Final Temperature (min) |
|---|---|---|---|
| 100 | — | 100 | — |
| 100 | 7.5 | 220 | 4 |

**Carrier gas:** Helium
**Injection size:** 0.5 µL
**Linear velocity:** 38 cm/s
**Injection type:** Split ratio, about 10:1
**System suitability**
**Sample:** *System suitability solution*
**Suitability requirements**
**Resolution:** NLT 7.0 between diethylene glycol and glycerin
**Analysis**
**Sample:** *Sample solution*
Calculate the percentage of each impurity, excluding any solvent peaks and diethylene glycol, in the portion of Glycerin taken:

$$\text{Result} = (r_U/r_T) \times 100$$

$r_U$ = peak response of each individual impurity from the *Sample solution*
$r_T$ = sum of the responses of all the peaks from the *Sample solution*

**Acceptance criteria**
**Individual impurities:** NMT 0.1%
**Total impurities:** NMT 1.0%

- **PROCEDURE 2: LIMIT OF CHLORINATED COMPOUNDS**

**Sample:** 5 g of Glycerin
**Analysis:** Transfer the *Sample* into a dry, round-bottom, 100-mL flask. Add 15 mL of morpholine, and connect the flask by a ground joint to a reflux condenser. Reflux gently for 3 h. Rinse the condenser with 10 mL of water, receiving the washings in the flask, and cautiously acidify with nitric acid. Transfer the solution to a suitable comparison tube, add 0.50 mL of silver nitrate TS, and dilute with water to 50.0 mL.
**Acceptance criteria:** The turbidity is not greater than that of a blank to which 0.20 mL of 0.020 N hydrochloric acid has been added, the refluxing being omitted (NMT 30 ppm of Cl).

- **PROCEDURE 3: FATTY ACIDS AND ESTERS**

**Sample solution:** Mix 50 g of Glycerin with freshly boiled water and 5 mL of 0.5 N sodium hydroxide VS. Boil the mixture for 5 min, cool, and add phenolphthalein TS.
**Analysis:** Titrate the excess alkali with 0.5 N hydrochloric acid VS. Perform a blank determination (see *Titrimetry* ⟨541⟩, *Residual Titrations*).
**Acceptance criteria:** NMT 1 mL of 0.5 N sodium hydroxide is consumed.

**SPECIFIC TESTS**

- **COLOR:** When viewed downward against a white surface in a 50-mL color-comparison tube, the color is not darker than the color of a standard made by diluting 0.40 mL of ferric chloride CS with water to 50 mL and similarly viewed in a color-comparison tube of approximately the same diameter and color as that containing the Glycerin.
- **SPECIFIC GRAVITY ⟨841⟩:** NLT 1.249
- **WATER DETERMINATION,** *Method I* **⟨921⟩:** NMT 5.0%

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Diethylene Glycol RS
USP Ethylene Glycol RS
USP Glycerin RS
1,2,3-Propanetriol.
$C_3H_8O_3$ 92.10

## Glycerin Ophthalmic Solution

» Glycerin Ophthalmic Solution is a sterile, anhydrous solution of Glycerin, containing not less than 98.5 percent of glycerin ($C_3H_8O_3$). It may contain one or more suitable antimicrobial preservatives. [NOTE—In the preparation of this Ophthalmic Solution, use Glycerin that has a low water content, in order that the Ophthalmic Solution may comply with the *Water* limit. This may be ensured by using Glycerin having a specific gravity of not less than 1.2607, corresponding to a concentration of 99.5 per cent.]
NOTE—Do not use the Ophthalmic Solution if it contains crystals, or is cloudy or discolored, or contains a precipitate.

**Packaging and storage**—Preserve in tight containers of glass or plastic, containing not more than 15 mL, protected from light. The container or individual carton is sealed and tamper-proof so that sterility is ensured at time of first use.

**USP Reference standards** ⟨11⟩—
USP Glycerin RS

**Identification**—It responds to the *Identification* test under *Glycerin*.

**Sterility** ⟨71⟩: meets the requirements.

**pH** ⟨791⟩: between 4.5 and 7.5, determined potentiometrically in a solution prepared by the addition of 5 mL of Sodium Chloride Injection to 5 mL of Ophthalmic Solution.

**Water,** *Method I* ⟨921⟩: not more than 1.0%.

**Assay**—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 3 g of glycerin, to a 500-mL volumetric flask, dilute with water to volume, and mix. Transfer a 3-mL portion to a conical flask, add 100.0 mL of a solution of potassium periodate (prepared by dissolving 3 g of potassium periodate in about 500 mL of warm water, cooling to room temperature, and then diluting with water to 1000 mL), swirl, and allow to stand at room temperature for 10 minutes. Add 4 g of sodium bicarbonate and 2 g of potassium iodide, and titrate immediately with 0.1 N potassium arsenite VS, adding 3 mL of starch TS as the endpoint is approached. Perform a blank determination, using water in place of the Ophthalmic Solution, and note the difference in volumes required. Each mL of 0.1 N potassium arsenite is equivalent to 2.303 mg of glycerin ($C_3H_8O_3$).

## Glycerin Oral Solution

» Glycerin Oral Solution contains not less than 95.0 percent and not more than 105.0 per cent of the labeled amount of glycerin ($C_3H_8O_3$).

**Packaging and storage**—Preserve in tight containers.

**Identification**—Heat a few drops with about 500 mg of potassium bisulfate in a test tube: pungent vapors of acrolein are evolved.

**pH** ⟨791⟩: between 5.5 and 7.5.

**Assay**—Transfer an accurately measured volume of Oral Solution, equivalent to about 3 g of glycerin, to a 500-mL volumetric flask, dilute with water to volume, and mix. Transfer a 3-mL portion to a conical flask, add 100.0 mL of a solution of potassium periodate (prepared by dissolving 3 g of potassium periodate in about 500 mL of warm water, cooling to room temperature, and then diluting with water to 1000 mL), swirl, and allow to stand at room temperature for 10 minutes. Add 4 g of sodium bicarbonate and 2 g of potassium iodide, and titrate immediately with 0.1 N potassium arsenite VS, adding 3 mL of starch TS as the endpoint is approached. Perform a blank determination, using water in place of the Oral Solution, and note the difference in volumes required. Each mL of 0.1 N potassium arsenite is equivalent to 2.303 mg of glycerin ($C_3H_8O_3$).