(Note) The description of each of novel monographs "Dapagliflozin Propylene Glycolate Hydrate" [162KB] and "Dapagliflozin Propylene Glycolate Tablets" [193KB] differs from the description required in the Guideline for Drafting Monographs for The Japanese Pharmacopoeia, Nineteenth Edition (Partial revision) in that the final concentration of a solution is indicated in the procedure for preparing the solution. To be used as references for preparation of solutions, the preparation procedures of the solutions in accordance with the ordinary descriptions of the Japanese Pharmacopoeia describing specific weighing amounts are provided. The preparation procedure of solutions describing specific weighing amounts are provided as a reference and has been verified by the manufacturer who prepared the drafts. Please note that these procedures are not monographs listed in the Japanese Pharmacopoeia.

A reference for procedures for preparing solutions in the novel monograph "Dapagliflozin Propylene Glycolate Hydrate"

Purity Related substances—Perform the test with 10 μL of the sample solution obtained in the Assay as directed under Chromatography *<2.00>* according to the following conditions. Determine each peak area by the automatic integration method, and calculate their amounts by the area percentage method: the amount of the peak of related substance B having the relative retention time of 1.24 to dapagliflozin is not more than 0.15%, and the amount of the peak other than dapagliflozin and the peak mentioned above is not more than 0.10%. Furthermore, the total amount of the peaks other than dapagliflozin is not more than 0.30%. The reporting threshold is 0.05%.

Operating conditions—

Detector, column, column temperature, mobile phase, flowing of mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay.

Time span of measurement: For 39 minutes after injection, beginning after the solvent peak.

System suitability—

Peak symmetry and resolution: Proceed as directed in the system suitability in the Assay.

System sensitivity: To 1 mL of the standard solution obtained in the Assay add acetonitrile to make 100 mL. To 1 mL of this solution add acetonitrile to make 20 mL. When the procedure is run with 10 μL of this solution under the above operating conditions, the SN ratio of the peak of dapagliflozin is not less than 10.

Propylene glycol Weigh accurately about 0.1 g of Dapagliflozin Propylene Glycolate Hydrate, add exactly 5 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately about 75 mg of propylene glycol, add exactly 25 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 1.0 μL each of the sample solution and standard solution as directed under Chromatography *<2.00>* according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of propylene glycol to that of the internal standard. Determine the amount of propylene glycol by the following equation: 14.0 – 16.5%.

$$\text{Amount (\%) of propylene glycol } (C_3H_8O_2) = M_S / M_T \times Q_T / Q_S \times 20$$

M_S: Amount (g) of propylene glycol taken

M_T: Amount (g) of Dapagliflozin Propylene Glycolate Hydrate taken

Internal standard solution—A solution of ethylene glycol in *N*,*N*-dimethylacetamide (33 in 12,500)

Operating conditions—

Detector: A hydrogen flame-ionization detector.

Column: A fused silica column 0.32 mm in inside diameter and 15 m in length, coated the inside surface with polyethylene glycol 20 M for gas chromatography in 0.5 μm thickness.

Column temperature: Maintain the temperature at 150℃ for 2 minutes, then raise to 240℃ at a rate of 40℃ per minute, and maintain at 240℃ for 4 minutes.

Injection port temperature: A constant temperature of about 240℃

Detector temperature: A constant temperature of about 240℃

Carrier gas: Helium.

Flow rate: 3.5 mL per minute.

Split ratio: 1:24

System suitability—

Resolution: When the procedure is run with 1.0 μL of the standard solution under the above operating conditions, the resolution between propylene glycol and the internal standard is not less than 1.5.

System repeatability: When the test is repeated 6 times with 1.0 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratio of the peak area of propylene glycol to that of the internal standard is not more than 3.0%.

Assay Weigh accurately about 40 mg each of Dapagliflozin Propylene Glycolate Hydrate and Dapagliflozin Propylene Glycolate RS, dissolve each in acetonitrile to make exactly 200 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Chromatography <*2.00*> according to the following conditions, and determine the peak areas, A_T and A_S, of dapagliflozin in each solution.

$$\text{Amount (mg) of dapagliflozin } (C_{21}H_{25}ClO_6) = M_S \times A_T / A_S$$

M_S: Amount (mg) of Dapagliflozin Propylene Glycolate RS taken

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 220 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (3.5 μm in particle diameter).

Column temperature: A constant temperature of about 30℃.

Mobile phase A: A mixture of water and trifluoroacetic acid (2000:1).

Mobile phase B: A mixture of acetonitrile for liquid chromatography and trifluoroacetic acid (2000:1).

Flowing of mobile phase: Control the gradient by mixing the mobile phases A and B as directed in the following table.

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 – 2	85	15
2 – 36	85 → 10	15 → 90
36 – 39	10	90

Flow rate: 1 mL per minute (the retention time of dapagliflozin is about 17 minutes).

System suitability—

Peak symmetry: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the symmetry factor of the peak of dapagliflozin is 0.8 – 1.5.

Resolution: Dissolve 4 mg of Dapagliflozin Related Substance A for System Suitability RS in acetonitrile to make 25 mL. To 1 mL of this solution add acetonitrile to make 10 mL. Then, to 0.1 mL of this solution add the standard solution to make 10 mL. When the procedure is run with 10 μL of this solution under the above operating conditions, the resolution between dapagliflozin and the related substance A having the relative retention time of about 1.02 to dapagliflozin is not less than 2.0.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of dapagliflozin is not more than 0.85%, according to the Table 2.00-1 in Chromatography <*2.00*>.