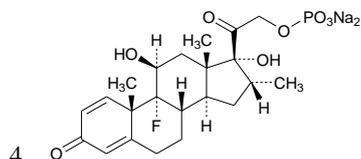


1 Dexamethasone Sodium Phosphate

2 デキサメタゾンリン酸エステルナトリウム
3



4 $C_{22}H_{28}FN_2O_8P$: 516.40

5 Disodium 9-fluoro-11 β ,17,21-trihydroxy-16 α -methylpregna-
6 1,4-
7 diene-3,20-dione 21-phosphate
8 [2392-39-4]

9
10
11 Dexamethasone Sodium Phosphate contains not
12 less than 97.0% and not more than 102.0% of dexa-
13 methasone sodium phosphate ($C_{22}H_{28}FN_2O_8P$), cal-
14 culated on the anhydrous and residual ethanol-free
15 basis.

16 **Description** Dexamethasone Sodium Phosphate occurs
17 as a white to pale yellow crystalline powder.

18 It is freely soluble in water, soluble in methanol, and
19 slightly soluble in ethanol (99.5).

20 It is hygroscopic.

21 **Identification** (1) Proceed with 10 mg of Dexamethasone Sodium Phosphate as directed under Oxygen Flask
22 Combustion Method <1.06>, using a mixture of 0.5 mL of
23 0.01 mol/L sodium hydroxide TS and 20 mL of water as
24 the absorbing liquid: the test solution responds to Qualita-
25 tive Tests <1.09> (1) for fluoride.

26
27 (2) Heat gradually 0.5 g of Dexamethasone Sodium
28 Phosphate to carbonize. After cooling, add a small amount
29 of sulfuric acid, and incinerate by ignition. After cooling,
30 dissolve the residue in 5 mL of water, and filter, if neces-
31 sary: the solution responds to Qualitative Tests <1.09> (2)
32 for phosphate.

33 (3) Determine the absorption spectrum of a solution of
34 Dexamethasone Sodium Phosphate (1 in 62,500) as di-
35 rected under Ultraviolet-visible Spectrophotometry <2.24>,
36 and compare the spectrum with the Reference Spectrum:
37 both spectra exhibit similar intensities of absorption at the
38 same wavelengths.

39 (4) Determine the infrared absorption spectrum of
40 Dexamethasone Sodium Phosphate as directed in the paste
41 method under Infrared Spectrophotometry <2.25>, and
42 compare the spectrum with the Reference Spectrum: both
43 spectra exhibit similar intensities of absorption at the same
44 wave numbers.

45 (5) The solution obtained in (2) responds to Qualitative
46 Tests <1.09> for sodium salt.

47 **Optical rotation** <2.49> $[\alpha]_D^{20}$: +74 – +82° (0.1 g
48 calculated on the anhydrous and residual ethanol-free basis,
49 water, 10 mL, 100 mm).

50 **pH** <2.54> Dissolve 0.10 g of Dexamethasone Sodium
51 Phosphate in 10 mL of water: the pH of the solution is be-
52 tween 7.5 and 10.0.

53 **Purity** (1) Clarity and color of solution—Dissolve 1.0
54 g of Dexamethasone Sodium Phosphate in 10 mL of water:
55 the solution is clear, and its absorbance at 440 nm deter-
56 mined as directed under Ultraviolet-visible Spectropho-
57 tometry <2.24> is not more than 0.15.

58 (2) Heavy metals <1.07>—Proceed with 1.0 g of Dex-
59 amethasone Sodium Phosphate according to Method 2, and
60 perform the test. Prepare the control solution with 2.0 mL
61 of Standard Lead Solution (not more than 20 ppm).

62 (3) Arsenic <1.11>—Prepare the test solution with 1.0
63 g of Dexamethasone Sodium Phosphate according to
64 Method 3, and perform the test (not more than 2 ppm).

65 (4) Free phosphoric acid—Weigh accurately about
66 0.25 g of Dexamethasone Sodium Phosphate, dissolve in
67 water to make exactly 100 mL, and use this solution as the
68 sample solution. Pipet 5 mL each of the sample solution
69 and Standard Phosphoric Acid Solution, add 2.5 mL of hex-
70 aammonium heptamolybdate-sulfuric acid TS and 1 mL of
71 1-amino-2-naphthol-4-sulfonic acid TS, shake, add water
72 to make exactly 25 mL, and allow to stand at $20 \pm 1^\circ\text{C}$ for
73 30 minutes. Perform the test with these solutions as directed
74 under Ultraviolet-visible Spectrophotometry <2.24>, using
75 a solution prepared with 5 mL of water in the same manner
76 as the blank. Determine the absorbances, A_T and A_S , of the
77 solutions obtained from the sample solution and Standard
78 Phosphoric Acid Solution at 740 nm: the amount of free
79 phosphoric acid is not more than 1.0%.

$$80 \quad \text{Amount (\%)} \text{ of free phosphoric acid (H}_3\text{PO}_4\text{)} \\ 81 \quad = 1/M \times A_T/A_S \times 258.0$$

82 M : Amount (mg) of Dexamethasone Sodium Phosphate
83 taken, calculated on the anhydrous and residual ethan-
84 ol-free basis

85 (5) Related substances—Dissolve 20 mg of Dexamethasone Sodium Phosphate in 5 mL of methanol, add the mobile phase A to make 50 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase A to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly
86 15 μL each of the sample solution and standard solution as
87 directed under Liquid Chromatography <2.01> according to
88 the following conditions. Determine each peak area by the
89
90
91
92
93

94 automatic integration method: the area of the peak other
95 than dexamethasone phosphate obtained from the sample
96 solution is not larger than 1/2 times the peak area of dexa-
97 methasone phosphate from the standard solution, and the
98 total area of the peaks other than dexamethasone phosphate
99 from the sample solution is not larger than 1.5 times the
100 peak area of dexamethasone phosphate from the standard
101 solution.

102 *Operating conditions*—

103 Detector, column, column temperature, mobile phases A
104 and B, and flow rate: Proceed as directed in the operating
105 conditions in the Assay.

106 Flowing of mobile phase: Control the gradient by mixing
107 the mobile phases A and B as directed in the following table.
108

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 — 8	88 → 80	12 → 20
8 — 15	80	20
15 — 30	80 → 60	20 → 40
30 — 31	60 → 88	40 → 12
31 — 45	88	12

109
110 Time span of measurement: About 2.5 times as long as
111 the retention time of dexamethasone phosphate, beginning
112 after the solvent peak.

113 *System suitability*—

114 System performance: Proceed as directed in the system
115 suitability in the Assay.

116 Test for required detectability: Pipet 1 mL of the stand-
117 ard solution, and add the mobile phase A to make exactly
118 10 mL. Confirm that the peak area of dexamethasone phos-
119 phate obtained with 15 μ L of this solution is equivalent to
120 7 to 13% of that with 15 μ L of the standard solution.

121 System repeatability: When the test is repeated 6 times
122 with 15 μ L of the standard solution under the above oper-
123 ating conditions, the relative standard deviation of the peak
124 area of dexamethasone phosphate is not more than 1.0%.

125 (6) Ethanol—Weigh accurately about 0.5 g of Dexa-
126 methasone Sodium Phosphate, add exactly 5 mL of the in-
127 ternal standard solution to dissolve, add water to make 10
128 mL, and use this solution as the sample solution. Separately,
129 pipet 1 mL of ethanol (99.5), and add water to make exactly
130 50 mL. Pipet 4 mL of this solution, add exactly 5 mL of the
131 internal standard solution, add water to make 10 mL, and
132 use this solution as the standard solution. Perform the test
133 with 3 μ L of the sample solution and standard solution as
134 directed under Gas Chromatography <2.02> according to
135 the following conditions. Calculate the ratios, Q_T and Q_S ,
136 of the peak area of ethanol to that of the internal standard:
137 the amount of ethanol is not more than 3.0%.

138 Amount (%) of ethanol = $1/M \times Q_T/Q_S \times 8 \times$
139 0.790

140 M : Amount (g) of Dexamethasone Sodium Phosphate
141 taken

142 0.790: Density (g/mL) of ethanol (99.5) at 20°C

143 *Internal standard solution*—A solution of 2-propanol (1 in
144 100).

145 *Operating conditions*—

146 Detector: A hydrogen flame-ionization detector.

147 Column: A glass column 3 mm in inside diameter and 2
148 m in length, packed with spherical porous ethyldivinylben-
149 zene-divinylbenzene copolymer for gas chromatography
150 (149 – 177 μ m in particle diameter).

151 Column temperature: A constant temperature of about
152 150°C.

153 Temperature of sample vaporization chamber: A con-
154 stant temperature of about 150°C.

155 Carrier gas: Nitrogen.

156 Flow rate: Adjust so that the retention time of ethanol is
157 about 6 minutes.

158 *System suitability*—

159 System performance: When the procedure is run with 3
160 μ L of the standard solution under the above operating con-
161 ditions, ethanol and the internal standard are eluted in this
162 order with the resolution between these peaks being not less
163 than 2.0.

164 System repeatability: When the test is repeated 6 times
165 with 3 μ L of the standard solution under the above operat-
166 ing conditions, the relative standard deviation of the ratio
167 of the peak area of ethanol to that of the internal standard
168 is not more than 3.0%.

169 **Water** <2.48> Not more than 12.0% (0.2 g, volumetric ti-
170 tration, direct titration).

171 **Assay** Weigh accurately about 20 mg of Dexamethasone
172 Sodium Phosphate, dissolve in 5 mL of methanol, add the
173 mobile phase A to make exactly 50 mL, and use this solu-
174 tion as the sample solution. Separately, weigh accurately
175 about 20 mg of Dexamethasone Phosphate RS, previously
176 dried under reduced pressure (not exceeding 0.67 kPa) at
177 40°C for 3 hours, dissolve in 5 mL of methanol, add the
178 mobile phase A to make exactly 50 mL, and use this solu-
179 tion as the standard solution. Perform the test with exactly
180 15 μ L each of the sample solution and standard solution as
181 directed under Liquid Chromatography <2.01> according to
182 the following conditions, and determine the peak areas, A_T
183 and A_S , of dexamethasone phosphate in each solution.

184 Amount (mg) of dexamethasone sodium phosphate
185 ($C_{22}H_{28}FN_2O_8P$)
186 = $M_S \times A_T/A_S \times 1.093$

187 M_S : Amount (mg) of Dexamethasone Phosphate RS
188 taken

189 *Operating conditions—*

190 Detector: An ultraviolet absorption photometer (wave-
191 length: 242 nm).

192 Column: A stainless steel column 3.9 mm in inside di-
193 ameter and 15 cm in length, packed with octadecylsilanized
194 silica gel for liquid chromatography (5 μm in particle di-
195 ameter).

196 Column temperature: A constant temperature of about
197 25°C.

198 Mobile phase A: Dissolve 7.8 g of sodium dihydrogen
199 phosphate and 1.88 g of sodium 1-hexanesulfonate in 1900
200 mL of water, adjust to pH 3.0 with phosphoric acid, and
201 add water to make 2000 mL.

202 Mobile phase B: Acetonitrile.

203 Flowing of mobile phase: Control the gradient by mixing
204 the mobile phases A and B as directed in the following table.
205

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 — 8	88 → 80	12 → 20
8 — 15	80	20
15 — 30	80 → 60	20 → 40

206
207 Flow rate: 1.0 mL of per minute.

208 *System suitability—*

209 System performance: When the procedure is run with 15
210 μL of the standard solution under the above operating con-
211 ditions, the number of theoretical plates and the symmetry
212 factor of the peak of dexamethasone phosphate are not less
213 than 10,000 and not more than 2.0, respectively.

214 System repeatability: When the test is repeated 6 times
215 with 15 μL of the standard solution under the above oper-
216 ating conditions, the relative standard deviation of the peak
217 area of dexamethasone phosphate is not more than 1.0%.

218 **Containers and storage** Containers—Tight containers.

219 *Add the following to 9.01 Reference*
220 *Standards (1):*

221 **Dexamethasone Phosphate RS**

222 *Add the following to 9.42 Solid Sup-*
223 *ports/Column Packings for Chromatog-*
224 *raphy:*

225 **Spherical porous ethyldivinylbenzene-divinylben-**
226 **zene copolymer for gas chromatography** Prepared for
227 gas chromatography.