

1 **Chlorpromazine Hydrochloride,**
 2 **Phenobarbital and Promethazine**
 3 **Hydrochloride Tablets**

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 5 メタジン塩酸塩錠

6
 7 Chlorpromazine Hydrochloride, Phenobarbital and
 8 Promethazine Hydrochloride Tablets contain not less
 9 than 95.0% and not more than 105.0% of the labeled
 10 amounts of chlorpromazine hydrochloride
 11 ($C_{17}H_{19}ClN_2S.HCl$: 355.33), phenobarbital
 12 ($C_{12}H_{12}N_2O_3$: 232.24) and promethazine hydrochloride
 13 ($C_{17}H_{20}N_2S.HCl$: 320.88).

14 **Method of preparation** Prepare as directed under Tablets,
 15 with Chlorpromazine Hydrochloride, Phenobarbital and
 16 Promethazine Hydrochloride.

17 **Identification** (1) To an amount of powdered Chlor-
 18 promazine Hydrochloride, Phenobarbital and Promethazine
 19 Hydrochloride Tablets, equivalent to 12.5 mg of Chlor-
 20 promazine Hydrochloride, add 10 mL of ethanol (95), shake,
 21 filter, and use the filtrate as the sample solution. Separately,
 22 dissolve 12.5 mg of chlorpromazine hydrochloride for assay
 23 in 10 mL of ethanol (95), and use this solution as the stand-
 24 ard solution. Perform the test with these solutions as directed
 25 under Thin-layer Chromatography <2.03>. Spot 5 μ L each of
 26 the sample solution and standard solution on a plate of silica
 27 gel with fluorescent indicator for thin-layer chromatography.
 28 Develop the plate with a mixture of ethyl acetate and di-
 29 ethylamine (50:1) to a distance of about 10 cm, and air-dry
 30 the plate. Again, develop the plate with the same developing
 31 solvent to a distance of about 10 cm, and air-dry the plate.
 32 Examine under ultraviolet light (main wavelength: 254 nm):
 33 one of the three spots obtained from the sample solution and
 34 the spot obtained from the standard solution show the same
 35 Rf value.

36 (2) To an amount of powdered Chlorpromazine Hydro-
 37 chloride, Phenobarbital and Promethazine Hydrochloride
 38 Tablets, equivalent to 30 mg of Phenobarbital, add 10 mL of
 39 ethanol (95), shake, filter, and use the filtrate as the sample
 40 solution. Separately, dissolve 30 mg of phenobarbital for
 41 assay in 10 mL of ethanol (95), and use this solution as the
 42 standard solution. Perform the test with these solutions as
 43 directed under Thin-layer Chromatography <2.03>. Spot 5
 44 μ L each of the sample solution and standard solution on a
 45 plate of silica gel with fluorescent indicator for thin-layer
 46 chromatography. Develop the plate with a mixture of ethyl
 47 acetate and diethylamine (50:1) to a distance of about 10 cm,
 48 and air-dry the plate. Again, develop the plate with the same
 49 developing solvent to a distance of about 10 cm, and air-dry

50 the plate. Examine under ultraviolet light (main wavelength:
 51 254 nm): one of the three spots obtained from the sample
 52 solution and the spot obtained from the standard solution
 53 show the same Rf value.

54 (3) To an amount of powdered Chlorpromazine Hydro-
 55 chloride, Phenobarbital and Promethazine Hydrochloride
 56 Tablets, equivalent to 12.5 mg of Promethazine Hydrochlo-
 57 ride, add 10 mL of ethanol (95), shake, filter, and use the
 58 filtrate as the sample solution. Separately, dissolve 12.5 mg
 59 of promethazine hydrochloride for thin-layer chromatog-
 60 raphy in 10 mL of ethanol (95), and use this solution as the
 61 standard solution. Perform the test with these solutions as
 62 directed under Thin-layer Chromatography <2.03>. Spot 5
 63 μ L each of the sample solution and standard solution on a
 64 plate of silica gel with fluorescent indicator for thin-layer
 65 chromatography. Develop the plate with a mixture of ethyl
 66 acetate and diethylamine (50:1) to a distance of about 10 cm,
 67 and air-dry the plate. Again, develop the plate with the same
 68 developing solvent to a distance of about 10 cm, and air-dry
 69 the plate. Examine under ultraviolet light (main wavelength:
 70 254 nm): one of the three spots obtained from the sample
 71 solution and the spot obtained from the standard solution
 72 show the same Rf value.

73 **Uniformity of dosage units** <6.02> Perform the test ac-
 74 cording to the following method: it meets the requirement of
 75 the Content uniformity test. Conduct this procedure using
 76 light-resistant vessels.

77 (1) Chlorpromazine Hydrochloride—To 1 tablet of
 78 Chlorpromazine Hydrochloride, Phenobarbital and Pro-
 79 methazine Hydrochloride Tablets add 60 mL of a mixture of
 80 diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1),
 81 shake vigorously for 20 minutes, and add a mixture of di-
 82 luted phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to
 83 make exactly 100 mL. Pipet V mL of the solution, add a
 84 mixture of diluted phosphoric acid (1 in 500) and ethanol
 85 (99.5) (1:1) to make exactly V' mL so that each mL contains
 86 about 12.5 μ g of chlorpromazine hydrochloride
 87 ($C_{17}H_{19}ClN_2S.HCl$), centrifuge, and use the supernatant liq-
 88 uid as the sample solution. Then, proceed as directed in the
 89 Assay (1).

$$\begin{aligned} & \text{Amount (mg) of chlorpromazine hydrochloride} \\ & (C_{17}H_{19}ClN_2S.HCl) \\ & = M_S \times A_T / A_S \times V' / V \times 1 / 20 \end{aligned}$$

93 M_S : Amount (mg) of chlorpromazine hydrochloride for
 94 assay taken

95 (2) Phenobarbital—To 1 tablet of Chlorpromazine Hy-
 96 drochloride, Phenobarbital and Promethazine Hydrochloride
 97 Tablets add 60 mL of a mixture of diluted phosphoric acid
 98 (1 in 500) and ethanol (99.5) (1:1), shake vigorously for 20

99 minutes, and add a mixture of diluted phosphoric acid (1 in 100
 100 500) and ethanol (99.5) (1:1) to make exactly 100 mL. Pipet
 101 V mL of the solution, add a mixture of diluted phosphoric
 102 acid (1 in 500) and ethanol (99.5) (1:1) to make exactly V'
 103 mL so that each mL contains about 30 μg of phenobarbital
 104 ($\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$), centrifuge, and use the supernatant liquid as
 105 the sample solution. Then, proceed as directed in the Assay
 106 (2).

$$\begin{aligned} & \text{Amount (mg) of phenobarbital (C}_{12}\text{H}_{12}\text{N}_2\text{O}_3) \\ & = M_S \times A_T/A_S \times V'/V \times 1/10 \end{aligned}$$

109 M_S : Amount (mg) of phenobarbital for assay taken

110 (3) Promethazine Hydrochloride—To 1 tablet of Chlor-
 111 promazine Hydrochloride, Phenobarbital and Promethazine
 112 Hydrochloride Tablets add 60 mL of a mixture of diluted
 113 phosphoric acid (1 in 500) and ethanol (99.5) (1:1), shake
 114 vigorously for 20 minutes, and add a mixture of diluted
 115 phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to make
 116 exactly 100 mL. Pipet V mL of the solution, add a mixture
 117 of diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1)
 118 to make exactly V' mL so that each mL contains about 12.5
 119 μg of promethazine hydrochloride ($\text{C}_{17}\text{H}_{20}\text{N}_2\text{S.HCl}$), centri-
 120 fuge, and use the supernatant liquid as the sample solution.
 121 Then, proceed as directed in the Assay (3).

$$\begin{aligned} & \text{Amount (mg) of promethazine hydrochloride} \\ & (\text{C}_{17}\text{H}_{20}\text{N}_2\text{S.HCl}) \\ & = M_S \times A_T/A_S \times V'/V \times 1/20 \end{aligned}$$

125 M_S : Amount (mg) of promethazine hydrochloride for as-
 126 say taken

127 **Dissolution** <6.10> (1) Chlorpromazine hydrochloride—
 128 When the test is performed at 50 revolutions per minute
 129 according to the Paddle method, using 900 mL of 0.05
 130 mol/L acetic acid-sodium acetate buffer solution (pH 4.0) as
 131 the dissolution medium, the dissolution rate in 90 minutes of
 132 Chlorpromazine Hydrochloride, Phenobarbital and Pro-
 133 methazine Hydrochloride Tablets is not less than 75%.

134 Start the test with 1 tablet of Chlorpromazine Hydrochlo-
 135 ride, Phenobarbital and Promethazine Hydrochloride Tablets,
 136 withdraw not less than 20 mL of the medium at the specified
 137 minute after starting the test, and filter through a membrane
 138 filter with a pore size not exceeding 0.45 μm . Discard the
 139 first 10 mL of the filtrate, pipet V mL of the subsequent fil-
 140 trate, add the dissolution medium to make exactly V' mL so
 141 that each mL contains about 14 μg of chlorpromazine hy-
 142 drochloride ($\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S.HCl}$), and use this solution as the
 143 sample solution. Separately, weigh accurately about 14 mg
 144 of chlorpromazine hydrochloride for assay, previously dried
 145 at 105°C for 2 hours, dissolve in methanol to make exactly
 146 50 mL, and use this solution as the chlorpromazine hydro-

chloride standard stock solution. Pipet 5 mL of this solution,
 add the dissolution medium to make exactly 100 mL, and
 use this solution as the standard solution. Perform the test
 with exactly 10 μL each of the sample solution and standard
 solution as directed under Liquid Chromatography <2.01>
 according to the following conditions, and determine the
 peak areas, A_T and A_S , of chlorpromazine in each solution.

$$\begin{aligned} & \text{Dissolution rate (\%)} \text{ with respect to the labeled amount of} \\ & \text{chlorpromazine hydrochloride (C}_{17}\text{H}_{19}\text{ClN}_2\text{S.HCl}) \\ & = M_S \times A_T/A_S \times V'/V \times 1/C \times 90 \end{aligned}$$

157 M_S : Amount (mg) of chlorpromazine hydrochloride for
 158 assay taken

159 C : Labeled amount (mg) of chlorpromazine hydrochloride
 160 ($\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S.HCl}$) in 1 tablet

161 *Operating conditions* —

162 Detector: An ultraviolet absorption photometer
 163 (wavelength: 225 nm).

164 Column: A stainless steel column 4.6 mm in inside
 165 diameter and 15 cm in length, packed with
 166 octadecylsilanized silica gel for liquid chromatography (5
 167 μm in particle diameter).

168 Column temperature: A constant temperature of about
 169 25°C.

170 Mobile phase: Dissolve 3.9 g of sodium dihydrogen
 171 phosphate dihydrate in water to make 1000 mL. To 810 mL
 172 of this solution add 390 mL of acetonitrile for liquid
 173 chromatography.

174 Flow rate: Adjust so that the retention time of
 175 chlorpromazine is about 13 minutes.

176 *System suitability* —

177 System performance: To 5 mL of the chlorpromazine
 178 hydrochloride standard stock solution add 5 mL each of the
 179 phenobarbital standard stock solution obtained in (2) and
 180 promethazine hydrochloride standard stock solution
 181 obtained in (3), then add the dissolution medium to make
 182 100 mL. When the procedure is run with 10 μL of this
 183 solution under the above operating conditions, phenobarbital,
 184 promethazine and chlorpromazine are eluted in this order
 185 and the resolutions between the peaks of phenobarbital and
 186 promethazine and between the peaks of promethazine and
 187 chlorpromazine are not less than 6, respectively.

188 System repeatability: When the test is repeated 6 times
 189 with 10 μL of the standard solution under the above
 190 operating conditions, the relative standard deviation of the
 191 peak area of chlorpromazine is not more than 2.0%.

192 (2) Phenobarbital—When the test is performed at 50
 193 revolutions per minute according to the Paddle method, us-
 194 ing 900 mL of 0.05 mol/L acetic acid-sodium acetate buffer
 195 solution (pH 4.0) as the dissolution medium, the dissolution
 196 rate in 90 minutes of Chlorpromazine Hydrochloride, Phe-

197 nobarbitol and Promethazine Hydrochloride Tablets is not 247
 198 less than 70%. 248
 199 Start the test with 1 tablet of Chlorpromazine Hydrochloride, Phenobarbital and Promethazine Hydrochloride Tablets, 249
 200 withdraw not less than 20 mL of the medium at the specified 250
 201 minute after starting the test, and filter through a membrane 251
 202 filter with a pore size not exceeding 0.45 μm . Discard the 252
 203 first 10 mL of the filtrate, pipet V mL of the subsequent fil- 253
 204 trate, add the dissolution medium to make exactly V' mL so 254
 205 that each mL contains about 33 μg of phenobarbital 255
 206 ($\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$), and use this solution as the sample solution. 256
 207 Separately, weigh accurately about 33 mg of phenobarbital 257
 208 for assay, previously dried at 105°C for 2 hours, dissolve in 258
 209 methanol to make exactly 50 mL, and use this solution as 259
 210 the phenobarbital standard stock solution. Pipet 5 mL of this 260
 211 solution, add the dissolution medium to make exactly 100 261
 212 mL, and use this solution as the standard solution. Perform 262
 213 the test with exactly 10 μL each of the sample solution and 263
 214 standard solution as directed under Liquid Chromatography 264
 215 $\langle 2.01 \rangle$ according to the following conditions, and determine 265
 216 the peak areas, A_T and A_S , of phenobarbital in each solution. 266
 217
 218 Dissolution rate (%) with respect to the labeled amount of 268
 219 phenobarbital ($\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$) 269
 220
$$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 90$$
 270
 221 M_S : Amount (mg) of phenobarbital for assay taken 271
 222 C : Labeled amount (mg) of phenobarbital ($\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$) in 272
 223 1 tablet 273
 224 *Operating conditions* – 274
 225 Proceed as directed in the operating conditions in (1). 275
 226 *System suitability* – 276
 227 System performance: To 5 mL of the phenobarbital 277
 228 standard stock solution add 5 mL each of chlorpromazine 278
 229 hydrochloride standard stock solution obtained in (1) and 279
 230 promethazine hydrochloride standard stock solution 280
 231 obtained in (3), then add the dissolution medium to make 281
 232 100 mL. When the procedure is run with 10 μL of this 282
 233 solution under the above operating conditions, phenobarbital, 283
 234 promethazine and chlorpromazine are eluted in this order 284
 235 and the resolutions between the peaks of phenobarbital and 285
 236 promethazine and between the peaks of promethazine and 286
 237 chlorpromazine are not less than 6, respectively. 287
 238 System repeatability: When the test is repeated 6 times 288
 239 with 10 μL of the standard solution under the above 289
 240 operating conditions, the relative standard deviation of the 290
 241 peak area of phenobarbital is not more than 2.0%. 291
 242 (3) Promethazine hydrochloride—When the test is per- 292
 243 formed at 50 revolutions per minute according to the Paddle 293
 244 method, using 900 mL of 0.05 mol/L acetic acid-sodium 294
 245 acetate buffer solution (pH 4.0) as the dissolution medium, 295
 246 the dissolution rate in 90 minutes of Chlorpromazine Hy- 296
 drochloride, Phenobarbital and Promethazine Hydrochloride 297
 Tablets is not less than 75%. 298
 Start the test with 1 tablet of Chlorpromazine Hydrochloride, Phenobarbital and Promethazine Hydrochloride Tablets, 299
 withdraw not less than 20 mL of the medium at the specified 300
 minute after starting the test, and filter through a membrane 301
 filter with a pore size not exceeding 0.45 μm . Discard the 302
 first 10 mL of the filtrate, pipet V mL of the subsequent fil- 303
 trate, add the dissolution medium to make exactly V' mL so 304
 that each mL contains about 14 μg of promethazine hydro- 305
 chloride ($\text{C}_{17}\text{H}_{20}\text{N}_2\text{S.HCl}$), and use this solution as the sam- 306
 ple solution. Separately, weigh accurately about 14 mg of 307
 promethazine hydrochloride for assay, previously dried at 308
 105°C for 3 hours, dissolve in methanol to make exactly 50 309
 mL, and use this solution as the promethazine hydrochloride 310
 standard stock solution. Pipet 5 mL of this solution, add the 311
 dissolution medium to make exactly 100 mL, and use this 312
 solution as the standard solution. Perform the test with ex- 313
 actly 10 μL each of the sample solution and standard solu- 314
 tion as directed under Liquid Chromatography $\langle 2.01 \rangle$ ac- 315
 cording to the following conditions, and determine the peak 316
 areas, A_T and A_S , of promethazine in each solution. 317
 Dissolution rate (%) with respect to the labeled amount of 318
 promethazine hydrochloride ($\text{C}_{17}\text{H}_{20}\text{N}_2\text{S.HCl}$) 319

$$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 90$$
 320
 M_S : Amount (mg) of promethazine hydrochloride for as- 321
 say taken 322
 C : Labeled amount (mg) of promethazine hydrochloride 323
 ($\text{C}_{17}\text{H}_{20}\text{N}_2\text{S.HCl}$) in 1 tablet 324
Operating conditions – 325
 Proceed as directed in the operating conditions in (1). 326
System suitability – 327
 System performance: To 5 mL of the promethazine 328
 hydrochloride standard stock solution add 5 mL each of 329
 chlorpromazine hydrochloride standard stock solution 330
 obtained in (1) and phenobarbital standard stock solution 331
 obtained in (2), then add the dissolution medium to make 332
 100 mL. When the procedure is run with 10 μL of this 333
 solution under the above operating conditions, phenobarbital, 334
 promethazine and chlorpromazine are eluted in this order 335
 and the resolutions between the peaks of phenobarbital and 336
 promethazine and between the peaks of promethazine and 337
 chlorpromazine are not less than 6, respectively. 338
 System repeatability: When the test is repeated 6 times 339
 with 10 μL of the standard solution under the above 340
 operating conditions, the relative standard deviation of the 341
 peak area of promethazine is not more than 2.0%. 342
Assay Conduct this procedure using light-resistant vessels. 343

295 (1) Chlorpromazine hydrochloride—Weigh accurately 345
 296 the mass of not less than 20 Chlorpromazine Hydrochloride, 346
 297 Phenobarbital and Promethazine Hydrochloride Tablets, and 347
 298 powder. Weigh accurately a portion of the powder, equiva- 348
 299 lent to about 12.5 mg of chlorpromazine hydrochloride 349
 300 ($C_{17}H_{19}ClN_2S.HCl$), add 60 mL of a mixture of diluted 350
 301 phosphoric acid (1 in 500) and ethanol (99.5) (1:1), shake 351
 302 vigorously for 20 minutes, and add a mixture of diluted 352
 303 phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to make 353
 304 exactly 100 mL. Pipet 5 mL of the solution, add a mixture of 354
 305 diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to 355
 306 make exactly 50 mL, centrifuge, and use the supernatant 356
 307 liquid as the sample solution. Separately, weigh accurately 357
 308 about 25 mg of chlorpromazine hydrochloride for assay, 358
 309 previously dried at 105°C for 2 hours, dissolve in a mixture 359
 310 of diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1) 360
 311 to make exactly 200 mL, and use this solution as the chlor- 361
 312 promazine hydrochloride standard stock solution. Pipet 5 362
 313 mL of this solution, add a mixture of diluted phosphoric acid 363
 314 (1 in 500) and ethanol (99.5) (1:1) to make exactly 50 mL, 364
 315 and use this solution as the standard solution. Perform the 365
 316 test with exactly 10 μ L each of the sample solution and 366
 317 standard solution as directed under Liquid Chromatography 367
 318 <2.01> according to the following conditions, and determine 368
 319 the peak areas, A_T and A_S , of chlorpromazine in each solu- 369
 320 tion. 370

$$\begin{aligned} & \text{Amount (mg) of chlorpromazine hydrochloride} \\ & (C_{17}H_{19}ClN_2S.HCl) \\ & = M_S \times A_T / A_S \times 1/2 \end{aligned}$$

324 M_S : Amount (mg) of chlorpromazine hydrochloride for 375
 325 assay taken 376

326 *Operating conditions* —

327 Detector: An ultraviolet absorption photometer 378
 328 (wavelength: 225 nm). 379

329 Column: A stainless steel column 4.6 mm in inside 380
 330 diameter and 10 cm in length, packed with 381
 331 octadecylsilanized silica gel for liquid chromatography (3 382
 332 μ m in particle diameter). 383

333 Column temperature: A constant temperature of about 384
 334 25°C.

335 Mobile phase: Dissolve 3.9 g of sodium dihydrogen 385
 336 phosphate dihydrate in water to make 1000 mL. To 810 mL 386
 337 of this solution add 390 mL of acetonitrile for liquid 387
 338 chromatography. 388

339 Flow rate: Adjust so that the retention time of 389
 340 chlorpromazine is about 11 minutes. 390

341 *System suitability* —

342 System performance: To 5 mL of the chlorpromazine 392
 343 hydrochloride standard stock solution add 5 mL each of the 393
 344 phenobarbital standard stock solution prepared in (2) and the 394

promethazine hydrochloride standard stock solution 395
 prepared in (3), and add a mixture of diluted phosphoric acid 396
 (1 in 500) and ethanol (99.5) (1:1) to make 50 mL. When the 397
 procedure is run with 10 μ L of this solution under the above 398
 operating conditions, phenobarbital, promethazine and 399
 chlorpromazine are eluted in this order, and the resolutions 400
 between the peaks of phenobarbital and promethazine is not 401
 less than 5, and that between the peaks of promethazine and 402
 chlorpromazine is not less than 9. 403

System repeatability: When the test is repeated 6 times 404
 with 10 μ L of the standard solution under the above 405
 operating conditions, the relative standard deviation of the 406
 peak area of chlorpromazine is not more than 1.0%. 407

(2) Phenobarbital—Weigh accurately the mass of not 408
 less than 20 Chlorpromazine Hydrochloride, Phenobarbital 409
 and Promethazine Hydrochloride Tablets, and powder. 410
 Weigh accurately a portion of the powder, equivalent to 411
 about 30 mg of phenobarbital ($C_{12}H_{12}N_2O_3$), add 60 mL of a 412
 mixture of diluted phosphoric acid (1 in 500) and ethanol 413
 (99.5) (1:1), shake vigorously for 20 minutes, and add a 414
 mixture of diluted phosphoric acid (1 in 500) and ethanol 415
 (99.5) (1:1) to make exactly 100 mL. Pipet 5 mL of the solu- 416
 tion, add a mixture of diluted phosphoric acid (1 in 500) and 417
 ethanol (99.5) (1:1) to make exactly 50 mL, centrifuge, and 418
 use the supernatant liquid as the sample solution. Separately, 419
 weigh accurately about 30 mg of phenobarbital for assay, 420
 previously dried at 105°C for 2 hours, dissolve in a mixture 421
 of diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1) 422
 to make exactly 100 mL, and use this solution as the pheno- 423
 barbital standard stock solution. Pipet 5 mL of this solution, 424
 add a mixture of diluted phosphoric acid (1 in 500) and eth- 425
 anol (99.5) (1:1) to make exactly 50 mL, and use this solu- 426
 tion as the standard solution. Perform the test with exactly 427
 10 μ L each of the sample solution and standard solution as 428
 directed under Liquid Chromatography <2.01> according to 429
 the following conditions, and determine the peak areas, A_T 430
 and A_S , of phenobarbital in each solution. 431

$$\begin{aligned} & \text{Amount (mg) of phenobarbital } (C_{12}H_{12}N_2O_3) \\ & = M_S \times A_T / A_S \end{aligned}$$

M_S : Amount (mg) of phenobarbital for assay taken

385 *Operating conditions* —

Proceed as directed in the operating conditions in (1).

387 *System suitability* —

388 System performance: To 5 mL of the phenobarbital 392
 standard stock solution add 5 mL each of the 393
 chlorpromazine hydrochloride standard stock solution 394
 prepared in (1) and the promethazine hydrochloride standard 395
 stock solution prepared in (3), and add a mixture of diluted 396
 phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to make 397
 50 mL. When the procedure is run with 10 μ L of this 398

395 solution under the above operating conditions, phenobarbital, 445
 396 promethazine and chlorpromazine are eluted in this order, 446
 397 and the resolutions between the peaks of phenobarbital and 447
 398 promethazine is not less than 5, and that between the peaks 448
 399 of promethazine and chlorpromazine is not less than 9. 449

400 System repeatability: When the test is repeated 6 times 450
 401 with 10 μL of the standard solution under the above 451
 402 operating conditions, the relative standard deviation of the 452
 403 peak area of phenobarbital is not more than 1.0%.

404 **(3) Promethazine hydrochloride**—Weigh accurately the 453
 405 mass of not less than 20 Chlorpromazine Hydrochloride, 454
 406 Phenobarbital and Promethazine Hydrochloride Tablets, and
 407 powder. Weigh accurately a portion of the powder, equivalent
 408 to about 12.5 mg of promethazine hydrochloride
 409 ($\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}\cdot\text{HCl}$), add 60 mL of a mixture of diluted phosphoric
 410 acid (1 in 500) and ethanol (99.5) (1:1), shake vigorously for 20 minutes,
 411 and add a mixture of diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1)
 412 to make exactly 100 mL. Pipet 5 mL of the solution, add a mixture of
 413 diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to
 414 make exactly 50 mL, centrifuge, and use the supernatant
 415 liquid as the sample solution. Separately, weigh accurately
 416 about 25 mg of promethazine hydrochloride for assay, previously
 417 dried at 105°C for 3 hours, dissolve in a mixture of
 418 diluted phosphoric acid (1 in 500) and ethanol (99.5) (1:1) to
 419 make exactly 200 mL, and use this solution as the promethazine
 420 hydrochloride standard stock solution. Pipet 5 mL of
 421 this solution, add a mixture of diluted phosphoric acid (1 in
 422 500) and ethanol (99.5) (1:1) to make exactly 50 mL, and
 423 use this solution as the standard solution. Perform the test
 424 with exactly 10 μL each of the sample solution and standard
 425 solution as directed under Liquid Chromatography <2.01>
 426 according to the following conditions, and determine the
 427 peak areas, A_T and A_S , of promethazine in each solution.
 428

$$429 \quad \text{Amount (mg) of promethazine hydrochloride} \\
 430 \quad (\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}\cdot\text{HCl}) \\
 431 \quad = M_S \times A_T / A_S \times 1/2$$

432 M_S : Amount (mg) of promethazine hydrochloride for assay taken
 433

434 *Operating conditions* —

435 Proceed as directed in the operating conditions in (1).

436 *System suitability* —

437 System performance: To 5 mL of the promethazine
 438 hydrochloride standard stock solution add 5 mL each of the
 439 chlorpromazine hydrochloride standard stock solution
 440 prepared in (1) and the phenobarbital standard stock solution
 441 prepared in (2), and add a mixture of diluted phosphoric acid
 442 (1 in 500) and ethanol (99.5) (1:1) to make 50 mL. When the
 443 procedure is run with 10 μL of this solution under the above
 444 operating conditions, phenobarbital, promethazine and

chlorpromazine are eluted in this order, and the resolutions
 between the peaks of phenobarbital and promethazine is not
 less than 5, and that between the peaks of promethazine and
 chlorpromazine is not less than 9.

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 promethazine is not more than 1.0%.

Containers and storage Containers — Well-closed containers.

Add the following to 9.41 Reagents, Test Solutions:

Promethazine hydrochloride for assay
 $\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}\cdot\text{HCl}$ [Same as the monograph Promethazine Hydrochloride. When dried, it contains not less than 99.0% of promethazine hydrochloride ($\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}\cdot\text{HCl}$).]

Promethazine hydrochloride for thin-layer chromatography
 $\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}\cdot\text{HCl}$ [Same as the monograph Promethazine Hydrochloride]