

1 9536
2 1E-4 Rev 5/98

PRODUCT INFORMATION SHEET

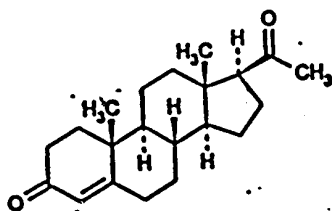
PROMETRIUM®

(progesterone, USP)

Capsules 100 mg

10 DESCRIPTION

11 Each PROMETRIUM® (progesterone, USP) Capsule contains 100 mg micronized
12 progesterone for oral administration. Progesterone has a molecular weight of
13 314.47 and an empirical formula of $C_{21}H_{30}O_2$. Progesterone,
14 (pregn-4-ene-3,20-dione) is a white or creamy white, odorless, crystalline
15 powder, practically insoluble in water, soluble in alcohol, acetone and dioxane,
16 and sparingly soluble in vegetable oils, stable in air, melting between 126° and
17 131°C. The structural formula is:



19
20 Each peach-colored, opaque, soft gelatin capsule contains 100 mg micronized
21 progesterone as the active ingredient. The inactive ingredients are peanut oil
22 NF, gelatin NF, glycerin USP, lecithin NF, titanium dioxide USP, D&C Yellow No.
23 10 and FD&C Red No. 40.

24
25

26

27 **CLINICAL PHARMACOLOGY**

28 PROMETRIUM® Capsules are an oral dosage form of micronized progesterone
29 which is chemically identical to progesterone of ovarian origin. The oral
30 bioavailability of progesterone is increased through micronization.

31

32 **Pharmacokinetics**

33 ***Absorption***

34 After oral administration of progesterone as a micronized soft gelatin capsule
35 formulation, maximum serum concentrations were attained within 3 hours. The
36 absolute bioavailability of micronized progesterone is not known. Table 1
37 summarizes the mean pharmacokinetic parameters in post-menopausal women
38 after five oral daily doses of PROMETRIUM® Capsules as a micronized soft
39 gelatin capsule formulation:

40

Table 1

| Parameter | PROMETRIUM® Capsules Dose QD | | |
|--------------------------|------------------------------|------------|-------------|
| | 100mg | 200mg | 300mg |
| Cmax (ng/mL) | 17.3 ±21.9 ^a | 38.1±37.8 | 60.6±72.5 |
| Tmax (hr) | 1.5±0.8 | 2.3±1.4 | 1.7±0.6 |
| AUC (0-10) (ng·hr/mL) | 43.3±30.8 | 101.2±66.0 | 175.7±170.3 |

41 ^a Mean ± S.D.

42



43 Serum progesterone concentrations appeared linear and dose proportional
44 following multiple dose administration of PROMETRIUM® Capsules over the dose
45 range 100 mg/day to 300 mg/day in post-menopausal women. Although doses
46 greater than 300 mg/day were not studied in females, serum concentrations
47 from a study in male volunteers appeared linear and dose proportional between
48 100 mg/day and 400 mg/day. The pharmacokinetic parameters in male
49 volunteers were generally consistent with those seen in post-menopausal
50 women.

51

52 ***Distribution***

53 Progesterone is approximately 96-99% bound to serum proteins, primarily to
54 serum albumin (50-54%) and transcortin (43-48%).

55

56 ***Metabolism***

57 Progesterone is metabolized primarily by the liver largely to pregnanediols and
58 pregnanolones. Pregnanediols and pregnanolones are conjugated in the liver to
59 glucuronide and sulfate metabolites. Progesterone metabolites which are
60 excreted in the bile may be deconjugated and may be further metabolized in the
61 gut via reduction, dehydroxylation, and epimerization.

62

63 ***Excretion***

64 The glucuronide and sulfate conjugates of pregnanediol and pregnanolone are
65 excreted in the bile and urine. Progesterone metabolites which are excreted in
66 the bile may undergo enterohepatic recycling or may be excreted in the feces.

67

68

69



70 ***Special Populations***

71 The pharmacokinetics of this formulation have not been assessed in low body
72 weight or obese patients.

73

74 ***Race:***

75 There is insufficient information available from trials conducted with
76 PROMETRIUM® Capsules to compare progesterone pharmacokinetics in different
77 racial groups.

78

79 ***Drug-Drug Interaction:***

80 The metabolism of progesterone by human liver microsomes was inhibited by
81 ketoconazole ($IC_{50} < 0.1 \mu M$). Ketoconazole is a known inhibitor of cytochrome
82 P450 3A4, hence these data suggest that other known inhibitors of this enzyme
83 may increase the bioavailability of progesterone. The clinical relevance of the *in*
84 *vitro* findings are unknown.

85

86 ***Food-Drug Interaction:***

87 Concomitant food ingestion increased the bioavailability of PROMETRIUM®
88 Capsules relative to a fasting state when administered to post-menopausal
89 women at a dose of 200 mg. This effect was further characterized at a single
90 dose of 300 mg in healthy male volunteers. Mean C_{max} was slightly increased
91 (9%) when PROMETRIUM® Capsules were administered with or 2 hours after a
92 high fat breakfast relative to the fasting state. In contrast, when the
93 PROMETRIUM® Capsules dose was administered 4 hours after the high fat
94 breakfast there was a significant increase in C_{max} (193%). The corresponding
95 increases in AUC were 47, 50, and 102% following administration with
96 breakfast, 2 hours and 4 hours after breakfast, respectively. There was no



97 effect on the time to maximum serum concentrations (T_{max}). High intra- and
98 intersubject variability was observed.

99

100 *Hepatic Insufficiency:*

101 No formal studies have evaluated the effect of hepatic disease on the disposition
102 of progesterone. However, since progesterone is metabolized by the liver, use
103 in patients with severe liver dysfunction or disease is contraindicated (See
104 **CONTRAINDICATIONS**). If treatment with progesterone is indicated in patients
105 with mild to moderate hepatic dysfunction, these patients should be monitored
106 carefully.

107

108 *Renal Insufficiency:*

109 No formal studies have evaluated the effect of renal disease on the disposition
110 of progesterone. Since progesterone metabolites are eliminated mainly by the
111 kidneys, PROMETRIUM[®] Capsules should be used with caution and only with
112 careful monitoring in patients with renal dysfunction. (See **PRECAUTIONS**)

113

114 **Clinical Studies**

115 In a single-center, randomized, double-blind clinical study that included pre-
116 menopausal women with secondary amenorrhea for at least 90 days,
117 administration of 10 days of micronized progesterone therapy resulted in 80%
118 experiencing withdrawal bleeding within 7 days of the last dose of
119 PROMETRIUM[®] Capsules, 300 mg/day (n=20), compared to 10% of women
120 experiencing withdrawal bleeding in the placebo group (n=21).

121

122 The rate of secretory transformation was evaluated in a multicenter,
123 randomized, double-blind clinical study in estrogen primed post-menopausal



124 women. Micronized progesterone administered orally for 10 days at 400
125 mg/day (n = 22) induced complete secretory changes in the endometrium in 45%
126 of women compared to 0% in the placebo group (n = 23).

127

128

129 INDICATIONS AND USAGE

130 Secondary amenorrhea.

131

132 CONTRAINDICATIONS

- 133 1. Known sensitivity to PROMETRIUM[®] Capsules or its ingredients.
134 PROMETRIUM[®] Capsules contain peanut oil and should never be used by
135 patients allergic to peanuts.
- 136 2. Known or suspected pregnancy.
- 137 3. Thrombophlebitis, thromboembolic disorders, cerebral apoplexy or
138 patients with a past history of these conditions.
- 139 4. Severe liver dysfunction or disease.
- 140 5. Known or suspected malignancy of breast or genital organs.
- 141 6. Undiagnosed vaginal bleeding.
- 142 7. Missed abortion.
- 143 8. As a diagnostic test for pregnancy.

144

145 WARNINGS

- 146 1. The physician should be alert to the earliest manifestations of thrombotic
147 disorders (thrombophlebitis, cerebrovascular disorders, pulmonary
148 embolism, and retinal thrombosis). Should any of these occur or be
149 suspected, the drug should be discontinued immediately.



- 150 2. Discontinue medication pending examination if there is sudden partial or
151 complete loss of vision, or if there is a sudden onset of proptosis, diplopia
152 or migraine. If examination reveals papilledema or retinal vascular lesions,
153 medication should be withdrawn.
- 154 3. The administration of any drug to nursing mothers should be done only
155 when clearly necessary since many drugs are excreted in human milk.
156 Detectable amounts of progestin have been identified in the milk of
157 mothers receiving progestins. The effect of this on the nursing infant has
158 not been determined.
- 159 4. Usage in pregnancy is not recommended. A case of cleft palate has been
160 observed in the child of a woman who was using PROMETRIUM[®]
161 Capsules during early pregnancy. Rare instances of fetal death have been
162 reported in pregnant women prescribed PROMETRIUM[®] Capsules for
163 unapproved indications. Definitive causality has not been established.
- 164 5. Retrospective studies of morbidity and mortality in Great Britain and
165 studies of morbidity in the United States have shown a statistically
166 significant association between thrombophlebitis, pulmonary embolism,
167 cerebral thrombosis and embolism, and the use of oral contraceptives.
168 The estimate of the relative risk of thromboembolism in the study by
169 Vessey and Doll was about seven fold, while Sartwell and associates in
170 the United States found a relative risk of 4.4, meaning that the users are
171 several times as likely to undergo thromboembolic disease without evident
172 cause as nonusers. The American study also indicated that the risk did
173 not persist after discontinuation of administration, and that it was not
174 enhanced by long continued administration. The American study was not
175 designed to evaluate a difference between products.
176



177 **PRECAUTIONS**

178 **General**

- 179 1. The pretreatment physical examination should include special reference to
180 breast and pelvic organs, as well as Papanicolaou smear.
- 181 2. Because progesterone may cause some degree of fluid retention,
182 conditions which might be influenced by this factor, such as epilepsy,
183 migraine, asthma, cardiac or renal dysfunction, require careful observation.
- 184 3. In cases of breakthrough bleeding, as in any cases of irregular bleeding per
185 vaginum, nonfunctional causes should be borne in mind. In cases of
186 undiagnosed vaginal bleeding, adequate diagnostic measures are indicated.
- 187 4. Patients who have a history of psychic depression should be carefully
188 observed and the drug discontinued if the depression recurs to a serious
189 degree.
- 190 5. Any possible influence of prolonged progestin therapy on pituitary, ovarian,
191 adrenal, hepatic or uterine functions awaits further study.
- 192 6. Diabetic patients should be carefully observed while receiving progestin
193 therapy.
- 194 7. The pathologist should be advised of progestin therapy when relevant
195 specimens are submitted.
- 196 8. Because of the occurrence of thrombotic disorders (thrombophlebitis,
197 pulmonary embolism, retinal thrombosis, and cerebrovascular disorders) in
198 patients taking estrogen-progestin combinations, the physician should be
199 alert to the earliest manifestation of these disorders, although the
200 mechanism is obscure.
- 201 9. Transient dizziness may occur in some patients. Use caution when driving
202 a motor vehicle or operating machinery.
- 203



204 **Information for the Patient**

205 See accompanying Patient Insert.

206

207 **Drug Lab Test Interactions**

208 The following laboratory results may be altered by the use of estrogen-progestin
209 combination drugs:

210 Increased sulfobromophthalein retention and other hepatic function tests.

211 Coagulation tests: increase in prothrombin factors VII, VIII, IX and X.

212 Metyrapone test.

213 Pregnanediol determination.

214 Thyroid function: increase in PBI, and butanol extractable protein bound
215 iodine and decrease in T3 uptake values.

216

217 In a three year study of micronized progesterone 200 mg/day administered for
218 12 days per 28 day cycle in combination with conjugated estrogens 0.625
219 mg/day, the concomitant use of conjugated estrogens and micronized
220 progesterone increased HDL-C and triglycerides and decreased LDL-C compared
221 to placebo, and did not impair glucose tolerance.

222

223 **Carcinogenesis, Mutagenesis, Impairment of Fertility**

224 Progesterone has not been tested for carcinogenicity in animals by the oral route
225 of administration. Other progestational drugs administered to experimental
226 animals by various routes of administration, including orally, have produced
227 tumors in several tissues after exposure to high dosages.

228

229 Progesterone did not show evidence of genotoxicity in *in vitro* studies for point
230 mutations or for chromosome damage. *In vivo* animal studies for chromosome



231 damage have yielded positive results in mice at oral doses of 1000 mg/kg and
232 2000 mg/kg (Med Sci Res 1987; 15:703-704).

233

234 Exogenously administered progesterone has been shown to inhibit ovulation in a
235 number of species and it is expected that high doses given for an extended
236 duration would impair fertility until the cessation of treatment.

237

238 **Pregnancy Category X**

239 Progesterone including PROMETRIUM® Capsules should not be used during
240 pregnancy.

241

242 **Nursing Mothers**

243 The administration of any drug to nursing mothers should be done only when
244 clearly necessary since many drugs are excreted in human milk. Detectable
245 amounts of progestin have been identified in the milk of nursing mothers
246 receiving progestins. The effect of this on the nursing infant has not been
247 determined.

248

249 **Pediatric Use**

250 The safety and effectiveness of PROMETRIUM® Capsules in pediatric patients
251 have not been established.

252



253

254 **ADVERSE REACTIONS**

255 Table 2 lists adverse experiences which were reported in $\geq 5\%$ of patients
256 receiving PROMETRIUM® Capsules, 400 mg/day, in a multicenter, randomized,
257 double blind, placebo controlled clinical trial in estrogen primed (6 weeks)
258 postmenopausal women receiving conjugated equine estrogens 0.625 mg/day
259 and cyclic (10 days per calendar month cycle) PROMETRIUM® Capsules at a
260 dose of 400 mg/day for 3 cycles.

261



262

Table 2

| Adverse Experiences (≥5%) Reported in Patients Using 400 mg/day in a Placebo-Controlled Trial in Estrogen Primed Post-menopausal Women | | |
|--|--|-------------------|
| Adverse Experience | PROMETRIUM® Capsules 400 mg N = 25 | Placebo N = 24 |
| | Percentage (%) of Patients | |
| Fatigue | 8 | 4 |
| Headache | 16 | 8 |
| Dizziness | 24 | 4 |
| Abdominal Distension (Bloating) | 8 | 8 |
| Abdominal Pain (Cramping) | 20 | 13 |
| Diarrhea | 8 | 4 |
| Nausea | 8 | 0 |
| Back Pain | 8 | 8 |
| Musculoskeletal Pain | 12 | 4 |
| Irritability | 8 | 4 |
| Breast Pain | 16 | 8 |
| Infection Viral | 12 | 0 |
| Coughing | 8 | 0 |

263



264 The most common adverse experiences reported in $\geq 5\%$ of patients in all
265 PROMETRIUM[®] Capsules dosage groups studied in this trial (100 mg/day to 400
266 mg/day) were: dizziness (16%), breast pain (11%), headache (10%), abdominal
267 pain (10%), fatigue (9%), viral infection (7%), abdominal distension (6%),
268 musculoskeletal pain (6%), emotional lability (6%), irritability (5%), and upper
269 respiratory tract infection (5%).

270

271 Other adverse events reported in $< 5\%$ of patients taking PROMETRIUM[®]
272 Capsules include:

273 *Autonomic Nervous System Disorders:* dry mouth

274 *Body As A Whole:* accidental injury, chest pain, fever

275 *Cardiovascular System Disorders:* hypertension

276 *Central and Peripheral Nervous System Disorders:* confusion, somnolence,
277 speech disorder

278 *Gastrointestinal System Disorders:* constipation, dyspepsia,
279 gastroenteritis, hemorrhagic rectum, hiatus hernia, vomiting

280 *Hearing and Vestibular Disorders:* earache

281 *Heart Rate and Rhythm Disorders:* palpitation

282 *Metabolic and Nutritional Disorders:* edema, edema peripheral

283 *Musculoskeletal System Disorders:* arthritis, leg cramps, hypertonia, muscle
284 disorder, myalgia

285 *Myo/Endo/Pericardial and Valve Disorders:* angina pectoris

286 *Psychiatric Disorders:* anxiety, depression, impaired concentration, insomnia,
287 personality disorder

288 *Reproductive System Disorders:* leukorrhea, uterine fibroid, vaginal dryness,
289 fungal vaginitis, vaginitis

290 *Resistance Mechanism Disorders:* abscess, herpes simplex



291 *Respiratory System Disorders:* bronchitis, nasal congestion, pharyngitis,
292 pneumonitis, sinusitis

293 *Skin and Appendages Disorders:* acne, verruca, wound debridement

294 *Urinary System Disorders:* urinary tract infection

295 *Vision Disorders:* abnormal vision

296 *White Cell and Resistance Disorders:* lymphadenopathy

297

298 The following adverse experiences have been reported with PROMETRIUM®
299 Capsules in other U.S. clinical trials: increased sweating, asthenia, tooth
300 disorder, anorexia, increased appetite, nervousness, and breast enlargement.

301

302 The following spontaneous adverse events have been reported during the foreign
303 marketing of PROMETRIUM® Capsules: reversible cases of hepatitis and
304 elevated transaminases. These events occurred mainly in patients receiving high
305 doses of up to 1200 mg.

306

307 The following additional adverse experiences have been observed in women
308 taking progestins in general: breakthrough bleeding, spotting, change in
309 menstrual flow, amenorrhea, changes in weight (increase or decrease), changes
310 in the cervical squamo-columnar junction and cervical secretions, cholestatic
311 jaundice, anaphylactoid reactions and anaphylaxis, rash (allergic) with and
312 without pruritus, melasma or chloasma, pyrexia, and insomnia.

313

314

315

316

317



318 **OVERDOSAGE**

319 No studies on overdose have been conducted in humans. In the case of
320 overdose, PROMETRIUM[®] Capsules should be discontinued, and the patient
321 should be treated symptomatically.

322

323

324 **DOSAGE AND ADMINISTRATION**

325 PROMETRIUM[®] Capsules may be given as a single daily dose of 400 mg in the
326 evening for 10 days.

327

328

329 **HOW SUPPLIED**

330 PROMETRIUM[®] (progesterone USP) Capsules 100 mg are round, peach colored
331 capsules branded with black imprint "SV", available in bottles of 100 capsules
332 (NDC 0032-1708-01).

333

334 **Store at controlled room temperature at 25°C (77°F).**

335

336 **Dispense in tight, light resistant container as defined in USP/NF, accompanied**
337 **by a Patient Insert.**

338

339 **Rx only**

340

341 **Manufactured By:**

342 **R. P. Scherer North America**

343 **St. Petersburg, FL 33716**

344



345 Marketed By:
346 Solvay
347 Pharmaceuticals, Inc.
348 Marietta, GA 30062
349
350 © 1998 Solvay Pharmaceuticals, Inc.



351

PATIENT INSERT

352

PROMETRIUM®

353

(progesterone, USP)

354

Capsules 100 mg

355

356

357 Please read this information carefully before you start to use PROMETRIUM®
358 Capsules, and each time your prescription is renewed, in case anything has
359 changed. This patient information leaflet does not take the place of discussions with
360 your doctor. If you have any questions, ask your doctor or health-care provider.

361

362 **THIS PRODUCT CONTAINS PEANUT OIL AND SHOULD NOT BE USED IF YOU**
363 **ARE ALLERGIC TO PEANUTS.**

364

365 **ABOUT PROMETRIUM® CAPSULES**

366 PROMETRIUM® Capsules are an oral formulation which contains the natural
367 female hormone called progesterone. It is chemically identical to progesterone of
368 ovarian origin. PROMETRIUM® Capsules are used for the treatment of secondary
369 amenorrhea (absence of menstrual periods in women who have previously had a
370 menstrual period) due to progesterone deficiency.

371



372 **UNDERSTANDING THE ROLE OF PROMETRIUM® CAPSULES IN THE**
373 **TREATMENT OF YOUR MENSTRUAL IRREGULARITIES**

374 Progesterone is one of the hormones essential for regular menstrual periods. If your
375 doctor has determined your body does not produce enough progesterone on its
376 own, PROMETRIUM® Capsules may be prescribed to provide the progesterone you
377 need. When you do not produce enough progesterone, menstrual irregularities can
378 occur. PROMETRIUM® Capsules can provide you with the progesterone needed
379 during a normal menstrual cycle.

380

381 **YOU SHOULD NOT USE PROMETRIUM® CAPSULES**

- 382 • If you are allergic to progesterone, progesterone-like drugs, or any of the
383 inactive ingredients in the capsules. Note that PROMETRIUM® Capsules
384 contain peanut oil and should not be used if you are allergic to peanuts.
- 385 • If you are pregnant or suspect that you are pregnant.
- 386 • If you have or have had blood clots in the legs, lungs, eyes, brain, or elsewhere.
- 387 • If you have liver disease.
- 388 • If you have known or suspected cancer of the breast or reproductive organs.
- 389 • If you have unusual bleeding from the vagina which has not been evaluated by
390 your doctor.



- 391 • If you have a miscarriage and your physician suspects some tissue is still in the
392 uterus.
- 393 • If you are nursing.

394

395 RISKS OF PROMETRIUM® CAPSULES

396

- 397 • *Risk to the Fetus.* A case of cleft palate has been reported in the child of a
398 woman who was using PROMETRIUM® Capsules during early pregnancy
399 Although definitive causality has not been established, you should check with
400 your doctor about the risks to your unborn child of any medication taken during
401 pregnancy.

402

- 403 • *Abnormal Blood Clotting.* Use of progestational drugs has been associated with
404 changes in the blood clotting system. These changes allow the blood to clot
405 more easily, possibly allowing clots to form in the bloodstream. If blood clots do
406 form in your bloodstream, they can cut off the blood supply to vital organs,
407 causing serious problems. These problems may include a stroke (by cutting off
408 blood to part of the brain), a heart attack (by cutting off blood to part of the
409 heart), a pulmonary embolus (by cutting off blood to part of the lungs), visual loss
410 or blindness (by cutting off blood vessels in the eye), or other problems. Any of



411 these conditions may cause death or serious long-term disability. Call your
412 doctor immediately if you suspect you have any of these conditions. He or she
413 may advise you to stop using this drug.

414

- 415 • *Eye Abnormalities.* Discontinue medication and call your physician immediately
416 if you experience sudden partial or complete loss of vision, blurred vision, or
417 sudden onset of bulging eyes, double vision, or migraine.

418

419 POSSIBLE SIDE EFFECTS OF PROMETRIUM® CAPSULES

420 Consult your doctor if you experience any of the side effects mentioned below, or
421 other side effects.

422

423 SIDE EFFECTS REPORTED IN GREATER THAN OR EQUAL TO 5% OF
424 PATIENTS AT DOSES OF 100 MG/DAY to 400 MG/DAY:

- 425 • Dizziness*
- 426 • Abdominal Pain (Cramping)
- 427 • Headache
- 428 • Breast Pain
- 429 • Muscle or Bone Pain
- 430 • Viral Infection



- 431 • Fatigue
- 432 • Bloating
- 433 • Diarrhea
- 434 • Nausea
- 435 • Back Pain
- 436 • Irritability
- 437 • Coughing
- 438 • Mood Swings
- 439 • Upper Respiratory Tract Infection

440

441 SIDE EFFECTS REPORTED IN LESS THAN 5% OF PATIENTS:

442 Dry mouth, chest pain, fever, high blood pressure, confusion, drowsiness*,
443 constipation, heartburn, indigestion, stomach pain, intestinal pain, vomiting,
444 pounding or racing of the heart, fluid retention, swelling in legs or arms,
445 arthritis, leg cramps, muscle cramps, anxiety, depression, decreased
446 concentration, sleep disorder, personality disorder, vaginal discharge, uterine
447 fibroid, vaginal dryness, fungal vaginal infection, inflammation of vagina,
448 infections, bronchitis, nasal congestion, sore throat, swelling of lungs,
449 swelling or fluid in sinus cavities, acne, urinary tract infection, blurred vision,
450 swelling of the lymph nodes.

451

452 *Use caution when driving a motor vehicle or operating machinery as dizziness or



453 drowsiness may occur.

454

455 **PRECAUTIONS**

456 Be alert for unusual signs and symptoms. If any of these warning signals (or any
457 other unusual symptoms) happen while you are using PROMETRIUM® Capsules,
458 call your doctor immediately:

- 459 • Breast lumps, (Ask your doctor or health-care provider to show you how to
460 examine your breasts monthly).
- 461
- 462 • Pain, swelling or tenderness in the abdomen.
- 463
- 464 • Tremors or seizures, migraine headaches, shortness of breath or asthma, heart
465 problems, kidney problems.
- 466
- 467 • Abnormal bleeding from the vagina
- 468
- 469 • Feelings of depression.
- 470
- 471 • Pains in the calves or chest, a sudden shortness of breath or coughing blood,
472 indicating possible clots in the legs, heart or lungs.
- 473
- 474 • Severe headache, vomiting, dizziness, faintness, or changes in vision or speech,
475 weakness or numbness in an arm or leg, indicating possible clots in the brain or
476 eye.
- 477

478 Use caution when driving a motor vehicle or operating machinery as
479 dizziness or drowsiness may occur.

480

481 Inform your doctor if you are diabetic.

482

483 You should inform your doctors that you are taking a hormone before lab
484 tests or biopsies are performed.

485



486

487 **OTHER INFORMATION**

- 488 • Your doctor has prescribed this drug for you and you alone. Do not give this drug
489 to anyone else.
- 490 • This medication was prescribed for your particular medical condition. Do not use
491 it for another condition.
- 492 • Keep this and all drugs out of the reach of children.

493

494 **HOW SUPPLIED**

495 PROMETRIUM® Capsules 100 mg are round, peach colored capsules branded with
496 black imprint "SV".

497

498 PROMETRIUM® Capsules should be stored at controlled room temperature at 25°C
499 (77 °F).

500

501 **Manufactured By:**

502 R. P. Scherer North America

503 St. Petersburg, FL 33716

504

505 **Marketed By:**



506 Solvay
507 Pharmaceuticals, Inc.
508 Marietta, GA 30062.
509
510
511 Copyright© 1998 Solvay Pharmaceuticals, Inc.



512

PROMETRIUM[®] Capsules

513

Label for 100 Capsules in Bottle

514

515 MAIN PANEL

516

100 CAPSULES

517

NDC-0032-1708-01

518

PROMETRIUM[®]

519

(progesterone, USP)

520

Capsules

521

100 mg

522

523

Rx only

524

Keep bottle tightly closed.

525

Keep out of Reach of Children

526

527

528 SIDE PANELS

529

530

Each capsule contains: 100 mg micronized progesterone

531

532

Usual Dose: See package insert

533

534

Read accompanying directions carefully

535

536

Dispense in tight, light resistant container as defined in USP/NF,

537

accompanied by a Patient Insert

538



539 **Store at controlled room temperature at 25°C (77°F).**

540

541 Manufactured By: R.P. Scherer North America, St. Petersburg, FL
542 33716.

543 Marketed By: Solvay Pharmaceuticals, Inc., Marietta, GA 30062.

544

545 LOT:

546 EXP:

547



548 **PROMETRIUM® Capsules**
549 **IPFC for Professional Sample (24 capsules) 100 mg**

550

551 MAIN PANEL, FRONT

552

Solvay Pharmaceuticals

553

Professional Sample - Not for Resale

554

24 Capsules (2 Blister Cards of 12 Capsules each)

555

NDC 0032-1708-24

556

557

PROMETRIUM®

558

(progesterone, USP)

559

Capsules

560

100mg

561

562

Not Child Resistant

563

Keep Out of Reach of Children

564

Rx only

565

566

MAIN PANEL, BACK

567

Professional Sample - Not for Resale

568

Each capsule contains: 100 mg micronized progesterone

569

570

Usual Dose: See package insert

571

Read accompanying directions carefully

572

573

Store at controlled room temperature at 25°C (77°F).

574

Protect from light and excessive moisture.



575

576 Manufactured By: R.P. Scherer North America, St. Petersburg, FL 33716.

577 Marketed By: Solvay Pharmaceuticals, Inc., Marietta, GA 30062.

578

579 LOT:

580 EXP:

581

582

583 TOP AND SIDE FLAPS

584 24 CAPSULES

585 PROMETRIUM® (progesterone, USP) Capsules

586 100mg



587

PROMETRIUM® Capsules

588

Professional Sample Blister Backing

589

590

PROMETRIUM®

591

(progesterone, USP)

592

Capsules

593

100 mg

594

595

Marketed by:

596

Solvay Pharmaceuticals, Inc.

597

Marietta, GA 30062

598



This label may not be the latest approved by FDA.
For current labeling information, please visit <https://www.fda.gov/drugsatfda>

NDA 19-781
PROMETRIUM CAPSULES

REVISED DRAFT LABELING
March 19, 1998

PROMETRIUM® Capsules
Professional Sample Blister Backing

CODE AREA CODE AREA
PROMETRIUM®
(progesterone, USP)
100 mg Capsules
Marketed by:
Solvay Pharmaceuticals, Inc.
Marietta, GA 30062
1E0198

CODE AREA CODE AREA
PROMETRIUM®
(progesterone, USP)
100 mg Capsules
Marketed by:
Solvay Pharmaceuticals, Inc.
Marietta, GA 30062
1E0198

PLEASE NOTE:
[CODE AREA]
WILL NOT BE PRINTED
IT IS REFERENCING
WHERE THE LOT AND
EXPIRATION DATE
WILL APPEAR

NDA 19-781
PROMETRIUM CAPSULES

MAR 20 1998

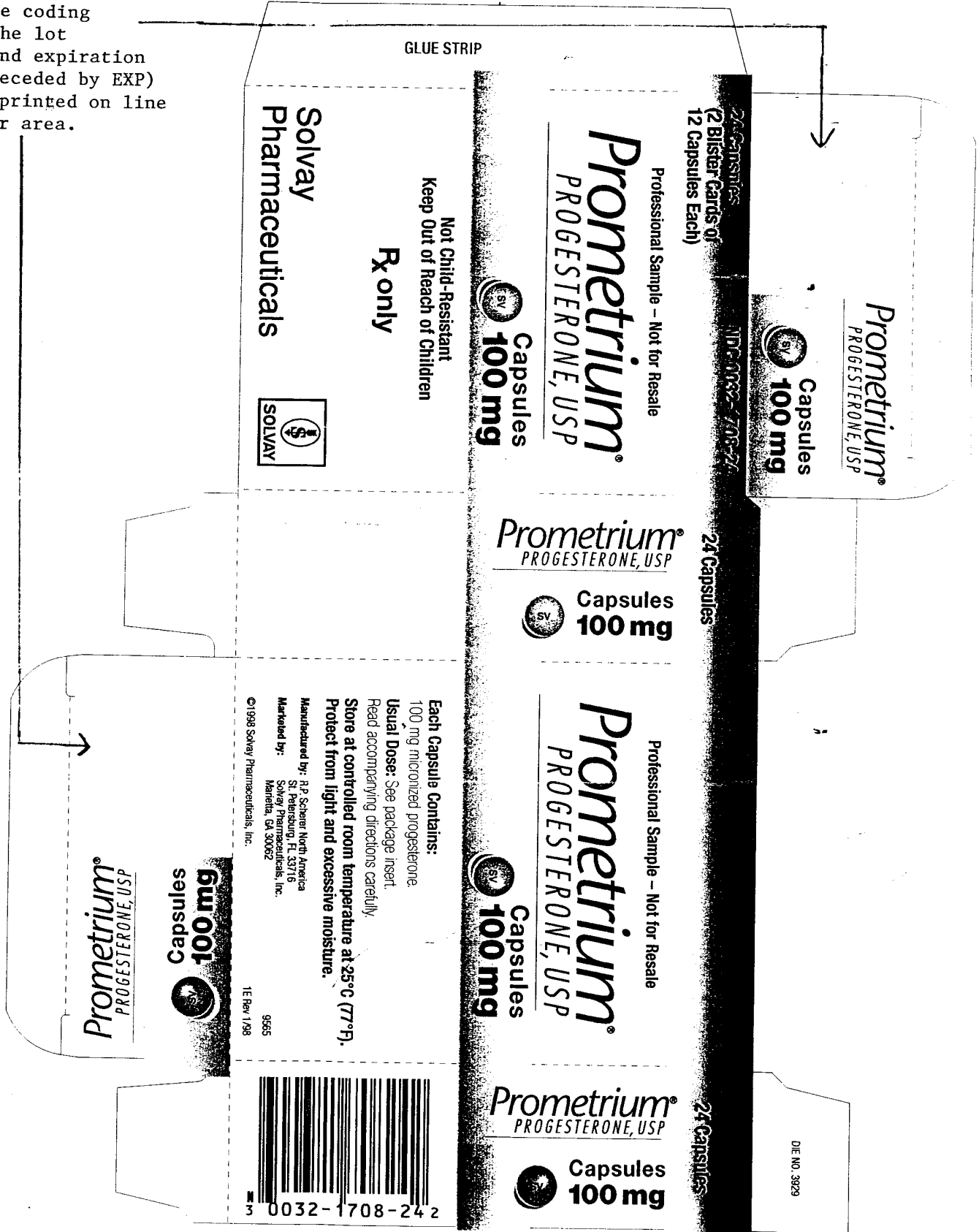
TOP
AP

REVISED DRAFT LABELING
MARCH 19, 1998

PROMETRIUM® Capsules

IPFC for Professional Sample (12 Capsules) 100 mg

These are coding areas. The lot number and expiration date (preceded by EXP) will be printed on line in either area.



Solvay
Pharmaceuticals



Not Child-Resistant
Keep Out of Reach of Children
Rx only

Prometrium®
PROGESTERONE, USP
Capsules
100 mg

Prometrium®
PROGESTERONE, USP
Capsules
100 mg

Prometrium®
PROGESTERONE, USP
Capsules
100 mg

Prometrium®
PROGESTERONE, USP
Capsules
100 mg

Prometrium®
PROGESTERONE, USP
Capsules
100 mg

Each Capsule Contains:
100 mg micronized progesterone
Usual Dose: See package insert.
Read accompanying directions carefully.
Store at controlled room temperature at 25°C (77°F).
Protect from light and excessive moisture.
Manufactured by: R.P. Scherer North America
St. Petersburg, FL 33716
Marketed by: Solvay Pharmaceuticals, Inc.
Marietta, GA 30062
©1998 Solvay Pharmaceuticals, Inc.
1E Rev 1/98
9565



0032-1708-24 2
3

DIE NO. 3929