9536

PRODUCT INFORMATION SHEET

1E-4 Rev 5/98

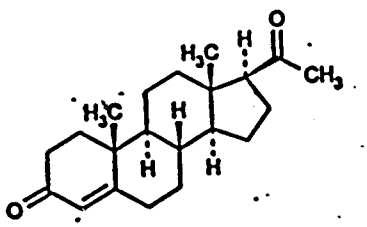
PROMETRIUM®

(progesterone, USP)

Capsules 100 mg

DESCRIPTION

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



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

CLINICAL PHARMACOLOGY

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

Pharmacokinetics

Absorption

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

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

[a] Mean ± S.D.

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

Distribution

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

Metabolism

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

Excretion

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

Special Populations

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

Race:

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

Drug-Drug Interaction:

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

Food-Drug Interaction:

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

effect on the time to maximum serum concentrations (Tmax). High intra- and intersubject variability was observed.

Hepatic Insufficiency:

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

Renal Insufficiency:

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

Clinical Studies

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

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

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

INDICATIONS AND USAGE

Secondary amenorrhea.

CONTRAINDICATIONS

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

WARNINGS

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

2. Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

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

4. Usage in pregnancy is not recommended. A case of cleft palate has been observed in the child of a woman who was using PROMETRIUM® Capsules during early pregnancy. Rare instances of fetal death have been reported in pregnant women prescribed PROMETRIUM® Capsules for unapproved indications. Definitive causality has not been established.

5. Retrospective studies of morbidity and mortality in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, cerebral thrombosis and embolism, and the use of oral contraceptives. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll was about seven fold, while Sartwell and associates in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration, and that it was not enhanced by long continued administration. The American study was not designed to evaluate a difference between products.

PRECAUTIONS

General

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

Information for the Patient

See accompanying Patient Insert.

Drug Lab Test Interactions

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

Increased sulfobromophthalein retention and other hepatic function tests.

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

Metyrapone test.

Pregnanediol determination.

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

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

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

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

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

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

Pregnancy Category X

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

Nursing Mothers

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

Pediatric Use

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

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254 **ADVERSE REACTIONS**

255 Table 2 lists adverse experiences which were reported in ≥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.

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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

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

Other adverse events reported in <5% of patients taking PROMETRIUM® Capsules include:

Autonomic Nervous System Disorders: dry mouth

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

Cardiovascular System Disorders: hypertension

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

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

Hearing and Vestibular Disorders: earache

Heart Rate and Rhythm Disorders: palpitation

Metabolic and Nutritional Disorders: edema, edema peripheral

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

Myo/Endo/Pericardial and Valve Disorders: angina pectoris

Psychiatric Disorders: anxiety, depression, impaired concentration, insomnia, personality disorder

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

Resistance Mechanism Disorders: abscess, herpes simplex

Respiratory System Disorders: bronchitis, nasal congestion, pharyngitis, pneumonitis, sinusitis

Skin and Appendages Disorders: acne, verruca, wound debridement

Urinary System Disorders: urinary tract infection

Vision Disorders: abnormal vision

White Cell and Resistance Disorders: lymphadenopathy

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

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

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

OVERDOSAGE

No studies on overdosage have been conducted in humans. In the case of overdosage, PROMETRIUM® Capsules should be discontinued, and the patient should be treated symptomatically.

DOSAGE AND ADMINISTRATION

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

HOW SUPPLIED

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

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

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

℞ only

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

Marketed By:

Solvay

Pharmaceuticals, Inc.

Marietta, GA 30062

351 **PATIENT INSERT**

352 PROMETRIUM®

353 (progesterone, USP)

354 Capsules 100 mg

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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.

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

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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.

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

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

YOU SHOULD NOT USE PROMETRIUM® CAPSULES

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

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

RISKS OF PROMETRIUM® CAPSULES

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

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

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

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

POSSIBLE SIDE EFFECTS OF PROMETRIUM® CAPSULES

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

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

- Dizziness*
- Abdominal Pain (Cramping)
- Headache
- Breast Pain
- Muscle or Bone Pain
- Viral Infection

- Fatigue
- Bloating
- Diarrhea
- Nausea
- Back Pain
- Irritability
- Coughing
- Mood Swings
- Upper Respiratory Tract Infection

SIDE EFFECTS REPORTED IN LESS THAN 5% OF PATIENTS:

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

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

drowsiness may occur.

PRECAUTIONS

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

- Breast lumps, (Ask your doctor or health-care provider to show you how to examine your breasts monthly).
- Pain, swelling or tenderness in the abdomen.
- Tremors or seizures, migraine headaches, shortness of breath or asthma, heart problems, kidney problems.
- Abnormal bleeding from the vagina
- Feelings of depression.
- Pains in the calves or chest, a sudden shortness of breath or coughing blood, indicating possible clots in the legs, heart or lungs.
- Severe headache, vomiting, dizziness, faintness, or changes in vision or speech, weakness or numbness in an arm or leg, indicating possible clots in the brain or eye.

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

Inform your doctor if you are diabetic.

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

OTHER INFORMATION

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

HOW SUPPLIED

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

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

Manufactured By:

R. P. Scherer North America

St. Petersburg, FL 33716

Marketed By:

506 Solvay

507 Pharmaceuticals, Inc.

508 Marietta, GA 30062.

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PROMETRIUM® Capsules

Label for 100 Capsules in Bottle

MAIN PANEL

100 CAPSULES

NDC-0032-1708-01

PROMETRIUM®

(progesterone, USP)

Capsules

100 mg

℞ only

Keep bottle tightly closed.

Keep out of Reach of Children

SIDE PANELS

Each capsule contains: 100 mg micronized progesterone

Usual Dose: See package insert

Read accompanying directions carefully

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

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

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

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

LOT:

EXP:

PROMETRIUM® Capsules

IPFC for Professional Sample (24 capsules) 100 mg

MAIN PANEL, FRONT

Solvay Pharmaceuticals

Professional Sample - Not for Resale

24 Capsules (2 Blister Cards of 12 Capsules each)

NDC 0032-1708-24

PROMETRIUM®

(progesterone, USP)

Capsules

100mg

Not Child Resistent

Keep Out of Reach of Children

℞ only

MAIN PANEL, BACK

Professional Sample - Not for Resale

Each capsule contains: 100 mg micronized progeserone

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.

LOT:
EXP:

TOP AND SIDE FLAPS

24 CAPSULES

PROMETRIUM® (progesterone, USP) Capsules

100mg

PROMETRIUM® Capsules

Professional Sample Blister Backing

PROMETRIUM®

(progesterone, USP)

Capsules

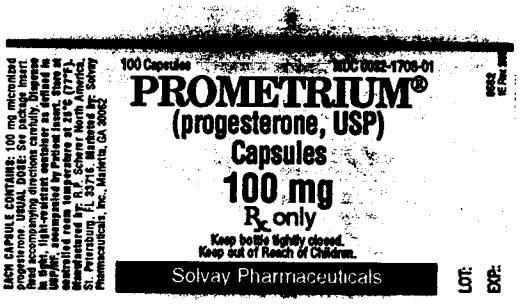
100 mg

Marketed by:

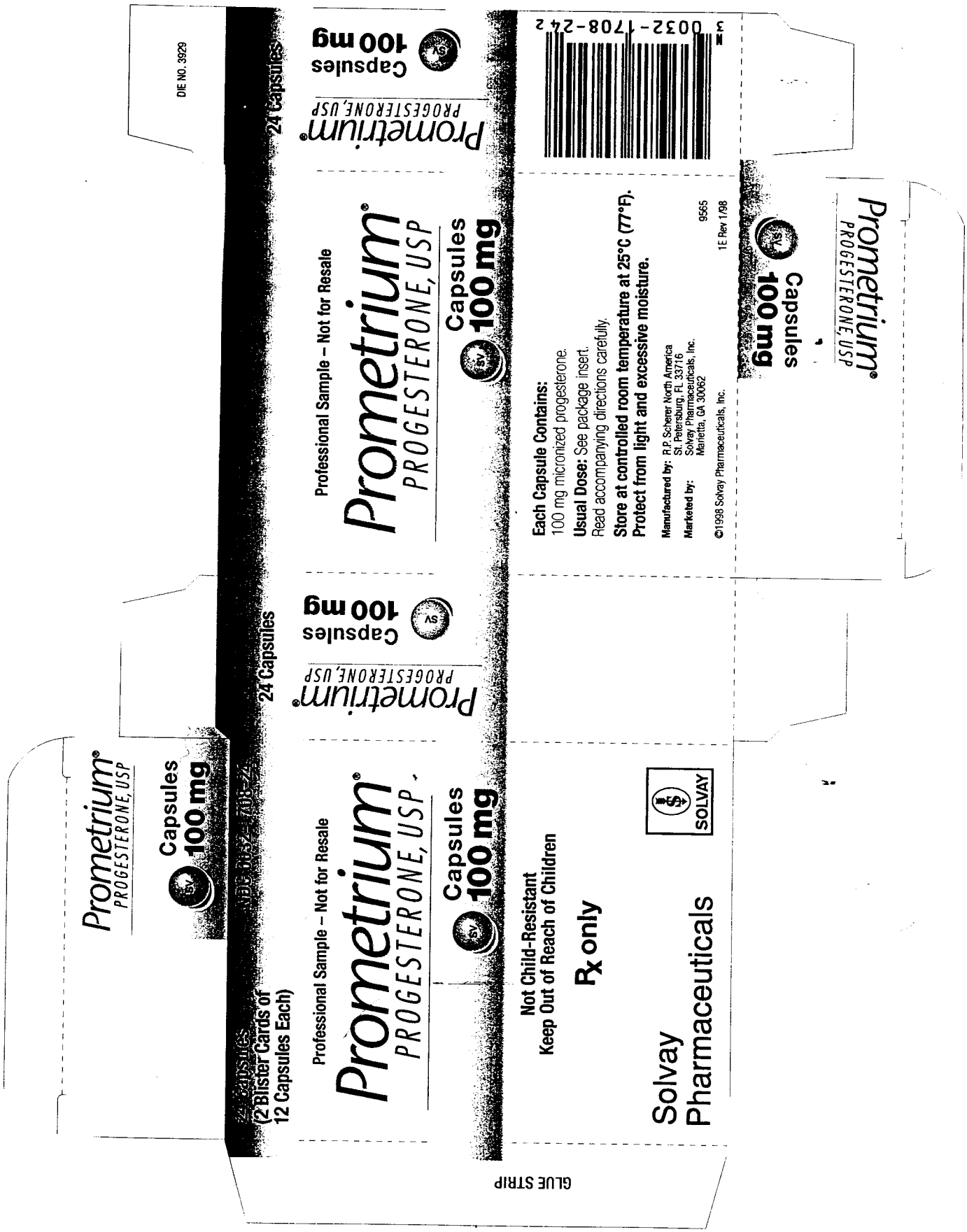
Solvay Pharmaceuticals, Inc.

Marietta, GA 30062

PROMETRIUM® Capsules
Label for 100 Capsules in Bottle



PROMETRIUM® Capsules
IPFC for Professional Sample (12 capsules) 100 mg



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

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.