ATTACHMENT A

DES product information prepared by Lilly in June 1997, published in Physician Desk Reference (1998-last appearance)

Darvon—Cont.

Selected Darvon Products

Maximum Daily Dosage		
6	Dark Orange, Capsule Shaped, Film Coated Tablets Imprinted with Script "Lilly" on the one side and "Darvocet-N 100" on the other, using edible black ink	DARVOCET-N® 100 ℂ Propoxyphene Napsylate and Acetaminophen Tablets
6	Parabolic-Shaped Capsules Imprinted with Script "Lilly" and "3111" on the opaque gray cap and "Darvon Comp 65" on the opaque red body, using edible black ink	DARVON® COMPOUND-65 ℂ Propoxyphene Hydrochloride, Aspirin, and Caffeine Pulvules®
6	Parabolic-Shaped Capsules Imprinted with Script "Lilly" and "H03" on the opaque pink cap and "Darvon" on the opaque pink body, using edible black ink	DARVON® ℂ Propoxyphene Hydrochloride Pulvules, 65 mg

Literature revised July 18, 1996

[071896]

DIETHYLSTILBESTROL ℞
[dī-eth 'il-stil-bĕs 'trōl]
USP

1. USE OF ESTROGENS HAS BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA

Three independent case-control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than 1 year.[1-3] This risk was independent of other known risk factors for endometrial cancer. These studies are further supported by the finding that, since 1969, the incidence rate of endometrial cancer has increased sharply in 8 different areas of the United States which have population-based cancer reporting systems.[4]

The 3 case-control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both the duration of treatment[1] and the dose of estrogen.[3] In view of these findings, the lowest dose that will control symptoms should be utilized when estrogens are used for the treatment of menopausal symptoms, and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, a reassessment should be made on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than does continuous administration;[3] it therefore appears prudent to utilize such a regimen.

Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy.

At present, there is no evidence that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equivalent estrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY

The use of female sex hormones, both estrogens and progestagens, during early pregnancy may affect the offspring. It has been reported that females exposed *in utero* to diethylstilbestrol, a nonsteroidal estrogen, may have an increased risk of developing later in life a rare form of vaginal or cervical cancer.[5, 6] This risk has been estimated to be 0.14 to 1.4 per 1000 exposures.[7] Further, other estrogens, it cannot be presumed that they would not induce similar changes.

Several reports suggest that there is an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb-reduction defects.[13-16] One case-control study[16] estimated a 4.7-fold increased risk of limb-reduction defects in infants exposed *in utero* to sex hormones (oral contraceptives, hormonal withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb-reduction defects in exposed fetuses is somewhat less than 1 per 1,000.

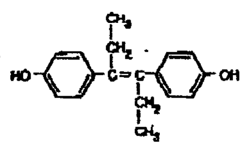
In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion; however, their efficacy was never conclusively proved or disproved.

If diethylstilbestrol is administered during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus and of the advisability of pregnancy continuation.

THIS DRUG PRODUCT SHOULD NOT BE USED AS A POSTCOITAL CONTRACEPTIVE[17].

DESCRIPTION

Diethylstilbestrol is a crystalline synthetic estrogenic substance capable of producing all the pharmacologic and therapeutic responses attributed to natural estrogens. Diethylstilbestrol may be administered orally. The structural formula is as follows: Chemically, diethylstilbestrol is α,α'-Diethyl-(E)-4,4'-stilbenediol.



The tablets contain corn starch, lactose, magnesium stearate, and talc.

INDICATIONS AND USAGE

Diethylstilbestrol is indicated in the treatment of:

1. Breast cancer (for palliation only) in appropriately selected women and men with metastatic disease
2. Prostatic carcinoma—palliative therapy of advanced disease

DIETHYLSTILBESTROL SHOULD NOT BE USED FOR ANY PURPOSE DURING PREGNANCY. ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

CONTRAINDICATIONS

Estrogens should not be used in women (or men) with any of the following conditions:

1. Known or suspected cancer of the breast, except in appropriately selected patients being treated for metastatic disease
2. Known or suspected estrogen-dependent neoplasia[18]
3. Known or suspected pregnancy (see boxed Warning)
4. Undiagnosed abnormal genital bleeding
5. Active thrombophlebitis or thromboembolic disorders
6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous use of estrogen (except when used in treatment of breast or prostatic malignancy).

WARNINGS

1. *Induction of malignant neoplasms.* In certain animal species, long-term continuous administration of natural and synthetic estrogens increases the frequency of carcinomas of the breast, cervix, vagina, kidney, and liver. There are now reports that prolonged use of estrogens increases the risk of carcinoma of the endometrium in humans. (*See* boxed Warning.)

At the present time, there is no satisfactory evidence that administration of estrogens to postmenopausal women increases the risk of cancer of the breast.[18] This possibility, however, has been raised by a recent long-term follow-up of one physician's practice.[19] Because of the animal data, there is a need for caution in prescribing estrogens for women with a family history of breast cancer or for women who have breast nodules, fibrocystic disease, or abnormal mammograms.

2. *Gallbladder disease:* A recent study reported a 2 to 3-fold increase in the risk of gallbladder disease ...

fects associated with the use of oral contr... ever, most of these adverse effects have... umented as consequences of postmenopausal... apy. This may reflect the comparatively... estrogen used in postmenopausal women... pected that these adverse effects are more likely... following administration of the larger doses... used for treating prostatic or breast cancer. It has... been shown that there is an increased risk of... with the administration of estrogens for prostatic... men and for postpartum breast engorgement...

a. *Thromboembolic disease.* It is... lished that women taking oral contraceptives... creased risk of various thromboembolic and thrombotic... cular diseases, such as thrombophlebitis, pulmonary... lism, stroke, and myocardial infarction.[20-22] Cases... thrombosis, mesenteric thrombosis, and optic... been reported in users of oral contraceptives. Th... dence that the risk of several of these adverse... related to the dose of the drug.[23, 24] An increase... postsurgical thromboembolic complications has... reported in users of oral contraceptives.[25, 26] If... trogen therapy should be discontinued at least... fore surgery such as that associated with an in... of thromboembolism, or that requiring periods of... immobilization.

Although an increased rate of thromboembolic and... botic disease has not been noted in postmenopausal... estrogen,[18, 27] this does not rule out the possibility... an increase may be present or that it exists in... women who have underlying risk factors or who... ing relatively large doses of estrogens. Therefore... should not be used in persons with active thrombo... or thromboembolic disorders, nor should they... cept in treatment of malignancy) in persons with... of such disorders associated with estrogen therapy... gens should be administered cautiously to patients... ebral vascular or coronary artery disease and... such therapy is clearly needed.

In a large prospective clinical trial in men,[28] large doses... estrogen (5 mg of conjugated estrogens per day)... to those used to treat cancer of the prostate and... been shown to increase the risk of nonfatal myocardial in... farction, pulmonary embolism, and thrombophlebitis... such large doses of estrogen are used, any of the... embolic and thrombotic adverse effects associated... use of oral contraceptives should be considered...

b. *Hepatic adenoma.* Benign hepatic adenomas ap... pear to be associated with the use of oral contracep... tives.[29-31] Although these adenomas are benign... they may rupture and may cause death by intra-abdominal... hemorrhage. Such lesions have not yet been reported in as... sociation with the administration of other estrogen or pro... stagen preparations, but they should be considered... abdominal pain and tenderness, abdominal mass... volemic shock occurs in persons receiving estrogen... Hepatocellular carcinoma has also been reported... taking estrogen-containing oral contraceptives... tionship of this malignancy to these drugs is not... this time.

c. *Elevated blood pressure.* Increased blood... is not uncommon in women taking oral contr... There is now one report that this may occur with... trogens in the menopause,[32] and blood pressure... monitored during estrogen therapy, especially... are used.

d. *Glucose tolerance.* A decrease in glucose... has been observed in a significant percentage of... estrogen-containing oral contraceptives. For this... abetic patients should be carefully observed... estrogen.

4. *Hypercalcemia.* Administration of estrogen... lead to severe hypercalcemia in patients with... and bone metastases. If this occurs, the drug... stopped and appropriate measures taken... serum calcium level.

PRECAUTIONS

General—1. A complete medical and family... be taken prior to initiation of any estrogen... pretreatment and periodic physical examinations... consideration should be given to blood pressure... domen, and pelvic organs, and a Papanicolaou... be performed. As a general rule, estrogen should... scribed for over a year without another physical... tion.

2. Fluid retention—Because estrogens... degree of fluid retention, conditions which... enced by this factor, such as epilepsy... or renal dysfunction, require careful observation...

3. Certain patients may develop undesirable... tions of excessive estrogenic stimulation... or excessive uterine bleeding, mastodynia...

should be advised of estrogen therapy
are submitted.
past history of jaundice during preg-
risk of recurrence of jaundice while
taining oral contraceptive therapy. If
any patient receiving estrogen, the
be discontinued while the cause is inves-

poorly metabolized in patients with
and they should therefore be ad-
caution in such patients.
influence the metabolism of cal-
they should be used with caution in
bone diseases associated with hy-
patients with renal insufficiency.
the effects of estrogens on epiphyseal clo-
be used judiciously in young patients in
is not complete.
and liver function tests may be af-
containing oral contraceptives. The fol-
may be expected with larger doses of

sulfobromophthalein retention.
prothrombin and factors VII, VIII, IX,
antithrombin 3; increased norepinephrine-
aggregability.
thyroid-binding globulin (TBG) leading to
total thyroid hormone, as measured by
or T4 by radioimmunoassay. Free T3
decreased, reflecting the elevated TBG; free
is unaltered.
glucose tolerance.
pregnanediol excretion.
response to metyrapone test.
serum folate concentration.
serum triglyceride and phospholipid con-

the Patient —See text of Patient Package In-
below.

gory X—See Contraindications and boxed

—As a general principle, the administra-
g to nursing mothers should be done only
necessary since many drugs are excreted in

—Safety and effectiveness in pediatric pa-
been established.

ACTIONS

regarding induction of neoplasia, adverse
fetus, increased incidence of gallbladder
adverse effects similar to those of oral
including thromboembolism.) The following
se reactions have been reported with estro-
including oral contraceptives:

inary system
ough bleeding, spotting, change in menstru-

orrhea
strual-like syndrome
hea during and after treatment
in size of uterine fibromyomata
candidiasis
in cervical eversion and in degree of cervical
ion
like syndrome

ess, enlargement, secretion
testinal
vomiting
al cramps, bloating
tic jaundice

a or melasma, which may persist when drug
continued
ma multiforme
ma nodosum
hagic eruption
scalp hair

ing of corneal curvature
nce to contact lenses

migraine, dizziness
pression

or decrease in weight
carbohydrate tolerance
on of porphyria
in libido

OVERDOSAGE

Signs and Symptoms —Symptoms of acute overdose include anorexia, nausea, vomiting, abdominal cramps, and diarrhea. Withdrawal vaginal bleeding may follow large doses. Chronic toxicity may include salt and water retention, edema, headache, vertigo, leg cramps, gynecomastia, cholasma, and porphyria cutanea tarda. Polydipsia, polyuria, fatigue, and an abnormal glucose tolerance may occur in some patients with preclinical diabetes mellitus.

No information is available on the following: LD_{50}, concentration of diethylstilbestrol in biologic fluids associated with toxicity and/or death, the amount of drug in a single dose usually associated with symptoms of overdosage, or the amount of diethylstilbestrol in a single dose likely to be life threatening.

Treatment —Chronic diethylstilbestrol toxicity should be treated by discontinuing all estrogenic medications and providing supportive care for any symptoms that may be present.

To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the *Physicians' Desk Reference (PDR)*. In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

In treating acute overdose, protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Forced diuresis, peritoneal dialysis, hemodialysis, or charcoal hemoperfusion have not been established as beneficial for an acute overdose of diethylstilbestrol.

DOSAGE AND ADMINISTRATION

Given chronically:

Inoperable progressing prostatic cancer
1 to 3 mg daily initially, increased in advanced cases; the dosage may later be reduced to an average of 1 mg daily.

Inoperable progressing breast cancer in appropriately selected men and postmenopausal women (see Indications)
15 mg daily.

Patients with an intact uterus should be closely monitored for signs of endometrial cancer, and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

HOW SUPPLIED

Diethylstilbestrol, USP, Tablets are available in:

Tablets:

The 1 mg tablets are white, round, and engraved with script "Lilly" and "J52".

Bottles of 100 NDC 0002-0122-02 (TA 1649)

The 5 mg tablets are white, round, and engraved with script "Lilly" and "J53".

Bottles of 100 NDC 0002-1054-02 (TA 1686)

Store at controlled room temperature 15° to 30°C (59° to 86°F).

CAUTION—Federal (USA) law prohibits dispensing without prescription.

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Continued on next page

* Identi-Code® symbol. This product information was prepared in June 1997. Current information on these and other products of Eli Lilly and Company may be obtained by direct inquiry to Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, Indiana 46285, (800) 545-5979.

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INFORMATION FOR THE PATIENT DIETHYLSTILBESTROL, USP

FACTS THAT YOU SHOULD KNOW ABOUT ESTROGENS

Estrogens are female hormones produced by the ovaries. The ovaries produce several different kinds of estrogens. In addition, scientists have been able to develop a variety of synthetic estrogens. As far as we know, all these estrogens have similar properties and, therefore, have much the same usefulness and side effects and involve the same risks. This leaflet is intended to help you understand what estrogens are given for, the possible risks involved in their use, and how to use them as safely as possible.

This leaflet contains the most important information about estrogens. If you want to know more, you may ask your doctor or pharmacist to let you read the package insert prepared for the doctor.

USES OF ESTROGEN

Estrogens are prescribed by physicians for a number of purposes, and they may be given:

1. To prevent certain uncomfortable symptoms of estrogen deficiency during a period of adjustment when a woman's ovaries no longer produce estrogen. (All women normally stop producing estrogens, generally between the ages of 45 and 55; this is called the menopause.)
2. To prevent symptoms of estrogen deficiency when a woman's ovaries have been removed surgically before the natural menopause.
3. To prevent pregnancy. (Estrogens are given along with a progestagen, another female hormone; these combinations are called oral contraceptives or birth control pills. Patient information is available to women taking oral contraceptives, and these will not be discussed in this leaflet.)
4. To treat certain cancers in women and men.

NOTE: PREGNANT WOMEN SHOULD NOT TAKE ESTROGENS.

THE USE OF ESTROGENS DURING THE MENOPAUSE

All women eventually experience a decrease in estrogen production during the natural course of life. This usually occurs between the ages of 45 and 55, but it may occur earlier or later. Sometimes, the ovaries may have to be removed by an operation before the natural menopause occurs, thus producing a "surgical menopause."

When the amount of estrogen in the body begins to decrease, many women may develop some of the following typical symptoms: feelings of warmth in the face, neck, and chest, or sudden intense episodes of heat and sweating throughout the body (called "hot flashes" or "hot flushes"). Sometimes these symptoms are quite uncomfortable. A few women may eventually develop changes in the vagina (called "atrophic vaginitis") which cause discomfort, especially during and after intercourse.

Estrogens can be prescribed to treat these symptoms of the menopause. Probably more than half of all women undergoing the menopause have only mild symptoms or none at all and thus do not need estrogens. Some women may require estrogen for only a few months while their bodies adjust to lower estrogen levels, whereas other women will need them for 6 months or longer. In an attempt to avoid overstimulation of the uterus (womb), estrogens are usually given on a cyclic basis each month, that is, 3 weeks of medication followed by 1 week with no medication.

Women sometimes experience nervous symptoms or depression during the menopause. There is no evidence that estrogens are effective for treating such symptoms, and they should not be used for this purpose; however, other treatment may be needed.

You may have heard that taking estrogens for a long period of time (years) after the menopause will keep your skin soft and supple and will keep you feeling young. Unfortunately, there is no evidence that this is true; on the other hand, there may be a significant risk involved in the use of such long-term treatment.

THE DANGER OF ESTROGENS

1. *Endometrial carcinoma.* There may be an increased risk of *endometrial carcinoma*, a form of cancer of the uterus, if estrogens are used for more than a year after the menopause. The chance of this cancer occurring may be approximately 5 to 10 times greater in women taking estrogen than in those women taking no estrogens. To put this another way, a woman who does not take estrogens after the menopause has 1 chance in 1,000 each year of having cancer of the uterus, whereas a woman who takes estrogens has 5 to 10 chances in 1,000 each year. For this reason, *it is important that estrogens be taken only when needed.*

It appears that the longer estrogens are taken, the greater the risk of this cancer; this risk seems to increase when larger doses are taken. For this reason, *it is important to take the lowest dose of estrogen that will control symptoms and to take it only as long as it is needed.* If estrogens are needed for longer periods of time, your doctor will want to reevaluate your need for estrogen at least every 6 months. Women using estrogens should report to their doctors any irregular vaginal bleeding; such bleeding may be of no importance, but it can also be an early warning of cancer of the uterus. If you have vaginal bleeding, you should *not* use estrogens until your doctor has made a diagnosis and has verified that there is no cancer of the uterus.

If your uterus has been completely removed (total hysterectomy), there is no danger of endometrial carcinoma occurring.

2. *Other possible cancers.* When given to animals for a long period of time, estrogens have caused development of other tumors, such as tumors of the breast, cervix, vagina, or liver. At present, there is no evidence that there is an increased risk that such tumors will occur in women taking estrogens during the menopause, but there is no way to be sure that there is no risk. One study raises the possibility that the use of estrogens during the menopause may increase the risk that cancer of the breast will develop many years later. This is another reason why estrogens should be used only when clearly needed. While you are taking estrogens, it is important for you to get to your doctor at least once a year for a physical examination. Your doctor may also want to make more frequent examinations of your breasts if members of your family have had breast cancer or if you have breast nodules (lumps) or abnormal mammograms (breast-x-rays).

3. *Gallbladder disease.* Women who use estrogens after the menopause are more likely to develop gallbladder disease than are women who do not use estrogens. Birth control pills have a similar effect.

4. *Abnormal blood clots.* Oral contraceptives increase the risk of blood clots developing in various parts of the body. In rare cases, this can result in a stroke (if the clot is in the brain), a heart attack (a clot in a blood vessel of the heart), or a pulmonary embolus (a clot which forms in the legs or pelvis and then breaks off and travels to the lungs). Any of these can be fatal.

At this time, the use of estrogens during the menopause is not known to cause such blood clots, but this has not been fully studied and could still prove to involve such a risk. If you have blood clots in the legs or lungs or had a heart attack while you were taking estrogens or birth control pills, you should not take estrogens (unless they are being prescribed by your doctor for treating cancer of the breast or prostate). If you have had a stroke or heart attack or if you have angina pectoris, estrogens should be taken with great caution and only if clearly needed (for example, if you have severe symptoms of the menopause).

SPECIAL WARNING ABOUT PREGNANCY

You should not take estrogens if you are pregnant, because, although the possibility remains small, there may be a greater than usual risk that the developing child may be born with a birth defect. In a female child, there may be an increased risk that cancer of the vagina or cervix will develop later in life (in the teens or 20's). If estrogens have been taken during pregnancy, see your doctor.

OTHER EFFECTS OF ESTROGENS

In addition to the serious known risks described above, estrogens have the following side effects and involve the following potential risks:

1. *Nausea and vomiting.* The most common side effect of estrogen therapy is nausea. Vomiting occurs less frequently.
2. *Effects on the breasts.* Estrogens may cause tenderness or enlargement of the breasts and may cause the breasts to secrete a liquid. These effects are not dangerous.
3. *Effects on the uterus.* Estrogens may cause enlargement of benign fibroid tumors of the uterus.

Some women will have menstrual bleeding when they stop taking estrogens; *however*, if bleeding occurs on days when you are still taking estrogens, you should report this to your doctor.

4. *Effects on the liver.* On very rare [illegible] taking oral contraceptives develop [illegible] which can rupture and bleed into the [illegible] tumors have not been reported in [illegible] during the menopause, but any swelling [illegible] tenderness in the abdomen should [illegible] tor immediately.

Women with a past history of jaundice [illegible] and the white parts of the eyes) [illegible] when estrogens are administered. [illegible] the estrogen and see your doctor.

5. *Other effects.* Estrogens may cause [illegible] tained in the body. This may worsen [illegible] as epilepsy, migraine, heart disease [illegible]

SUMMARY

Estrogens have important uses, but there [illegible] involved in their use. Together with your doctor, you [illegible] decide whether the risks are acceptable in your [illegible] benefits of estrogen therapy. Except [illegible] prescribed estrogens for treatment of special cases [illegible] of the breast or prostate, you should not use estrogens [illegible] have cancer of the breast or uterus; if you are pregnant [illegible] you have undiagnosed abnormal vaginal bleeding [illegible] in the legs or lungs, or if you have [illegible] heart attack, angina, or clotting in the legs or lungs [illegible]

You can use estrogens as safely as possible by [illegible] ing that your doctor will want you to have regular [illegible] examinations while you are taking estrogens, and [illegible] she will use the smallest dose possible and will [illegible] continue the drug as soon as possible. Be alert [illegible] trouble, including:

1. Abnormal bleeding from the vagina.
3. Pains in the calves or chest, sudden severe [illegible] or coughing up blood (indicating possible clots [illegible] heart, or lungs).
3. Severe headache, faintness, dizziness, or change [illegible] sion (indicating possible development of clots in the [illegible] eye).
4. Lumps in the breast. (You should ask your doctor [illegible] you how you can examine your own breasts.)
5. Jaundice (yellowing of the skin).
6. Mental depression.

On the basis of his or her assessment of your medical [illegible] your doctor has prescribed this drug for you. Do not give [illegible] drug to anyone else.

HOW SUPPLIED

Diethylstilbestrol is available for oral administration [illegible] lets.

Literature revised October 16, 1996

DOBUTREX® SOLUTION

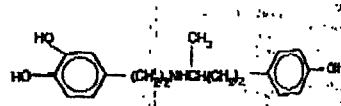
[dō 'bū-trĕks]

(dobutamine hydrochloride)

injection

DESCRIPTION

Dobutrex® Solution (Dobutamine Hydrochloride [illegible] is 1, 2-benzenediol, 4-[2-[[3-(4-hydroxyphenyl)-1-[illegible] pyl]amino]ethyl]-, hydrochloride, (±). It is a synthetic [illegible] echolamine.



Molecular Formula: $C_{18}H_{23}NO_3 \cdot HCl$
Molecular Weight: 337.85

The clinical formulation is supplied in a sterile [illegible] travenous use only. Each mL contains 12.5 mg [illegible] dobutamine, 0.24 mg sodium bisulfite (added [illegible] factors), and water for injection, q.s. Hydrochloric [illegible] and/or sodium hydroxide may have been added [illegible] ufacture to adjust the pH.

CLINICAL PHARMACOLOGY

Dobutrex Solution is a direct-acting inotropic [illegible] primary activity results from stimulation of the [illegible] of the heart while producing comparatively [illegible] tropic, hypertensive, arrhythmogenic, and [illegible] fects. It does not cause the release of endogenous [illegible] nephrine, as does dopamine. In animal studies [illegible] hydrochloride produces less increase in heart [illegible] decrease in peripheral vascular resistance for [illegible] tropic effect than does isoproterenol.

In patients with depressed cardiac function [illegible] utamine hydrochloride and isoproterenol increase [illegible] diac output to a similar degree. In the case of [illegible] hydrochloride, this increase is usually not accompanied [illegible] marked increases in heart rate (although tachycardia [illegible] casionally observed), and the cardiac stroke volume [illegible]