

Dear Pharmacist:

On May 28, 2010, Teva Pharmaceuticals introduced GianviTM (drospirenone and ethinyl estradiol tablets), AB rated and bioequivalent to Yaz[®]* Tablets. This letter serves as notification that the GianviTM Physician Prescribing Information is being updated to reflect a clarification in the inactive ingredients. Specifically, Teva's GianviTM product contains ethinyl estradiol which is not stabilized by betadex as a clathrate.

The Physician Prescribing Information included with initial shipments of GianviTM (revision code B 4/2010) has been updated. The new Physician Prescribing Information is included below and is accessible on our website at www.tevausa.com/Gianvi_PI. For your reference, the change is highlighted below:

Original Physician Prescribing Information, Revision B 4/2010

Description: GianviTM (drospirenone and ethinyl estradiol tablets) 3 mg/0.02 mg provides an oral contraceptive regimen consisting of 24 active film-coated tablets each containing 3 mg of drospirenone and 0.02 mg of ethinyl estradiol stabilized by betadex as a clathrate (molecular inclusion complex) and 4 inert film-coated tablets. Other ingredients are...

Updated Physician Prescribing Information, Revision D 6/2010

Description: GianviTM (drospirenone and ethinyl estradiol tablets) 3 mg/0.02 mg provides an oral contraceptive regimen consisting of 24 active film-coated tablets each containing 3 mg of drospirenone and 0.02 mg of ethinyl estradiol and 4 inert film-coated tablets. Other ingredients are...

Please accept our apology for any inconvenience this may have caused. And we thank you for your continued support of Teva's products.

Sincerely,

Maureen M. Cavanaugh

Maureer M Cavanaugh

Vice President, Customer Operations & Marketing

* Yaz® is a registered trademark of Bayer Schering Pharma.

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PATIENTS SHOULD BE COUNSELED THAT THIS PRODUCT DOES NOT PROTECT AGAINST HIV INFECTION (AIDS) AND Hepatic Dysfunction OTHER SEXUALLY TRANSMITTED DISEASES Trospirenone and ethi DESCRIPTION

(drospirenone and ethinyl estradiol tablets) 3 mg/0.02 mg provides an oral contraceptive regimen consisting of 24 active film-coated tablets each containing 3 mg of drospirenone and 0.02 mg of ethinyl estradiol and 4 inert film-coated tablets. Other ingredients are anhydrous lactose, corn starch, crospovidone, FD&C red no. 40 aluminum lake, PD&C yellow no. 6 aluminum lake, hypromellose, magnesium stearate, polyethylene glycol, polysorbate 80, povidone, polysorbate 80, polysorbate 80, povidone, polysorbate 80, povidone, polysorbate 80, povidone, polysorbate 80, polysor pregelatinized starch and titanium dioxide. The inert tablets contain anhydrous lactose, hypromellose, magnesium stearate, and BOLDED WARNING).

ompound. The structural formulas are as follows: Drospirenone

Ethinyl Estradiol

CLINICAL PHARMACOLOGY

mbination oral contraceptives (COCs) act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increases the difficulty of sperm entry into the uterus) and the endometrium (which reduces the likelihood of implantation).

Drospirenone is a spironolactone analogue with antimineralocorticoid activity. Preclinical studies in animals and *in vitro* have shown that drospirenone has no androgenic, estrogenic, glucocorticoid, or antiglucocorticoid activity. Preclinical studies in animals have also shown that drospirenone has antiandrogenic activity

Acne vulgaris is a skin condition with a multifactorial etiology including androgen stimulation of sebum production. While the e relationship between these changes and a decrease in the severity of facial acne in otherwise healthy women with this skin condition has not been established. The impact of the antiandrogenic activity of drospirenone on acne is not known Pharmacokinetics

The absolute bioavailability of drospirenone (DRSP) from a single entity tablet is about 76%. The absolute bioavailability of ethinyl estradiol (EE) is approximately 40% as a result of presystemic conjugation and first-pass metabolism. The absolute bioavailability of drospirenone and ethinyl estradiol tablets, which is a combination tablet of drospirenone and ethinyl estradiol stabilized by betadex as a clathrate (molecular inclusion complex), has not been evaluated. The bioavailability of EE is similar when dosed via a betadex clathrate formulation compared to when it is dosed as a free steroid. Serum concentrations of DRSP and EE reached peak levels within 1 to 2 hours after administration of drospirenone and ethinyl estradiol tablets.

The pharmacokinetics of DRSP are dose proportional following single doses ranging from 1 to 10 mg. Following daily dosing of drospirenone and ethinyl estradiol tablets, steady-state DRSP concentrations were observed after 8 days. There was about 2 to 3 fold accumulation in serum C_{max} and AUC $_{(0-24h)}$ values of DRSP following multiple dose administration of drospirence and ethinyl estradiol tablets (see Table I). For EE, steady-state conditions are reported during the second half of a treatment cycle. Following daily administration of drospirenon and ethinyl estradiol tablets serum C_{max} and AUC $_{(0-24h)}$ values of EE accumulate by a factor of about 1.5 to 2 (see Table I).

TABLE I: TABLE OF PHARMACOKINETIC PARAMETERS OF DROSPIRENONE AND ETHINYL ESTRADIOL TABLETS (Drospirenone 3 mg and Ethinyl Estradiol 0.02 mg)

Drospirenone								
Cycle / Day	No. of Subjects	C _{max} 1 (ng/mL)	T _{max} ² (h)	AUC _(0-24h) 1 (ng•h/mL)	t _{1/2} 1 (h)			
1/1	23	38.4 (25)	1.5 (1 to 2)	268 (19)	NA			
1/21	23	70.3 (15)	1.5 (1 to 2)	763 (17)	30.8 (22)			
	,	Ethin	yl Estradiol	`				
Cycle / Day	No. of Subjects	C _{max} 1 (pg/mL)	T _{max} ² (h)	AUC _(0-24h) 1 (pg•h/mL)	t _{1/2} 1 (h)			
1/1	23	32.8 (45)	1.5 (1 to 2)	108 (52)	NA			
1/21	23	45.1 (35)	1.5 (1 to 2)	220 (57)	NA			

geometric mean (geometric coefficient of variation)

3 8 1 R

FULL PRESCRIBING INFORMATION

Gianvi^{*}

(drospirenone and ethinyl estradiol tablets)

PATIENTS SHOULD BE COUNSELED THAT THIS PRODUCT

OTHER SEXUALLY TRANSMITTED DISEASES

Rev. D 6/2010

DOES NOT PROTECT AGAINST HIV INFECTION (AIDS) AND

ne rate of absorption of DRSP and FF following single administration of a formulation similar to drospirenone and ethinyl estradiol tablets was slower under fed (high fat meal) conditions with the serum C_{max} being reduced about 40% for both components. The extent of absorption of DRSP, however, remained unchanged. In contrast, the extent of absorption of EE was reduced by about 20% under fed conditions.

SP and EE serum levels decline in two phases. The apparent volume of distribution of DRSP is approximately 4 L/kg and that f EE is reported to be approximately 4 to 5 L/kg.

PRSP does not bind to sex hormone binding globulin (SHBG) or corticosteroid binding globulin (CBG) but binds about 97% to

other serum proteins. Multiple dosing over 3 cycles resulted in no change in the free fraction (as measured at trough levels). EE is reported to be highly but non-specifically bound to serum albumin (approximately 98.5%) and induces an increase in the serum concentrations of both SHBG and CBG. EE induced effects on SHBG and CBG were not affected by variation of the DRSP dosage in the range of 2 to 3 mg.

he two main metabolites of DRSP found in human plasma were identified to be the acid form of DRSP generated by opening of the lactone ring and the 4,5-dihydrodrospirenone-3-sulfate. These metabolites were shown not to be pharmacologically ctive. In in vitro studies with human liver microsomes, DRSP was metabolized only to a minor extent mainly by Cytochrome

inically significant difference was observed between the pharmacokinetics of DRSP or EE in Japanese versus Caucasian women (age 20 to 35) when drospirenone and ethinyl estradiol tablets were administered daily for 21 days. Other ethnic groups

virenone and ethinyl estradiol tablets are contraindicated in patients with hepatic dysfunction (see CONTRAINDICATIONS and BOLDED WARNING). The mean exposure to DRSP in women with moderate liver impairment is approximately three times highe than the exposure in women with normal liver function. Drospirenone and ethinyl estradiol tablets have not been studied in women

The effect of renal insufficiency on the pharmacokinetics of DRSP (3 mg daily for 14 days) and the effect of DRSP on serum Drospirenone (6R,7R,8R,9S,10R,13S,14S,15S,16S,17S)-1,3',4',6,6a,7,8,9,10,11,12,13,14,15,15a,16-hexadecahydro-10,13-dimethylspiro-[17H-dicyclopropa-[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5H)-furan]-3,5'(2H)-dione) is a synthetic progestational compound. Ethinyl estradiol (19-nor-17\(\alpha\)-pregna 1,3,5(10)-triene-20-yne-3, 17-diol) is a synthetic estrogenic group with mild renal impairment (creatinine clearance CLcr. 50 to 80 mL/min) were comparable to those in the group with normal renal function (CLcr, >80 ml/min). The serum DRSP levels were on average 37% higher in the group with moderate renal impairment (CLcr, 30 to 50 ml/min) compared to those in the group with normal renal function. DRSP treatment was well tolerated by all groups. DRSP treatment did not show any clinicate refect on serum potassium concentration. Although hyperkalemia was not observed in the study, in five of the seven subjects who continued use of potassium sparing drugs during the study, mean serum potassium levels increased by up to 0.33 mEq/L. Therefore, potential exists for hyperkalemia to occur in subjects with renal impairment whose serum potassium is in the upper reference range, and who are concomitantly using potassium sparing drugs.

ATTOMORATE SOLUTION (drospirenone and ethinyl estradiol tablets) 3 mg/0.02 mg is indicated for the prevention of pregnancy in women CONTRAINDICATIONS who elect to use an oral contracentive Oral contraceptives are highly effective. Table II lists the typical unintended pregnancy rates for users of combination oral

• Renal insufficiency

contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization and

• Hepatic dysfunction implants and IUDs, depends upon the reliability with which they are used. Correct and consistent use of methods

• Adrenal insufficiency can result in lower failure rates.

Gianvi™ (drospirenone and ethinyl estradiol tablets) is indicated for the treatment of moderate acne vulgaris in women at least 14 years of age, who have no known contraindications to oral contraceptive therapy and have achieved menarche.

• Thrombophlebitis or thromboembolic disorders
• A past history of deep-vein thrombophlebitis or thrombophlebitis or thromboembolic disorders and ethinyl estradiol tablets) should be used for the treatment of acne only if the patient desires an ral contracentive for hirth control

TABLE II: PERCENTAGE OF WOMEN EXPERIENCING AN UNINTENDED PREGNANCY DURING THE FIRST YEAR OF TYPICAL USE AND FIRST YEAR OF PERFECT USE OF CONTRACEPTION AND THE PERCENTAGE CONTINUING USE AT THE END OF THE FIRST YEAR: UNITED STATES. • Valvalar heart disease with friendings • Severe hypertension • Diabetes with vascular involvement • Headaghes with friendings

	% of Women Experienci Within the	ng an Unintended Pregnancy First Year of Use	% of Women Continuing Use at One Year ³
Method (1)	Typical Use ¹ (2)	Perfect Use ² (3)	(4)
Chance ⁴	85	85	40
Spermicides ⁵	26	6	63
Periodic abstinence	25		
Calendar		9	
Ovulation method		3	
Sympto-thermal ⁶		2	
Post-ovulation		1	
Withdrawal	19	4	
Cap ⁷			
Parous women	40	26	42
Nulliparous women	20	9	56
Sponge			
Parous women	40	20	42
Nulliparous women	20	9	56
Diaphragm ⁷	20	6	56
Condom8			
Female (Reality)	21	5	56
Male	14	3	61
Pill	5		71
progestin only		0.5	
combined		0.1	
IUD			
Progesterone T	2	1.5	81
Copper T 380A	0.8	0.6	78
Lng 20	0.1	0.1	81
Depo Provera	0.3	0.3	70
Norplant and Norplant-2	0.05	0.05	88
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.1	100

Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnanc Lactational Amenorrhea Method: LAM is a highly effective, temporary method of contraception. 10

Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Guest F, Kowal D, aceptive Technology: Seventeenth Revised Edition. New York NY: Irvington Publishers, 1998.

1 Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year. ⁴ The percents becoming pregnant in columns (2) and (3) are based on data from populations where contraception is no used and from women who cease using contraception in order to become pregnant. Among such populations, about 8 become pregnant within one year. This estimate was lowered slightly (to 85%) to represent the percentage who would become

pregnant within one year among women now relying on reversible methods of contraception if they abandoned contracep ⁵ Foams, creams, gels, vaginal suppositories, and vaginal film.

6 Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in t post-ovulatory phases.

With spermicidal cream or jelly.

2 light-orange pills). Lo/Ovral (1 dose is 4 white pills). Triphasil or Tri-Levlen (1 dose is 4 vellow pills).

drospirenone and ethinyl estradiol tablets or placebor on six 28 day cycles. The primary efficacy endpoints were the percent change in inflammatory lesions, non-inflammatory lesions, total lesions, and the percentage of subjects with a "clear" or "almost clear" rating on the Investigator's Static Global Assessment (ISGA) scale on day 15 of cycle 6, as presented in Table III:

TABLE III: EFFICACY RESULTS FOR ACNE TRIALS

	Stud	ly 1	Study 2		
	Drospirenone and Ethinyl Estradiol Tablets N=228	Placebo N=230	Drospirenone and Ethinyl Estradiol Tablets N=218	Placebo N=213	
GA Success Rate	35 (15%)	10 (4%)	46 (21%)	19 (9%)	
flammatory Lesions Mean Baseline Count Mean Absolute (%) Reduction	33 15 (48%)	33 11 (32%)	32 16 (51%)	32 11 (34%)	
on-inflammatory esions Mean Baseline Count Mean Absolute (%) Reduction	47 18 (39%)	47 10 (18%)	44 17 (42%)	44 11 (26%)	
otal lesions Mean Baseline Count Mean Absolute (%) reduction	80 33 (42%)	80 21 (25%)	76 33 (46%)	76 22 (31%)	
Evaluated at day 15 of cy	cle 6, last observation carrie	ed forward for the Intent t	to treat population		

™ (drospirenone and ethinyl estradiol tablets) should not be used in women who have the following:

Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia

Thrombophlebitis or thromboembolic disorders

Valvular heart disease with thrombogenic complications

· Headaches with focal neurological symptoms . Major surgery with prolonged immobilization Known or suspected carcinoma of the breast

Undiagnosed abnormal genital bleeding

 Cholestatic jaundice of pregnancy or jaundice with prior pill use . Known or suspected pregnancy

· Liver tumor (benign or malignant) or active liver disease Heavy smoking (≥ 15 cigarettes per day) and over age 35

 Hypersensitivity to any component of this product WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases

2. Estimates of Mortality From Contraceptive Use with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke. Gianvi™ (drospirenone and ethinyl estradiol tablets) contains 3 mg of the progestin drospirenone that has

GianviTM (drospirenone and ethinyl estradiol tablets) should not be used in patients with conditions that predispose to

The observation of a possible increase in risk of mortality with age for oral contraceptive users is based on data gathered in the 1970's -

The use of oral contraceptives is associated with increased risks of several serious conditions including venous and arterial thrombotic and thromboembolic events (such as myocardial infarction, thromboembolism, stroke), hepatic neoplasia, gallbladder disease, and hypertension. The risk of serious morbidity or mortality is very small in healthy women (even with the newer low-dose formulations), there are greater potential health risks associated with pregnancy in older women and with the alternative surgical and medical procedures which may be necessary if such women do not have access to effective and acceptable means of contraception.

5. Fluid Retention

Oral contraceptives may cause some degree of fluid retention. They should be prescribed with caution, and only with careful monitoring, in patients with conditions which might be aggravated by fluid retention.

Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks The information contained in this package insert is based principally on studies carried out in patients who used oral contraceptives

with higher formulations of estrogens and progestogens than those in common use today. The effect of long-term use of the oral contraceptives with lower formulations of both estrogens and progestogens remains to be determined. Throughout this labeling, epidemiologic studies reported are of two types: retrospective or case control studies and prospective cohort studies. Case control studies provide a measure of the relative risk of a disease, namely, a ratio of the incidence of a diseas mong oral contraceptive users to that among nonusers. The relative risk does not provide information on the actual clinical occur of a disease. Cohort studies provide a measure of attributable risk, which is the difference in the incidence of disease between oral contraceptive users and nonusers. The attributable risk does provide information about the actual occurrence of a disease in the

population. For further information, the reader is referred to a text on epidemiologic methods. Thromboembolic Disorders and Other Vascular Problems

such as hypertension, hyperlipidemias, obesity and diabetes.

An increased risk of myocardial infarction has been attributed to oral contraceptive use. This risk is primarily in smokers of women with other underlying risk factors for coronary-artery disease such as hypertension, hypercholesterolemia, morbid obesity, and diabetes. The relative risk of heart attack for current oral contraceptive users has been estimated to be two to six. The risk is very low under the age of 30.

Smoking in combination with oral contraceptive use has been shown to contribute substantially to the incidence of myocardial infarctions in women in their mid-thirties or older with smoking accounting for the majority of excess cases. Mortality rates Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly). The percentage who experience an accidental pregnancy during the first year if they do not stop use for any reason.

TABLE IV: CIRCULATORY DISEASE MORTALITY RATES PER 100,000 WOMAN-YEARS BY AGE, SMOKING STATUS AND ORAL CONTRACEPTIVE US

come	AGE	EVER-USERS NON-SMOKERS	EVER-USERS SMOKERS	CONTROLS NON-SMOKERS	CONTR SMOKE	
ption	15 to 24	0	10.5	0	0	
	25 to 34	4.4	14.2	2.7	4.2	
n the	35 to 44	21.5	63.4	6.4	15.2	
	45+	52.4	206.7	11.4	27.9	
	(Adapted from P.M.	Lavde and V. Beral)				

Oral contraceptives may compound the effects of well-known risk factors, such as hypertension, diabetes, hyperlipidemias 9 The treatment schedule is one dose within 72 hours after unprotected intercourse, and a second dose 12 hours after the first age and obesity. In particular, some progestogens are known to decrease HDL cholesterol and cause glucose intolerance, while age and obesity. In particular, some progestogens are known to decrease HDL cholesterol and cause glucose intolerance, while dose. The Food and Drug Administration has declared the following brands of oral contraceptives to be safe and effective estrogens may create a state of hyperinsulinism. Oral contraceptives how been shown to increase blood pressure among users for emergency contraception: Ovral (1 dose is 2 white pills), Alesse (1 dose is 5 pink pills), Nordette or Levlen (1 dose is 6 pink pills), Alesse (1 dose is 6 pink pills), Alesse (1 dose is 7 pink pills), Alesse (1 do contraceptives must be used with caution in women with cardiovascular disease risk factors.

Significant in the state of the

(Lidegaard et al.4) suggested that the risk of venous thromboembolism occurring in Yasmin users was higher than that for users of levonorgestrel-containing COCs and lower than that for users of desogestrel/gestodene-containing COCs (so-called third generation COCs). In the case-control study, however, the number of Yasmin cases was very small (1.2% of all cases) making the risk estimates unreliable. The relative risk for Yasmin users in the retrospective cohort study was greater than that for users of other COC products when considering women who used the products for less than one year. However, these one-year estimates may not be reliable because the analysis may include women of varying risk levels. Among women who used the product for 1 to 4 years, the relative risk was similar for users of other COC products.

A corrobydrate and Lipid Metabolic Effects
Oral contraceptives have been shown to cause glucose intolerance in a significant percentage of users. Oral contraceptives ontaining greater than 75 micrograms of estrogens cause hyperinsulinism, while lower doses of estrogen cause less glucose intolerance. Progestogens increase insulin resistance, this effect varying with different progestational agents. However, in the nondiabetic woman, oral contraceptives appear to have no effect on fasting blood glucose. Because of these demonstrated effects, prediabetic and diabetic woman should be carefully observed while taking oral contraceptives.

A small proportion of women will have persistent hypertriplyceridemia while on the oil. As discussed earlier (see WARNINGS 1a. Cerebrovascular Diseases

Gianvi[™]

(drospirenone and ethinyl estradiol tablets)

Oral contraceptives have been shown to increase both the relative and attributable risks of cerebrovascular events (thrombotic and hemorrhagic strokes), although, in general, the risk is greatest among older (>35 years), hypertensive women who also **9. Elevated Blood Pressure** smoke. Hypertension was found to be a risk factor, for both users and nonusers, for both types of strokes, while smoking interacted to increase the risk for hemorrhagic strokes.

Women with severe hypertension should not be started on hormonal contraceptives (see CONTRAINDICATIONS).

An increase in blood pressure has been reported in women taking oral contraceptives and this increase is more likely

2.6 for smokers who did not use oral contraceptives, 7.6 for smokers who used oral contraceptives, 1.8 for normotensive users and 25.7 for users with severe hypertension. The attributable risk is also greater in older women. Oral contraceptives also increase the risk for stroke in women with other risk for stroke in women with other nost women, elevated blood hyperipidemias, and obesity. Women with migraine (particularly migraine with aura) who take combination oral contraceptives. may be at an increased risk of stroke.

d. Dose-Related Risk of Vascular Disease From Oral Contraceptives

A positive association has been observed between the amount of estrogen and progestogen in oral contraceptives and forms a seriogen sincreased incidence of ischemic heart disease. Because estrogen and progestogen combination, the dosage regimen prescribed should be considered in the choice of an oral contraceptive. For any particular estrogen/progestogen combination, the dosage regimen prescribed should be considered in a low failure rate and the needs of the individual patient. New acceptors of oral contraceptive and forms and progestogen and progestogen and progestogen and progestogen combination, the dosage regimen prescribed should be considered in progestogen and progestogen and progestogen combination, the dosage regimen prescribed should be considered and adducts with numan increased incidence of ischemic heart disease. Because from Oral Contraceptives and formal of the cause.

11. Pregnancy
Pregnancy Category X. (See CONTRAINDICATIONS and dwith numan increased unities in the patients of the cause.

12. Headach
The onset or exacerbation of migraine or development of headache with a new pattern which is recurrent, persistent or severe of security of the cause.

13. Headach
The onset or exacerbation of oral contraceptives and formal dwints intercased intercased unities in the patients of the cause.

13. Pregnancy
Pregnancy Category X. (See CONTRAINDICATIONS and number of progestogen and progestogen and progestogen in progestogen and progesto

progestogen that is compatible with a low failure rate and the needs of the individual patient. New acceptors of oral contraceptive progestogen that is compatible with a low failure rate and the needs of the individual patient. New acceptors of oral contraceptive Some women may encounter post-pill amenorrhea or oligomenorrhea, especially when such a condition was pre-existent. agents should be started on preparations containing the lowest estrogen content that is judged appropriate for the individual patient. e. Persistence of Risk of Vascular Disease

There are two studies which have shown persistence of risk of vascular disease for ever-users of oral contraceptives. In a study in the United States, the risk of developing myocardial infarction after discontinuing oral contraceptives persists for at least 9 years for women aged 40 to 49 years who had used oral contraceptives for five or more years, but this increased risk was not demonstrated diseases.

1. General Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

2. Physical Examination and Eulew Up in other age groups. In another study in Great Britain, the risk of developing cerebrovascular disease persisted for at least 6 years after discontinuation of oral contraceptives, although excess risk was very small. However, both studies were performed with oral contraceptive formulations containing 50 micrograms or higher of estrogens.

2. Physical Examination and Follow-Up
A periodic personal and family medical history and complete physical examination are appropriate for all women, including women using oral contraceptives. The physical examination, however, may be deferred until after initiation of oral contraceptives are periodic personal and family medical history and complete physical examination are appropriate for all women, including women using oral contraceptives. The physical examination, however, may be deferred until after initiation of oral contraceptives.

One study gathered data from a variety of sources which have estimated the mortality rate associated with different methods of contraception at different ages (Table V). These estimates include the combined risk of death associated with contraceptive methods rospirenone and ethinyl estradiol tablets) contains 3 mg of the progestin drospirenone that has corticoid activity, including the potential for hyperkalemia in high-risk patients, comparable to a 25 mg dose tone.

Contraception and ethinyl estradiol tablets) contains 3 mg of the progestin drospirenone that has publisher isk attributable to pregnancy in the event of method failure. Each method of contraception has its specific benefits and risks. The study concluded that with the exception of oral contraceptive users 35 and older who smoke and 40 and older who smoke and 40 and older who smoke, mortality associated with control is below that associated with childbirth.

Suppose the risk attributable to pregnancy in the event of method failure. Each method of contraceptive users 35 and older who smoke and 40 and older who smoke and 40 and older who smoke, mortality associated with childbirth.

Suppose the risk attributable to pregnancy in the event of method failure. Each method of contraceptive users 35 and older who smoke and 40 and progestogens may elevate LDL levels and may render the control of hyperlipidemias more difficult. (See WARNINGS 1d.)

In conservation or a possible increase in risk of mortality with age for oral contraceptive users is based on data gathered in the 1970's but not reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations, combined with rearment for chronic conditions or diseases with medications that may increase serum potassium should have their serum potassium should have their serum potassium include ACE inhibitors, angiotensin — Il receptor antagonists, potassium-sparing diuretics, potassium supplementation, heparin, aldosterone antagonists, and NSAIDs.

The use of oral contraceptives is associated with increased risks of several serious conditions or notating vision and adequal insufficiency.) Women receiving daily, long-term but not reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations combined with the various risk factors listed in this labeling.

In patients with familial defects of lipoprotein metabolism receiving of oral contraceptive users is based on data gathered in the 1970's but not reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations combined with particular particular variety of reports of significant elevations of placentar indications reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations combined with reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations combined with particular variety of significant elevations of placentar indications that may increase earing restroin of oral contraceptive users is based on data gathered in the 1970's but not reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations combined with particular variety in the various risk factors of significant elevations of placentar in the various risk factors of significant elevations of placentar in the various risk factor

inderlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors

Therefore, the Committee recommended that the benefits of oral contraceptive use by healthy nonsmoking women over 40 may

6. Emotional Disorders formulation that is effective

TABLE V: ANNUAL NUMBER OF BIRTH-RELATED OR METHOD-RELATED DEATHS ASSOCIATED WITH CONTROL OF

FERTILITY PER 100,000 NONSTERILE WOMEN, BY FERTILITY-CONTROL METHOD ACCORDING TO AGE						
Method of Control and Outcome	15 to 19 years	20 to 24 years	25 to 29 years	30 to 34 years	35 to 39 years	40 to 44 years
No fertility control methods\1\	7	7.4	9.1	14.8	25.7	28.2
Oral contraceptives non-smoker \2\	0.3	0.5	0.9	1.9	13.8	31.6
Oral contraceptives smoker \2\	2.2	3.4	6.6	13.5	51.1	117.2
IUD \2\	0.8	0.8	1	1	1.4	1.4
Condom \1\	1.1	1.6	0.7	0.2	0.3	0.4
Diaphragm/spermicide \1\	1.9	1.2	1.2	1.3	2.2	2.8
Periodic abstinence \1\	2.5	1.6	1.6	1.7	2.9	3.6
\1\ Deaths are hirth related	*			•		

dapted from H.W. Orv. Family Planning Perspectives, 15:57-63, 1983. 3. Carcinoma of the Reproductive Organs and Breasts

Numerous epidemiological studies have been performed on the incidence of breast, endometrial, ovarian and cervical cancer in women using oral contraceptives.

Atorvastatin: Coadministration of atorvastatin and an estradiol by approximately 30% and 20%, respectively.

oral contraceptives (RR=1.24), this excess risk decreases over time after combination oral contraceptive discontinuation and by 10 years after cessation the increased risk disappears. The risk does not increase with duration of use and no consistent relationships have been found with dose or type of steroid. The patterns of risk are also similar regardless of a woman's reproductive history or her family breast cancer history. The subgroup for whom risk has been found to be significantly elevated inhibition of conjugation.

P450) and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations are supported by the following contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive significantly after discretizations and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contracepti is women who first used oral contraceptives before age 20, but because breast cancer is so rare at these young ages, the number Effects of Drospirenone on Other Drugs of cases attributable to this early oral contraceptive use is extremely small.

of cases attributable to this early oral contraceptive use is extremely small.

Metabolic Interactions

Metabolic Interactions

Metabolic Interactions

Metabolism of DRSP and potential effects of DRSP on hepatic cytochrome P450 (CYP) enzymes have been investigated in *in vitro*And *in vivro* studies DRSP did not affect turnover of model substrates of CYP1A2 and CYP2D6, and *in vivro* studies of CYP1A1, CYP2C9, CYP2C19 and CYP3A4 with CYP2C19 being because breast cancer is a better of model substrates of CYP1A1, CYP2C9, CYP2C19 and CYP3A4 with CYP2C19 being because breast cancer.

relationship has not been established

prior to pregnancy. Studies also do not suggest a teratogenic effect, particularly in so far as cardiac anomalies and limb-reduction defects are concerned, when taken inadvertently during early pregnancy.

Gianvi[™]

Two additional epidemiological studies, one case-control study (van Hylckama Vlieg et al.³) and one retrospective cohort study contraceptive users may be minimal. The recent findings of minimal risk may be related to the use of oral contraceptive formulations containing lower hormonal doses of estrogens and progestogens.

A small proportion of women will have persistent hypertriglyceridemia while on the pill. As discussed earlier (see WARNINGS 1a.

An increase in blood pressure has been reported in women taking oral contraceptives and this increase is more likely in older oral

In a large study, the relative risk of thrombotic strokes has been shown to range from 3 for normotensive users to 14 for users with severe hypertension. The relative risk of hemorrhagic stroke is reported to be 1.2 for nonsmokers who used oral contraceptives, shown that the incidence of hypertension increases with increasing concentrations of progestogens.

among ever- and never-users.

if requested by the woman and judged appropriate by the clinician. The physical examination should include special reference

12. Nursing Mothers to blood pressure, breasts, abdomen and pelvic organs, including cervical cytology and relevant laboratory tests. In case of undiagnosed, persistent or recurrent abnormal vaginal bleeding, appropriate measures should be conducted to rule out malignancy. Women with a strong family history of breast cancer or who have breast nodules should be monitored with particular care.

of this product before menarche is not indicated.

outweigh the possible risks. Of course, women of all ages who take oral contraceptives should take the lowest possible dose

Women with a history of depression should be carefully observed and the drug discontinued if depression recurs to a serious degree. Patients becoming significantly depressed while taking oral contraceptives should stop the medication and use an alternate

method of contraception in an attempt to determine whether the symptom is drug related. **Contact Lenses** tact lens wearers who develop visual changes or changes in lens tolerance should be assessed by an ophthalmologist.

rug Interactions ets of Other Drugs on Combined Hormonal Contraceptive: pin: Metabolism of ethinyl estradiol and some progestins (e.g., norethindrone) is increased by rifampin. A reduction in

• Hepatic adenomas or benign liver tumors

raceptive effectiveness and an increase in menstrual irregularities have been associated with concomitant use of rifampin.

There is evidence of an association between the following conditions and the use of oral contraceptives: excline: Minocycline-related changes in estradiol, progesterone, FSH and LH plasma levels, breakthrough bleeding, or Mesenteric thrombosis aceptive failure cannot be ruled out.

polism of ethinyl estradiol and/or some progestins, which could result in a reduction of contraceptive effectiveness. tibiotics: Pregnancy while taking combined hormonal contraceptives has been reported when the combined hormonal ontraceptives were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical of activities were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. contraceptives were administered with aniimicrousias such as anipolinin, tenasyonin, and grootstand pharmacokinetic studies have not demonstrated any consistent effects of antibiotics (other than rifampin-see above) on plasma

Breakthrough bleeding

Atorvastatin: Coadministration of atorvastatin and an oral contraceptive increased AUC values for norethindrone and ethinyl

In women using oral contraceptives.

Although the risk of having breast cancer diagnosed may be slightly increased among current and recent users of combined and polycoprotein transporter and may reduce the effectiveness of oral contraceptives (RR=1.24) this excess risk decreases over time after combination and increased among current and recent users of combined and polycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive and emergency contraceptive.

Amenorrhea

*Temporary infertility after discontinuation of treatment and recent users of combined and polycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive.

hormonally-sensitive tumor.

Some studies suggest that oral contraceptive use has been associated with an increase in the risk of cervical intraepithelial neoplasia in some populations of women. However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behavior and other factors.

In spite of many studies of the relationship between oral contraceptive use and breast and cervical cancers, a cause-and-effect relationship has not been established.

but nad a liminolory of moder substrates of CYP2A1, CYP2A9, CYP2A9 (CYP2A9 GYP2A9 With CYP2A9 W

Several studies have investigated the relative risks of thromboembolism in women using a different drospirenone-containing COC (Yasmin, which contains 0.030 mg of ethinyl estradiol and 3 mg of drospirenone) compared to those in women using a contraceptives should not be used as a test for pregnancy. Oral contraceptives on Other Drugs

The administration of oral contraceptives on Other Drugs

The following adverse recontaining ethinyl estradiol may inhibit the metabolism of other compounds. Increased on the plasma concentrations of cyclosporine, prednisolone, and theophylline have been reported with concomitant administration of oral contraceptives should not be used as a test for pregnancy. Oral contraceptives on Other Drugs

The administration of oral contraceptives on Other Drugs

Combined oral contraceptives on Other Drugs

Combined Hormonal Contraceptives on Other Drugs

Combined oral contraceptives containing ethinyl estradiol may inhibit the metabolism of other compounds. Increased into contraceptives containing ethinyl estradiol may inhibit the metabolism of other compounds. Increased on the plasma concentrations of cyclosporine, prednisolone, and theophylline have been reported with concomitant administration of oral contraceptives. In addition, oral contraceptives in contraceptives on Other Drugs

The administration of oral contraceptives on Other Drugs

Combined oral contraceptives on Other Drugs

Combined oral contraceptives on Other Drugs

Combined oral contraceptives on Other Drugs

It is recommended that for any patient who has missed two consecutive periods, pregnancy should be considered at the time of the first in contraceptives in addition, oral contraceptives. In addition, oral contraceptives in other compounds. Decreased plasma on centraceptive in contraceptives on Other Drugs

It is recommended that for any patient who plasma concentrations of cyclosporine, prednisolone, and theophylline have been reported with concomitant administration of oral contraceptives. In addition, oral contraceptives may induce the conjugation of other compounds. Decreased plasma

• Acne
• Budd-Chiari syndrome

Glucose tolerance may be decreased.

a. Increased prothrombin and factors VII, VIII, IX and X; decreased antithrombin 3; increased norepinephrine-induced platelet • Cystitis-like syndrome b. Increased thyroid-binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by protein-

pound iodiné (PBI), T4 by column or by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG tree T4 concentration is unaltered. Other binding proteins may be elevated in serum.

d. Sex-hormone-binding globulins are increased and result in elevated levels of total circulating sex steroids and corticoids; however, free or biologically active levels remain unchanged.

Headache

Hemolytic ur · Hemolytic uremic syndrom e. Triglycerides may be increased.

g. Serum folate levels may be depressed by oral contraceptive therapy. This may be of clinical significance if a woman becomes pregnant shortly after discontinuing oral contraceptives.

10. Carcinogenesis, Mutagenesis, Impairment of Fertility
In a 24 month oral carcinogenicity study in mice dosed with 10 mg/kg/day drospirenone alone or 1 + 0.01, 3 + 0.03 and 10 + 0.1 mg/kg/day of drospirenone and ethinyl estradiol, 0.1 to 2 times the exposure (AUC of drospirenone) of women taking a 4-optic neuritis, which may lead to partial or complete loss of vision contraceptive dose, there was an increase in carcinomas of the harderian gland in the group that received the high dose of drospirenone

Pancreatitis

Pancreatitis · Pre-menstrual syndrome

human lymphocytes) and *in vivo* (mouse micronucleus) genotoxicity tests. Drospirenone increased unsch hepatocytes and formed adducts with rodent liver DNA but not with human liver DNA. (See WARNINGS).

Twelve pregnancies that occurred with drospirenone and ethinyl estradiol tablets exposure *in utero* (none with more than a single cycle of exposure) have been identified. There were no known cases of congenital anomalies.

A teratology study in pregnant rats given drospirenone orally at doses of 5, 15 and 45 mg/kg/day, 6 to 50 times the human bronchitis, rinnitis, amenorrhea, and urine abnormality. exposure based on AUC of drospirenone, resulted in an increased number of fetuses with delayed ossification of bones of the OVERDOSAGE

WENDOSAGE

The two higher doses. A similar study in rabbits dosed orally with 1, 30 and 100 mg/kg/day drospirenone, 2 to 27 times the human exposure, resulted in an increase in fetal loss and retardation of fetal development (delayed ossification of small bones, multiple fusions of ribs) at the high dose only. When drospirenone was administered with ethinyl estradiol (100:1) during analogue which has antimineralocorticoid properties. Serum concentration of potassium and sodium, and evidence of metabolic bones, multiple fusions of ribs) at the high dose only. When drospirenone was administered with ethinyl estradiol (100:1) during late pregnancy (the period of genital development) at doses of 5, 15 and 45 mg/kg, there was a dose dependent increase in acidosis, should be monitored in cases of overdose. feminization of male rat fetuses. In a study in 36 cynomolgous monkeys, no teratogenic or feminization effects were observed with orally administered drospirenone and ethinyl estradiol (100:1) at doses up to 10 mg/kg/day drospirenone, 30 times the human exposure.

Small amounts of oral contraceptive steroids have been identified in the milk of nursing mothers, and a few adverse effects on the child have been reported, including jaundice and breast enlargement. In addition, oral contraceptives given in the postpartum period may interfere with lactation by decreasing the quantity and quality of breast milk. If possible, the nursing mother should be advised not to use oral contraceptives but to use other forms of contraception until she has completely weared her child.

After oral administration of 3 me DSEMIO 20 me 5. Technical behavior 20 me 1.0 me 1. After oral administration of 3 mg DRSP/0.03 mg EE tablets about 0.02% of the drospirenone dose was excreted into the breast Effects related to inhibition of ovulation:

13. Pediatric Usage
Safety and efficacy of drospirenone and ethinyl estradiol tablets has been established in women of reproductive age. Safety and Effects from long-term use: efficacy are expected to be the same for post-pubertal adolescents under the age of 16 and for users 16 years and older. Use

• decreased incidence of fibroadenomas and fibrocystic disease of the breast

Information for the Patient ADVERSE REACTIONS

n increased risk of the following serious adverse reactions has been associated with the use of oral contraceptives (see WARNINGS). Arterial thromboembolisn

 Pulmonary embolism Mvocardial infarction · Cerebral hemorrhage

 Hypertension Gallbladder disease

Retinal thrombosis

convulsants: Anticonvulsants such as phenobarbital, phenytoin, and carbamazepine have been shown to increase the The following adverse reactions have been reported in patients receiving oral contraceptives and are believed to be drug-related:

Change in menstrual flow

· Breast changes: tenderness, enlargement, secretion Change in weight or appetite (increase or decrease)

The following adverse reactions have been reported in users of oral contraceptives and a causal association has been neither

 Dizziness Dvsmenorrhea

Frythema nodosum

· Hemorrhagic eruption Hirsutism

Loss of scalp hair

The most frequent (> 1%) treatment-emergent adverse events, listed in descending order, reported with the use of drospirenone and ethinyl estradiol tablets in the contraception clinical trials, which may or may not be drug related, included; upper respiratory infection, headache, breast pain, vaginal moniliasis, leukorrhea, diarrhea, nausea, vomiting, vaginitis, abdominal pain, flu syndrome, dysmenorrhea, moniliasis, allergic reaction, urinary tract infection, accidental injury, cystitis, tooth disorder, sore throat, infection, fever, surgery, sinusitis, back pain, emotional lability, migraine, suspicious Papanicolaou smear, dyspepsia,

rhinitis, acne, gastroenteritis, bronchitis, pharyngitis, skin disorder, intermenstrual bleeding, decreased libido, weight gain, pain, depression, increased cough, dizziness, menstrual disorder, pain in extremity, pelvic pain, and asthenia. The most frequent (> 1%) treatment-emergent adverse events, listed in descending order, reported with the use of drospirenone and ethinyl estradiol tablets in the acne clinical trials, which may or not be drug related, included: upper respiratory infection, metrorrhagia, headache, suspicious Papanicolaou smear, nausea, sinusitis, vaginal moniliasis, flu syndrome, menorrhagia

ocorticoid properties. Serum concentration of potassium and sodium, and evidence of metabolic

e following non-contraceptive health benefits related to the use of oral contraceptives are supported by epidemiological studies which largely utilized oral contraceptive formulations containing doses exceeding 0.035 mg of ethinyl estradiol or 0.05 mg mestranol.

milk of postpartum women within 24 hours. This results in a maximal daily dose of about 3 mcg drospirenone in an infant.

• decreased incidence of functional ovarian cysts

decreased incidence of ectopic pregnancies

 decreased incidence of acute pelvic inflammatory disease decreased incidence of endometrial cancer

· decreased incidence of ovarian cancer DOSAGE AND ADMINISTRATION

Sunday Start

To achieve maximum contraceptive effectiveness. Gianvi tablets must be taken exactly as directed at intervals not exceeding Gianvi tablets consist of 24 pink active tablets of a monophasic combined hormonal preparation plus 4 inert white tablets. The

dosage of Gianvi tablets is one pink tablet daily for 24 consecutive days followed by 4 white inert tablets per menstrual cycle. A patient should begin to take Gianvi tablets either on the first day of her menstrual period (Day 1 Start) or on the first Sunday after the onset of her menstrual period (Sunday Start).

During the first cycle of Gianvi tablet use, the patient should be instructed to take one pink Gianvi tablet daily, beginning on Day one (1) of her menstrual cycle. (The first day of menstruation is Day one.) She should take one pink Gianyi tablet daily for 24 consecutive days, followed by one white inert tablet daily on menstrual cycle days 25 through 28. It is recommended that Gianvi tablets be taken at the same time each day, preferably after the evening meal or at bedtime. Gianvi tablets can be taken without regard to meals. If Gianvi tablets are first taken later than the first day of the menstrual cycle, Gianvi tablets should not be considered effective as a contraceptive until after the first 7 consecutive days of product administration. The possibility of evulation and conception prior to initiation of medication should be considered.

During the first cycle of Gianvi tablet use, the patient should be instructed to take one pink Gianvi tablet daily, beginning on the first Sunday after the onset of her menstrual period. She should take one pink Gianvi tablet daily for 24 consecutive days, followed by one white inert tablet daily on menstrual cycle days 25 through 28. It is recommended that Gianvi tablets be taken at the same time each day, preferably after the evening meal or at bedtime. Gianvi tablets can be taken without regard to meals. Gianvi tablets should not be considered effective as a contraceptive until after the first 7 consecutive days of product administration. The possibility of ovulation and conception prior to initiation of medication should be considered. The patient should begin her next and all subsequent 28-day regimens of Gianvi tablets on the same day of the week that she

began her first regimen, following the same schedule. She should begin taking her pink tablets on the next day after ingestion of the last white tablet, regardless of whether or not a menstrual period has occurred or is still in progress. Anytime a subsequent cycle of Gianvi tablets is started later than the day following administration of the last white tablet, the patient should use another method of contraception until she has taken a pink Gianvi tablet daily for seven consecutive days. When switching from another oral contraceptive, Gianvi tablets should be started on the same day that a new pack of the

previous oral contraceptive would have been started. . Withdrawal bleeding usually occurs within 3 days following the last pink tablet. If spotting or breakthrough bleeding occurs while taking Gianvi, the patient should be instructed to continue taking her Gianvi tablets as instructed and by the regimen described above. She should be instructed that this type of bleeding is usually transient and without significance; however, if the bleeding is persistent or prolonged, the patient should be advised to consult her physician.

Although the occurrence of pregnancy is low if Gianvi tablets are taken according to directions, if withdrawal bleeding does not occur, the possibility of pregnancy must be considered. If the patient has not adhered to the prescribed dosing schedule (missed one or more active tablets or started taking them on a day later than she should have), the possibility of pregnancy should be considered at the time of the first missed period and appropriate diagnostic measures taken. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out. Hormonal contraceptives should

be discontinued if pregnancy is confirmed.

on the other side, each containing 3 mg of drospirenone and 0.02 mg of ethinyl estradiol, and 4 inert white, round, unscored tablets debossed with stylized b on one side and 208 on the other side.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN. Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

2. Seeger JD, Loughlin J, Eng PM, et al: Risk of thromboembolism in women taking ethinyl estradiol/drospirenone and other oral contraceptives. Obstetrics & Gynecology 2007;110(3):587-593.

BRIEF SUMMARY PATIENT PACKAGE INSERT

ne and ethinyl estradiol tablets) containing the following:

and other sexually transmitted diseases GianviTM (drospirenone and ethinyl estradiol tablets) is different from other birth control pills because it contains the or about using another method of birth control.

Other drugs may also increase potassium. If you are currently on daily, long-term treatment for a chronic condition with any 1 DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL

blood test to check your potassium level.

NSAIDs (ibuprofen [Motrin*, Advil*], naprosyn [Aleve* and others] when taken long-term and daily for treatment of pills (without hormones) to be taken for four days. arthritis or other problems)

Potassium-sparing diuretics (spironolactone and others)

- Potassium supplementation ACE inhibitors (Capoten*, Vasotec*, Zestril* and others)
- Angiotensin-II receptor antagonists (Cozaar*, Diovan*, Avapro* and others)

Gianvi™ (drospirenone and ethinyl estradiol tablets) is an oral contraceptive, also known as a "birth control pill" or "the pill. Oral contraceptives are taken to prevent pregnancy, and, when taken correctly without missing any pills, have a failure rate of approximately 1% per year (1 pregnancy per 100 women per year of use). The typical failure rate in pill users is appro % per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. Forgetting to take pills considerably increases the chances of pregnancy.

nvi™ (drospirenone and ethinyl estradiol tablets) may also be taken to treat moderate acne in women who are able to and wish to use the pill for birth control. Any woman who needs contraception (birth control) and chooses to use an oral contraceptive should understand the benefits

and risks of using the pill. This leaflet will give you much of the information you will need to help you decide if you should use the pill for contraception and will also help you determine if you are at risk of developing any of the serious side effects of the pill. It will tell you how to use the pill properly so that it will be as effective as possible. However, this leaflet is not a replacement or a careful discussion between you and your healthcare professional. You should discuss the information provided in this AN EXTRA, FULL PILL PACK. leaflet with him or her, both when you first start taking the pill and during your revisits. You should also follow your healthcare professional's advice with regard to regular check-ups while you are on the pill.

AN EXTRA, FULL PILL PACK.

WHEN TO START THE FIRST PACK OF PILLS

For the majority of women, oral contraceptives can be taken safely. But there are some women who are at high risk of developing certain serious diseases that can be life-threatening or may cause temporary or permanent disability or death. The risks associated with taking oral contraceptives increase significantly if you:

Note the majority of women, oral contraceptives can be taken safely. But there are some women who are at high risk of developing certain serious diseases that can be life-threatening or may cause temporary or permanent disability or death. The risks associated with taking oral contraceptives increase significantly if you:

Note the majority of women, oral contraceptives can be taken safely. But there are some women who are at high risk of developing certain serious diseases that can be life-threatening or may cause temporary or permanent disability or death. The risks associated with taking oral contraceptives increase significantly if you:

have high blood pressure, diabetes, high cholesterol, or are obese • have or have had clotting disorders, heart attack, stroke, angina pectoris (severe chest pains), cancer of the breast or sex

organs, jaundice, or malignant or benign liver tumors. You should not take the pill if you suspect you are pregnant or have unexplained vaginal bleeding.

Although cardiovascular disease risks may be increased with oral contraceptive use after age 40 in healthy, non-smoking

omen (even with the newer low-dose formulations), there are also greater potential health risks associated with pregnancy WHEN YOU SWITCH FROM A DIFFERENT BIRTH CONTROL PILL

Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from oral contraceptive like. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women WHATTO DO DURING THE MONT

over 35 years of age. Women who use oral contraceptives should not smoke. Most side effects of the pill are not serious. The most common such effects are nausea, vomiting, bleeding between menstrual Do not skip pills even if you are spotting or bleeding between monthly periods or feel sick to your stomach (nausea) Do not skip pills even if you do not have sex very often.

Most side effects of the pill are not serious. The most common such enects are mausea, vormang, occurring sources and vomiting periods, weight gain, breast tenderness, and difficulty wearing contact lenses. These side effects, especially nausea and vomiting 2. WHEN YOU FINISH A PACK OF PILLS:

The serious side effects of the pill occur very infrequently, especially if you are in good health and are young. However, you should know that the following medical conditions have been associated with or made worse by the pill:

1. Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), blockage or rupture of a blood vessel in the brain (stroke), blockage of blood vessels in the heart (heart attack and angina pectoris) or other organs of the body. As mentioned above, smoking increases the risk of heart attacks and strokes and subsequent serious medical consequences. Women with graine headaches also may be at increased risk of stroke when taking the pill.

2. You do not need to use a back-up birth control method if you have sex. If you MISS 2 pink "active" pills in a row in WEEK 1 or WEEK 2 of your par

the pill and liver cancer. However, liver cancers are extremely rare. The chance of developing liver cancer from using the pill 2. Then take one pill a day until you finish the pack.

3. High blood pressure, although blood pressure usually returns to normal when the pill is stopped.

4. Cartied of the breast. Various studies give conflicting reports of the relationship between breast cancer and of an confraceptive use may slightly increases your chance of having breast cancer of diagnosed, particularly after using hormonal contraceptives at a younger age. After you stop using hormonal contraceptives, the chances of getting breast cancer is begin to go back down. You should have regular breast examinations by a healthcare provider and examine your own breasts monthly. Tell your healthcare provider if you have a family history of breast cancer or if you have had breast cancer or if you have had breast cancer or if you have had breast cancer should not use oral contraceptives because breast cancer is a hormone-sensitive tumor.

In If you are a Day 1 Starter:

THROW OUT the rest of the pill pack and start a new pack that same day.

If you are a Sunday Starter:

Keep taking one pill every day until Sunday. On Sunday, THROW OUT the rest of the pack and start a new pack of pills that abnormal mammogram. Women who currently have or have had breast cancer should not use oral contraceptive because breast cancer is a hormone-sensitive tumor.

If you are a Day 1 Starter:

THROW OUT the rest of the pill pack and start a new pack of pills that a new pack of pills that

Some studies have found an increase in the incidence of cancer or precancerous lesions of the cervix in women who use the pill.

2. Tou GOLD BECOME THE ORDER THY YOU have 5 and 18 or 7 agreements of the cervix in women who use the pill. However, this finding may be related to factors other than the use of the pill. The symptoms associated with these serious side effects are discussed in the detailed leaflet given to you with your supply of healthcare provider because you might be pregnant.

pills. Notify your doctor or healthcare provider if you notice any unusual physical disturbances while taking the pill. In addition Irugs such as rifampin, as well as some anticonvulsants, some antibiotics and some herbal products such as St. John's Wort, may decrease oral contraceptive effectiveness.

Taking the pill may provide some important non-contraceptive benefits. These include less painful menstruation, less menstrual large and favor cancers of the overvand the lining of the uterus.

THROW OUT the rest of the lift you are a Sunday Starter:

Be sure to discuss any medical condition you may have with your healthcare provider. Your healthcare provider will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be delayed to another time if you request it and the healthcare provider believes that it is appropriate to postpone it. You should be reexamined at least once a year while taking oral contraceptives. The detailed patient information booklet gives you further information, which you should read and while taking oral contraceptives. The detailed patient information booklet gives you further information, which you should read and while taking oral contraceptives. The detailed patient information booklet gives you further information, which you should read and while taking oral contraceptives. The detailed patient information booklet gives you further information, which you should read and while taking oral contraceptives. The detailed patient information booklet gives you further information, which you should read and taking the provider will take a medical and tenting the total contraceptives and with your healthcare provider will take a medical and tenting the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and will examine and the mining of the total contraceptives and the mining of the t

infection (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

If you MISS ANY of the 4 white "reminder" pills in WEEK 4:

• THROW AWAY the pills you missed.

INSTRUCTIONS TO PATIENTS

IMPORTANT POINTS TO REMEMBER

1. BE SURE TO READ THESE DIRECTIONS

. Before you start taking your pills

pregnant. See "WHAT TO DO IF YOU MISS PILLS" below

. Anytime you are not sure what to do

2. THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME. GIANVI™ TABLETS CAN BE TAKEN WITHOUT

Gianvi™

(drospirenone and ethinyl estradiol tablets)

3. van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, et al: The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ 2009;339:b2921. 4. Lidegaard O, Lokkegaard E, Svendsen AL, et al: Hormonal contraception and risk of venous thromboembolism: national follow-up study. *BMJ* 2009: 339:b2890.

On the days you take two pills, to make up for missed pills, you could also feel a little sick to your stomach.

5. IF YOU HAVE VOMITING (within 3 to 4 hours after you take your pill), you should follow the instructions for "WHAT TO DO IF YOU MISS PILLS". IF YOU HAVE DIARRHEA, or IF YOU TAKE CERTAIN MEDICINES, including some antibiotics and some herbal products such as St. John's Wort, your pills may not work as well.

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS)

Use a back-up method (such as condoms or spermicides) until you check with your healthcare provider 6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your healthcare provider about how to make pill-taking easier GianviTM (drospirenone and ethinyl estradiol tablets) may also be taken to treat moderate acne in women who are able to and

• Diabetes with complications of the kidneys, eyes, nerves, or blood vessels

Trogestin drospirenone. Drospirenone may increase potassium. Therefore, you should not take drospirenone and ethinyl straight of the drugs may also increase notassium. It was a currently on daily long-term treatment for a charge provider.

of the medications below, you should consult your healthcare provider about whether drospirenone and ethinyl estradiol tablets is right for you, and during the first month that you take drospirenone and ethinyl estradiol tablets, you should have The Gianvi tablets-pill pack has 24 pink "active" pills (with hormones) to be taken for 24 days, followed by 4 white "reminder"

> Where on the nack to start taking nills 2) In what order to take the pills (follow the arrows)

3) The week numbers are shown on the blister card picture below

ANOTHER KIND OF BIRTH CONTROL (such as condoms or spermicides) to use as a back-up in case you miss pills.

13. Take the first pink "active" pill of the first pack during the first 24 hours of your period.

2. You will not need to use a back-up method of birth control, since you are starting the pill at the beginning of your period.

SUNDAY START:1. Take the first pink "active" pill of the first pack on the *Sunday after your period starts*, even if you are still bleeding. If your p

begins on Sunday, start the pack that same day.

/hen switching from another birth control pill, Gianvi tablets should be started on the same day that a new pack of the previous birth

1. TAKE ONE PILL AT THE SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY

Start the next pack on the day after your last white "reminder" pill. Do not wait any days between packs.

If you MISS 2 pink "active" pills in a row in WEEK 1 or WEEK 2 of your pack: 2. Liver tumors, which may rupture and cause severe bleeding. A possible but not definite association has been found with 1. Take two pills on the day you remember and two pills the next day.

You COULD BECOME PREGNANT if you have sex in the *T days* after you restart your pills. You MUST use another birth con method (such as condoms or spermicides) as a back-up for those *T* days.

4. Cancer of the breast. Various studies give conflicting reports on the relationship between breast cancer and oral contraceptive If you MISS 2 pink "active" pills in a row in WEEK 3 or WEEK 4 of your pack.

2. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use another birth control

3. You may not have your period this month but this is expected. However, if you miss your period two months in a row, call your

1. If you are a Day 1 Starter:

THROW OUT the rest of the pill pack and start a new pack that same day. Keep taking 1 pill every day until Sunday. On Sunday, THROW OUT the rest of the pack and start a new pack of pills that

discuss with your healthcare provider.

This product (like all oral contraceptives) is intended to prevent pregnancy. Oral contraceptives do not protect against HIV healthcare provider because you might be pregnant.

For additional information see "Detailed Patient Labeling"

Keep taking one pill each day until the pack is empty.

FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED: Use a BACK-UP METHOD (such as condoms or spermicides) anytime you have sex KEEP TAKING ONE ACTIVE PINK PILL EACH DAY until you can contact your healthcare provider. DETAILED PATIENT PACKAGE INSERT

Gianvi[™] (drospirenone and ethinyl estradiol tablets) is product (like all oral contraceptives) is intended to prevent pregnancy. Oral contraceptives do not protect against HIV section (AIDS) and other sexually transmitted diseases.

GianviTM (drospirenone and ethinyl estradiol tablets) is different from other intro control take drospirenone and ethinyl estradiol tablets if you have kidney, liver or adrenal disease because this could cause serious heart and health problems. Other drugs may also increase potassium. If you are currently on daily, long-term treatment for a chronic condition with any of the medications below, you should not not health and the medications below, you should consult your healthcare provider about whether drospirenone and ethinyl estradiol tablets is right for you, and during the first month that you take drospirenone and ethinyl estradiol tablets, you should have a blood test to check your potassium level.

28 associated with profice of deaths exceeds the WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES

Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.

1. Dinger JC, Heinemann LAJ, et al: The safety of a drospirenone-containing oral contraceptive shared on 142,475 women-years of observation. Contraceptive based on 142,475 women-years of observation. Contraceptive shared on 142,475 women-years of observation. See "WHAT TO DO IF YOU MISS PILLS" heliow

**NSAIDS (ibuprofen [Motrin*, Advil*], naprosyn [Aleve* and others] when taken long-term and daily for treatment of pregnant. This includes starting the pack late. The more pills you could get pregnant. This includes starting the pack late. The more pills you miss, the more likely you are pregnant or think you or other problems)

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 Potassium-sparing diuretics (spironolactone and others) Potassium supplementation

• ACE inhibitors (Capoten*, Vasotec*, Zestril* and others) • Angiotensin-II receptor antagonists (Cozaar*, Diovan*, Avapro* and others)

nsiderably increases the chances of pregnancy

Aldosterone antagonist

Gianvi™ (drospirenone and ethinyl estradiol tablets) is an oral contracentive, also known as a "hirth control pill" or "the pill" Oral contraceptives are taken to prevent pregnancy, and, when taken correctly without missing any pills, have a failure rate of approximately 1% per year (1 pregnancy per 100 women per year of use). The typical failure rate in pill users is approximately 5% per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. Forgetting to take pills

• Known or suspected pregnancy

INTRODUCTION

y woman who needs contraception (birth control) and chooses to use an oral contraceptive should understand the benefits and

• Headaches with neurological symptoms

Any woman who needs contraception (pirm control) and critiouses to use an oral contraception and included pure should understand the pill. This leaflet will give you much of the information you will need to help you decide if you should use the pill for contraception and will also help you determine if you are at risk of developing any of the serious side effects of the pill. It will tell you how to use the pill properly so that it will be as effective as possible. However, this leaflet is not a replacement for a careful discussion between you and your healthcare professional. You should discuss the information provided in this leaflet with him or her, both when you first start taking the pill and during your revisits. You should also follow your healthcare professional's advice with regard to regular to regular to the pill and during your revisits. You should also follow your healthcare professional's advice with regard to regular to regular to the pill properly so that it will be as effective as possible. However, this leaflet with him or her, both when you first start taking the pill and during your revisits. You should also follow your healthcare professional's advice with regard to regular to regular to the pill properly so that it will be as effective as possible. However, this leaflet with him or her, both when you first start taking the pill and during your revisits. You should also follow your healthcare professional's advice with regard to regular to repair the pill and during your revisits. You should also follow your healthcare professional's advice with regard to regular to the pill to

Cral contraceptives or "birth control pills" or "the pill" are used to prevent pregnancy and are more effective than most other nonsurgical methods of birth control. When they are taken correctly, the chance of becoming pregnant is less than 1% one pregnancy per 100 women who don't always follow the instructions exactly, are about 5% per year. The chance of becoming pregnant increases with each missed pill during a menstrual cycle.

NAIDS (ibuprofen, naprosyn and others)

**Occurs in more than one cycle or lasts for more than a few days, talk to your doctor or healthcare provider. Tell your healthcare provider if you have ever had any of the above conditions (Your healthcare provider can recommend another method of birth control). If you are currently on daily, long-term treatment for a chronic condition with any of the following method of birth control). If you are currently on daily, long-term treatment for a chronic condition with any of the following provider.

**SAIDS (ibuprofen, naprosyn and others)*

**NAIDS (ibuprofen, naprosyn and others)*

**NAIDS (ibuprofen, naprosyn and others)*

**SAIDS (ibuprofen, naprosyn a In comparison, typical failure rates for other population methods of hirth control during the first year of use are as follows:

• Potassium supplementation

PERCENTAGE OF WOMEN EXPERIENCING AN UNINTENDED PREGNANCY DURING THE FIRST YEAR OF TYPICAL USE

• ACE inhibitors (captopril, enalapril, lisinopril and others) AND FIRST YEAR OF PERFECT USE OF CONTRACEPTION AND THE PERCENTAGE CONTINUING USE AT THE END OF THE

• Angiotensin-II receptor antagonists (Cozaar*, Diovan*, Avapro* and others)

			encing an Unintended the First Year of Use	% of Women Continuing Use at One Year ³
	Method (1)	Typical Use ¹ (2)	Perfect Use ² (3)	(4)
	Chance ⁴	85	85	
	Spermicides ⁵	26	6	40
	Periodic abstinence	25		63
	Calendar		9	
r you.	Ovulation method		3	
n you.	Sympto-thermal ⁶		2	
	Post-ovulation		1	
od.	Withdrawal	19	4	
ou.	Cap ⁷			
period	Parous women	40	26	42
	Nulliparous women	20	9	56
unday	Sponge			
	Parous women	40	20	42
control	Nulliparous women	20	9	56
	Diaphragm ⁷	20	6	56
	Condom ⁸			
	Female (Reality)	21	5	56
	Male	14	3	61
	Pill	5		71
	progestin only		0.5	
	combined		0.1	
<i>'</i> .	IUD:			
•	Progesterone T	2	1.5	81
	Copper T 380A	0.8	0.6	78
	Lng 20	0.1	0.1	81
	Depo Provera	0.3	0.3	70
ontrol	Nornlant and Nornlant-2	0.05	0.05	88

Male sterilization Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy

Contraceptive Technology: Seventeenth Revised Edition. New York NY: Irvington Publishers, 1998

Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently

Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently

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Saminations of a method (not necessarily for the first time) and who use it perfectly for the first time) and who use it perfectly for the first time (not necessarily for the first time) and the first time (not necessarily for the first time) and the first time (not necessarily for the first time) and the first time (not necessarily for the first time) and the first time (not necessarily for the first time) and the

and correctly). The percentage who experience an accidental pregnancy during the first year if they do not stop use for any this finding may be related to factors other than the use of oral contraceptives.

become pregnant within one year among women now relying on reversible methods of contraception if they abandoned

Foams, creams, gels, vaginal suppositories, and vaginal film.

Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in

ost-ovulatory phases. Vith spermicidal cream or jelly.

Female sterilization

The treatment schedule is one dose within 72 hours after unprotected intercourse, and a second dose 12 hours after the 1 dose. The Food and Drug Administration has declared the following brands of oral contraceptives to be safe and effector emergency contraception: Ovral (1 dose is 2 white pills), Alesse (1 dose is 5 pink pills), Nordette or Levlen (1 dose).

10 effletgeincy contraception. Over (1 dose is 2 wine pins), hosse (1 dose is 4 yellow pills).

10 However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches the provided of the provided in the provid

(drospirenone and ethinyl estradiol tablets)

GianviTM (drospirenone and ethinyl estradiol tablets) may also be taken to treat moderate acne if all of the following are true: users over the age of 35 who smoke and pill users over the age of 40 even if they do not smoke. It can be seen in the table

Gianvi[™] (drospirenone and ethinyl estradiol tablets) is different from other birth control pills because it contains • You have started having menstrual periods

A history of heart attack or stroke

• A history of blood clots in the legs (deep vein thrombosis), lungs (pulmonary embolism),

or eyes (retinal thrombosis Chest pain (angina pectoris)

• Known or suspected breast cancer or cancer of the lining of the uterus, cervix or vagina

• Yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during previous use of the pill or other

• Sudden severe headache or vomiting, dizziness or fainting, disturbances of vision or speech, weakness, or numbness in an DAY 1 START: Liver tumor (benian or cancerous)

• Heart valve or heart rhythm disorders that may be associated with formation of blood clots

 Severe high blood pressure A need for surgery with prolonged bedrest

Adrenal Disease

4. Liver Tumors

\2\ Deaths are method-relate

Potassium-sparing diuretics (spironolactone and others)

Use | • Aldosterone antagonists

t	ne First Year of Use	at One Year ³	OTHER CONSIDERATIONS BEFORE TAKING ORAL CONTRACEPTIVES
	Perfect Use ² (3)	(4)	Tell your healthcare provider if you have or ever had:
			Breast nodules, fibrocystic disease of the breast, an abnormal breast X-ray or mammogram
	85		Diabetes
	6	40	Elevated cholesterol or triglycerides
		63	High blood pressure
	Q	55	A blood test indicating a higher risk of having blood clots
	3		Migraine or other headaches or epilepsy
_	0		Mental depression
-	۷		Gallbladder, heart or kidney disease
_	1		History of scanty or irregular menstrual periods
_	4		Women with any of these conditions should be checked often by their healthcare provider if they choose to use oral contraceptives.
			Also, be sure to inform your doctor or healthcare provider if you smoke, are on any medications, recently had a baby or
	26	42	miscarriage, or are breast feeding.
	9	56	RISKS OF TAKING ORAL CONTRACEPTIVES
			1. Risk of Developing Blood Clots

Blood clots and blockage of blood vessels are the most serious side effects of taking oral contraceptives and can be fatal. In particular, a clot in the legs (deep vein thrombosis) can cause pain and swelling, and a clot that travels to the lungs can cause sudden blocking of the vessel carrying blood to the lungs. Rarely, clots occur in the blood vessels of the eye and may cause blindness, double vision, or impaired vision. If you take oral contraceptives and need elective surgery, need to stay in bed for a prolonged illness or have recently delivered a baby, you may be at risk of developing blood clots. You should consult your doctor about stopping oral contraceptives three to four weeks before surgery and not taking oral contraceptives for two weeks after surgery or during bed rest. You should also not take oral contraceptives

songlety and not admit got a contraceptives of two weeks are surgery of uning year less. To should not take or an other contraceptives or son after delivery of a baby or a mid-trimester pregnancy loss or termination. It is advisable to wait for at least four to six weeks after delivery if you are not breast feeding. If you are breast feeding, you should wait until you have weaned your child before using the pill. (See also the section on Breast Feeding in GENERAL PRECAUTIONS.) 2. Heart Attacks and Strokes Oral contraceptives may increase the tendency to develop strokes (stoppage or rupture of blood vessels in the brain) and angina pectoris and heart attacks (blockage of blood vessels in the heart). Any of these conditions can cause death or serious disability.

contraceptives greatly increase the chances of developing and dying of heart disease. 3. Gallbladder Disease Dral contraceptive users probably have a greater risk than nonusers of having gallbladder disease, although this risk may be related to pills containing high doses of estrogens

e cases, oral contraceptives can cause benign but dangerous liver tumors. These benign liver tumors can rupture and cause fatal ternal bleeding. In addition, a possible but not definite association has been found with the pill and liver cancers in two studies, in which a few women who developed these very rare cancers were found to have used oral contraceptives for long periods. However, iver cancers are extremely rare. The chance of developing liver cancer from using the pill is thus even rarer. 5. Cancer of the Reproductive Organs and Breasts

by at least 75%.9

Various studies give conflicting reports on the relationship between breast cancer and oral contraceptive use. Oral contraceptive use of having breast cancer diagnosed, particularly after using hormonal contraceptives at a younger age. After Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Guest F, Kowal D, you stop using hormonal contraceptives, the chances of getting breast cancer begin to go back down. You should have regular breast younger age. After Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Guest F, Kowal D, you stop using hormonal contraceptives, the chances of getting breast cancer begin to go back down. You should have regular breast cancer begin to go back down. You should have regular breast cancer begin to go back down. You should have regular breast cancer begin to go back down. You should have regular breast on the proposal breast of the proposal breast cancer begin to go back down. You should have regular breast on the proposal breast cancer begin to go back down. You should have regular breast on the proposal breast cancer begin to go back down. You should have regular breast on the proposal breast of the proposal breast cancer begin to go back down. You should have regular breast on the proposal breast of the examinations by a healthcare provider and examine your own breasts monthly. Tell your healthcare provider if you have a family history of 3 PACKS OF PILLS.

ESTIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY

Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year.

Among couples attempting to avoid pregnancy are associated with a risk of developing certain diseases, which may lead to disability
The percents becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cases using contraception in order to become pregnants with one year. This actimate use lowered libebtu (8° 25°) to repost the control and pregnancy are associated with different methods of birth control and pregnancy has been products such as \$Y. John's Wort, your pills may not work as well.

Is a hack-up method (such as condance or pregnants).

SETIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY

All methods of birth control and pregnancy are associated with a risk of developing certain diseases, which may lead to disability or death. An estimate of the number of deaths associated with different methods of birth control and pregnancy has been products such as \$Y. John's Wort, your pills may not work as well.

SETIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY

All methods of birth control and pregnancy are associated with different methods of birth control and pregnancy has been products such as \$Y. John's Wort, your pills may not work as well.

SETIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY

All methods of birth control and pregnancy are associated with different methods of birth control and pregnancy are associated with different methods of birth control and pregnancy are associated with different methods of birth control and pregnancy are associated with a risk of developing certain diseases, which may lead to disability or death. An estimate of the number of deaths associated with different methods of birth control and pregnancy are associated with different methods of birth control and pregnancy are associated with different m

loned	100,000 NONSTERILE WOMEN, BY FERTILITY-CONTROL METHOD ACCORDING TO AGE							
n the	Method of Control and Outcome	15 to 19 years	20 to 24 years	25 to 29 years	30 to 34 years	35 to 39 years	44	
	No fertility control methods\1\	7	7.4	9.1	14.8	25.7		
	Oral contraceptives non-smoker \2\	0.3	0.5	0.9	1.9	13.8		
e first ective ose is	Oral contraceptives smoker \2\	2.2	3.4	6.6	13.5	51.1	1	
	IUD \2\	0.8	0.8	1	1	1.4		
	Condom \1\	1.1	1.6	0.7	0.2	0.3		
	Diaphragm/spermicide \1\	1.9	1.2	1.2	1.3	2.2		
on as	Periodic abstinence \1\	2.5	1.6	1.6	1.7	2.9		

Adapted from H.W. Ory, Family Planning Perspectives, 15:57-63, 1983. In the above table, the risk of death from any birth control method is less than the risk of childbirth, except for oral contraceptive that for women aged 15 to 39, the risk of death was highest with pregnancy (7 to 26 deaths per 100,000 women, depending on age). Among pill users who do not smoke, the risk of death was always lower than that associated with pregnancy for any age group, except for those women over the age of 40, when the risk increases to 32 deaths per 100,000 women, compared to .8 associated with pregnancy at that age. However, for pill users who smoke and are over the age of 35, the estimated number of deaths exceeds those for other methods of birth control. If a woman is over the age of 40 and smokes, her estimated risk

(drospirenone and ethinyl estradiol tablets)

f death is four times higher (117/100,000 women) than the estimated risk associated with pregnancy (28/100,000 women) The suggestion that women over 40 who do not smoke should not take oral contraceptives is based on information from olde high-dose pills and on less-selective use of pills than is practiced today. An Advisory Committee of the FDA discussed this issue in 1989 and recommended that the benefits of oral contraceptive use by healthy, non-smoking women over 40 years of age may outweigh the possible risks. However, all women, especially older women, are cautioned to use the lowest-dose pill

that is effective WARNING SIGNALS

If any of these adverse effects occur while you are taking oral contraceptives, call your doctor immediately • Sharp chest pain, coughing of blood, or sudden shortness of breath (indicating a possible clot in the lung) Pain in the calf (indicating a possible clot in the leg)

arm or leg (indicating a possible stroke) • Sudden partial or complete loss of vision (indicating a possible clot in the eye) Breast lumps (indicating possible breast cancer or fibrocystic disease of the breast; ask your doctor or healthcare provider to

show you how to examine your breasts) Severe pain or tenderness in the stomach area (indicating a possibly ruptured liver tumor) 2. Use another method of hirth control (such as condoms or spermicides) as a back-up method if you have sex anytime from the Sunday

• Difficulty in sleeping, weakness, lack of energy, fatigue, or change in mood (possibly indicating severe depression) . Jaundice or a light yellowing of the skin or eyeballs, accompanied frequently by fever, fatigue, loss of appetite, dark-colored urine, or -colored bowel movements (indicating possible liver problems)

SIDE EFFECTS OF ORAL CONTRACEPTIVES

5. Other Side Effects

HOW TO TAKE THE PILL

IMPORTANT POINTS TO REMEMBE

REFORE YOU START TAKING YOUR PILLS

In what order to take the pills (follow the arrows) 3) The week numbers are shown on the blister card picture below

Crushing chest pain or heaviness in the chest (indicating a possible heart attack)

I. Vaginal Bleeding rregular vaginal bleeding or spotting may occur while you are taking the pills. Irregular bleeding may vary from slight staining between WHAT TO DO DURING THE MONTH megual vagnial becausing or sporting may occur while you are taking the pins. Tregular because may any normalism advisors most often during the menstrual periods to breakthrough bleeding, which is a flow much like a regular period. Irregular bleeding occurs most often during the first few months of oral contraceptive use, but may also occur after you have been taking the pill for some time. Such bleeding may be emporary and usually does not indicate any serious problems. It is important to continue taking your pills on schedule. If the bleeding

ral contraceptives may cause edema (fluid retention) with swelling of the fingers or ankles and may raise your blood pressure.

2. You do not need to use a back-up birth control method if you have sex. If you experience fluid retention, contact your doctor or healthcare provider spotty darkening of the skin is possible, particularly of the face.

side effects may include nausea, vomiting, change in appetite, headache, nervousness, depression, dizziness, loss of 3. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use another birth control scalp hair, rash, and vaginal infections

If any of these side effects bother you, call your doctor or healthcare provide GENERAL PRECAUTIONS
1. Missed Periods and Use of Oral Contraceptives Before or During Early Pregnancy

1. Missed Periods and Use of Oral Contraceptives Before or During Early Pregnancy
There may be times when you may not menstruale regularly after you have completed taking a cycle of pills. If you have taken your pills regularly and miss one menstrual period, continue taking your pills for the next cycle but be sure to inform your healthcare provider. If you have not taken the pills daily as instructed and missed a menstrual period, or if you missed two consecutive menstrual periods, you may be pregnant. Check with your healthcare provider immediately to determine the office taking and consecutive menstrual periods, you may be pregnant. Check with your healthcare provider immediately to determine the determined that the consecutive menstrual periods, you may be pregnant. Check with your healthcare provider immediately to determine the determined to the provider of the pack and start a new pack of pills that same day.

2. You COULD BECOME PREGNANT if you have sex in the 7 days after you restart your pills. You MUST use another birth control method (such as condoms or spermicide) as a back-up for those 7 days.

two consecutive menstrual periods, you may be pregnant. Check with your healthcare provider immediately to determine whether you are pregnant. Stop taking oral contraceptives if pregnancy is confirmed. There is no conclusive evidence that oral contraceptive use is associated with an increase in birth defects when taken inadvertently during early pregnancy. Previously, a few studies had reported that oral contraceptives might be associated with birth defects, but these studies have not been confirmed. Nevertheless, oral contraceptives should not be used during pregnancy. You should check with your doctor about risks to your unborn child of any medication taken during pregnancy.

2 While Breast Feeding

contraceptives while breast feeding. You should use another method of contraception since breast feeding provides only partial method (such as condoms or spermicides) as a back-up for those 7 days ordection from becoming pregnant, and this partial protection decreases significantly as you breast feed for longer periods of time.

3. You may not have your period this month but this is expected. However, if you miss your period two months in a row, call your If you are scheduled for any laboratory tests, tell your doctor you are taking birth control pills. Certain blood tests may be affected by birth control pills.

• THROW AWAY the pills you missed.

4. Drug Interactions 4. Drug Interactions
Certain drugs may interact with birth control pills to make them less effective in preventing pregnancy or cause an increase in breakthrough bleeding. Such drugs include rifampin, drugs used for epilepsy such as barbiturates (for example, phenobarbital) and phenytoin (Dilantin is one brand of this drug), phenylbutazone (Butazolidin is one brand) and possibly certain antibiotics. Herbal products containing St. John's Wort (hypericum perforatum) may reduce the effectiveness of oral contraceptives. This may also such as a products containing St. John's Wort (hypericum perforatum) may reduce the effectiveness of oral contraceptives. This may also such as a products containing St. John's Wort (hypericum perforatum) may reduce the effectiveness of oral contraceptives. This may also such as a product of the product of th result in breakthrough bleeding. You may need to use an additional method of contraception during any cycle in which you take drugs

PREGNANCY AFTER STOPPING THE PILL that can make oral contraceptives less effective (See BOLDED TEXT AT BEGINNING).

5. Sexually Transmitted Diseases pectors and heart attacks (blockage of blood vessels in the heart). Any of these conditions can cause death or serious disability.

Smoking greatly increases the possibility of suffering heart attacks and strokes. Furthermore, smoking and the use of oral other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against transmission of HIV (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

There does not protect against transmission of HIV (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis. NSTRUCTIONS TO PATIENTS

> 1 BE SLIBE TO BEAD THESE DIRECTIONS Before you start taking your pills. Anytime you are not sure what to do

2. THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME. GIANVI™ TABLETS CAN BE TAKEN WITHOUT

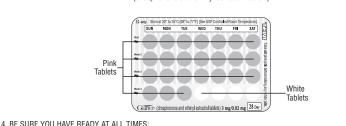
If you do have spotting or light bleeding or feel sick to your stomach, do not stop taking the pill. The problem will usually go away. If it In addition to preventing pregnancy, use of oral contraceptives may provide certain benefits. They are: does not go away, check with your healthcare provider. 4. MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING, even when you make up these missed pills.

On the days you take two pills, to make up for missed pills, you could also feel a little sick to your stomach.

6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your healthcare provider about how to make pill-taking easier about using another method of birth control 7. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your healthcare provider.

CIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL. It is important to take Gianvi tablets at about the same time every day. Gianvi tablets can be taken without regard to meals. 2. LOOK AT YOUR PILL PACK: - IT HAS 28 PILLS

The Gianvi tablets-pill pack has 24 pink "active" pills (with hormones) to be taken for 24 days, followed by 4 white "reminder" KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN. pills (without hormones) to be taken for four days. 3. ALSO FIND: 1) Where on the pack to start taking pills.



ANOTHER KIND OF BIRTH CONTROL (such as condoms or spermicides) to use as a back-up in case you miss pills. AN EXTRA FIII PIII PACK

Gianvi™

(drospirenone and ethinyl estradiol tablets

WHEN TO START THE FIRST PACK OF PILLS

You have a choice for which day to start taking your first pack of pills. Decide with your healthcare provider which is the best day for you. Pick a time of day, which will be easy to remember. . Take the first pink "active" pill of the first pack during the first 24 hours of your period. 2. You will not need to use a back-up method of birth control, since you are starting the pill at the beginning of your period.

SUNDAY START: Take the first pink "active" pill of the first pack on the *Sunday after your period starts*, even if you are still bleeding. If your period

WHEN YOU SWITCH FROM A DIFFERENT BIRTH CONTROL PILL

birth control pill would have been started. 1. TAKE ONE PILL AT THE SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY

Do not skip pills even if you are spotting or bleeding bet Do not skip pills even if you do not have sex very often. 2. WHEN YOU FINISH A PACK OF PILLS:

. Take it as soon as you remember. Take the next pill at your regular time. This means you may take two pills in one day.

If you MISS 2 pink "active" pills in a row in WEEK 1 OR WEEK 2 of your pack: 2 Then take one nill a day until you finish the nack

method (such as condoms or spermicides) as a back-up for those 7

with any of these conditions should be checked often by their healthcare provider if they choose to use oral contraceptives.

2. While Breast reguing

If you are a Sunday Starter:

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If you are breast feeding, consult your doctor before starting oral contraceptives. Some of the drug will be passed on to the child in the milk. A few adverse effects on the child have been reported, including light yellowing of the skin (jaundice) and breast leading, or are breast feeding.

If you are a Sunday Starter:

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Keep taking 1 pill every day until Sunday. On Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day. enlargement. In addition, oral contraceptives may decrease the amount and quality of your milk. If possible, do not use oral enlargement. In addition, oral contraceptives may decrease the amount and quality of your milk. If possible, do not use oral enlargement. In addition, oral contraceptives may decrease the amount and quality of your milk. If possible, do not use oral enlargement. In addition, oral contraceptives.

If you MISS ANY of the 4 white "reminder" pills in WEEK 4

Keep taking one pill each day until the pack is empty

here may be some delay in becoming pregnant after you stop using oral contraceptives, especially if you had irregular nenstrual cycles before you used oral contraceptives. It may be advisable to postpone conception until you begin menstruating

of drospirenone and ethinyl estradiol tablets may cause nausea and withdrawal bleeding in females and may increase blood levels of otassium or decrease blood levels of sodium, which could be dangerous. In case of overdosage, contact your healthcare provider OTHER INFORMATION r healthcare provider will take a medical and family history before prescribing gral contracentives and will examine you. The

hysical examination may be delayed to another time if you request it and the healthcare provider believes that it is appropriate to postpone it. You should be re-examined at least once a year. Be sure to inform your healthcare provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your healthcare provider, because this is a time to determine if there are early signs of side effects of oral contraceptive u Do not use the drug for any condition other than the one for which it was prescribed. This drug has been prescribed specifically for you; do

Menstrual cycles may become more regular.

HEALTH BENEFITS FROM ORAL CONTRACEPTIVES

Oral contraceptive use may provide some protection against developing two forms of cancer: cancer of the ovaries and cancer of the lining of the uterus.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 *Other trademarks are the properties of their respective owners

Pomona, NY 10970

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tart the next pack on the day after your last white "reminder" pill. Do not wait any days between packs.

othly periods or feel sick to your stomach (nausea)

If you MISS 2 pink "active" pills in a row in WEEK 3 or WEEK 4 of your pack: 1. If you are a Day 1 Starter THROW OUT the rest of the pill pack and start a new pack that same day.

There does not appear to be any increase in birth defects in newborn babies when pregnancy occurs soon after stopping the pill.

rious ill effects have not been reported following ingestion of large doses of other oral contraceptives by young children. Overdosagi

• Blood flow during menstruation may be lighter and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.

· Acute pelvic inflammatory disease may occur less frequently.

If you want more information about birth control pills, ask your doctor or pharmacist. They have a more technical leaflet called the