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Documentation of Contraception and Pregnancy When Prescribing Potentially Teratogenic Medications for Reproductive-Age Women

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Abstract

Background—Certain medications are identified by the U.S. Food and Drug Administration (FDA) as class D or X because they increase the risk for birth defects if used during pregnancy.

Objective—To assess pregnancy rates and the frequency of contraceptive counseling documented with prescriptions for class D or X drugs filled by women of reproductive age.

Design—Description of prescriptions filled in 2001.

Setting—A large health maintenance organization in northern California in 2001.

Patients—488 175 women age 15 to 44 years who filled a total of 1 011 658 class A, B, D, or X prescriptions.

Measurements—Medications dispensed, contraceptive counseling, and pregnancy testing.

Results—A class D or X prescription was filled by 1 of every 6 women studied. Women who filled a prescription for class D or X medications were no more likely than women who filled prescriptions for safer, class A or B medications to have received contraceptive counseling, filled a contraceptive prescription, or been sterilized (48% vs. 51% of prescriptions). There was little variation by clinical indication in rates of contraceptive counseling with class D or X prescriptions, except for isotretinoin. Women who filled a class D or X prescription were only slightly less likely to have a pregnancy

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documented within 3 months than women filling a class A or B prescription (1.0% vs. 1.4% of prescriptions).

Limitations—International Classification of Diseases, Ninth Revision, codes underestimate contraceptive counseling. Documentation of a positive pregnancy test after filling a prescription may overestimate medication use in early pregnancy. Women who filled several prescriptions are overrepresented in prescription analyses.

Conclusion—Prescriptions for potentially teratogenic medications are frequently filled by women of childbearing age without documentation of contraceptive counseling.

Use of medications that can cause birth defects is at times necessary in the treatment of reproductive-age women. With concurrent use of contraception, the risk for birth defects associated with teratogenic medications can be substantially reduced. To increase awareness among women and clinicians of the adverse pregnancy outcomes associated with use of certain medications, the U.S. Food and Drug Administration (FDA) instituted a system to classify drugs into 5 categories. Class A and B medications are those for which there is no evidence of fetal harm in humans. Class C designates drugs for which adequate studies are not available. Classes D and X are used to identify potentially teratogenic medications. Specifically, a class D medication is a drug for which there is evidence of fetal risk but “the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks” (1). Class X medications are “contraindicated in women who are or may become pregnant” (1).

In the United States, women of reproductive age receive 11.7 million prescriptions for potentially teratogenic class D or X medications each year (2). Unfortunately, fewer than 20% of women using these medications receive contraceptive counseling during ambulatory care visits (2), and approximately 6% of U.S. pregnancies are exposed to potentially teratogenic class D or X medications (3,4). In some cases, women choose to terminate pregnancies exposed to teratogens, even when the absolute risk for a defect is low (5–7). Thus, inadvertent exposure to a potential teratogen may cause hardship even when it does not result in the birth of an affected child.

Our study was designed to estimate whether rates of pregnancy after a prescription for a potentially teratogenic class D or X medication was filled differed from those after a prescription for a safer class A or B drug. We examined documentation of contraceptive counseling, use of contraception, and history of sterilization among 488 175 women of reproductive age who received health care and prescription medications from a large health maintenance organization in northern California.

Methods

We conducted a retrospective cohort study using health care databases of women who were between 15 and 44 years of age and had continuous membership and pharmacy benefits with Kaiser Permanente Northern California, Oakland, California, during 2001. Kaiser Permanente Northern California, the largest health maintenance organization in northern California, has many facilities in 12 locations and serves approximately one third of the region's population. An estimated 96% of Kaiser Permanente members have pharmacy benefits that give them a financial incentive to fill prescriptions at a Kaiser Permanente pharmacy (8). This study was approved by the institutional review boards of the Kaiser Foundation Research Institute and the University of Pittsburgh.

We abstracted data from the Kaiser Permanente Northern California Pharmacy Information Management System related to class D and X medications that were prescribed and filled by women at Kaiser Permanente Northern California pharmacies during 2001. We excluded

prescriptions that patients never picked up and were thus returned to stock. In addition, we excluded medications (such as angiotensin-converting enzyme inhibitors) that were labeled class B or C if used in the first trimester, even if they were labeled class D or X if used in the second or third trimesters. We excluded contraceptive medications from the class D or X medications that we considered potentially teratogenic (9). Three sources were consulted to confirm FDA classification for each medication (10–12). When there was no consensus across all 3 sources in risk classification for first-trimester exposure, we classified the medication according to the highest risk estimate given by any of the 3 sources. For purposes of comparison, we also abstracted data about prescription episodes involving class A and B medications that are considered safe for use during pregnancy. The Appendix Table (available at www.annals.org) shows class A, B, D, and X medications included in this analysis.

We identified all contraceptive prescriptions filled by Kaiser Permanente Northern California pharmacies in 2001 by using the Pharmacy Information Management System databases. In addition, we reviewed the Outpatient Services Clinical Record System for evidence of insertion of an intrauterine contraceptive device in the previous 10 years, placement of a contraceptive implant in the previous 5 years, or diaphragm or cervical cap fitting in the previous 2 years. We searched admission, discharge, and transfer and alliance hospital databases for information indicating whether a sterilization procedure (for example, hysterectomy or tubal ligation) had been performed between 1985 and 2001 by a Kaiser Permanente Northern California physician or an affiliated hospital.

We considered a woman to be using contraception while taking a class A, B, D, or X medication if we found evidence of any of the following: the woman filled a prescription for contraceptive pills, patches, rings, or injections in the 3 months before the date on which she filled a prescription; she was fitted for a diaphragm or cervical cap in the previous 2 years; she had a contraceptive implant inserted in the previous 5 years; she had an intrauterine contraceptive device inserted in the previous 10 years; or she had sterilization (by hysterectomy or tubal ligation) between 1985 and 2001. We categorized the contraceptive methods into 3 groups: most effective (intrauterine devices, contraceptive implants, and surgical sterilization), highly effective (contraceptive pills, patches, rings, and injections), and moderately effective (diaphragms and cervical caps). In addition, because women who received contraceptive counseling at the time they were given a prescription for a class A, B, D, or X medication may have had some delay in obtaining the prescription, we considered contraceptive prescriptions filled in the following 3 months to indicate that a clinician had attempted to ensure concurrent use of contraception.

We considered a woman to have received contraceptive counseling if we found evidence of any of the following: She was practicing contraception (including having been surgically sterilized), as defined above; the Outpatient Services Clinical Record System showed that she received contraceptive counseling, oral contraceptive management, or family planning counseling (as indicated by an International Classification of Diseases, Ninth Revision, code V2541, V258, or V2509) in the 2 years before the date on which the class A, B, D, or X prescription was filled; or the Outpatient Services Clinical Record System showed that she was given a prescription for emergency contraception or a contraceptive agent or device, regardless of whether she filled the prescription.

To identify results of any pregnancy tests that were performed within 3 months of a woman filling a prescription for a class A, B, D, or X medication, we searched Kaiser Permanente Northern California laboratory databases.

Context

Many women of childbearing age receive prescriptions for potentially teratogenic drugs.

Contribution

In this review of administrative data from a large health maintenance organization in 2001, prescriptions for class D or X drugs were no more likely to be accompanied by documented claims for contraceptive services or for a subsequent pregnancy than were prescriptions for class A or B drugs.

Cautions

This study may overestimate the frequency of inadequate contraceptive counseling because the researchers did not have access to data about a patient's sexual activity or fertility potential, or about contraceptive advice that did not result in an administrative claim.

Implication

There is probably room for improvement in contraceptive counseling for women who receive prescriptions for potentially teratogenic drugs.

To explore whether clinician characteristics may have influenced the frequency with which contraceptive counseling was provided, we abstracted data on clinician training and specialty from employee databases compiled at the time clinicians joined the Permanente Medical Group.

We tabulated information about prescription of medications of different FDA classes, receipt of contraceptive counseling, use of contraceptive methods, and positive pregnancy test results. We measured the proportion of prescription episodes in which women who were using specific classes of drugs were also using contraception or had received contraceptive counseling. We expected rates of contraceptive counseling to be higher with the prescription of class D or X drugs (potentially teratogenic medications) than with the prescription of class A or B drugs (safer medications). Although we recognized that underreporting of contraceptive counseling might occur, we expected it to occur nondifferentially with respect to FDA medication class.

We conducted 3 parallel sets of analyses. In the first, the unit of analysis was the prescription episode. To address concerns that women who filled several prescriptions may be overrepresented in analyses of prescription episodes, we conducted a second analysis of prescription episodes that was limited to women who filled only 1 prescription in 2001. In the third analysis, the unit of analysis was each woman. In this analysis, women who filled both high-risk (class D or X) and low-risk (class A or B) prescriptions were categorized as having filled a high-risk prescription and were excluded from the comparison group, which included women who filled only prescriptions considered safe for use during pregnancy. In the per-woman analysis, we examined whether women had documented use of contraception at the time all prescriptions were filled, had documented use of contraception at the time some (but not all) prescriptions were filled, had received contraceptive counseling but had no documented use of contraception, or had no documented receipt of contraceptive counseling.

For all analyses, we used SAS, version 9.1 (SAS Institute, Cary, North Carolina).

Role of the Funding Sources

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manuscript. Dr. Schwarz was supported in part by a career development award from the National Institute of Child Health and Development.

Result

In 2001, 488 175 women of reproductive age had continuous membership and uninterrupted Kaiser Permanente pharmacy benefits with Kaiser Permanente Northern California. Many women (47%) had continuous membership with Kaiser Permanente Northern California for 5 years or more, and 29% had continuous membership for 10 years or more (1991–2000). At least 1 prescription for class D or X medication was filled by 77 378 of these women. In total, these women filled 801 354 prescriptions for class A or B medications, 177 663 prescriptions for class D medications, and 32 641 prescriptions for class X medications at Kaiser Permanente Northern California pharmacies (Table 1). The median number of class D or X prescriptions filled by women of reproductive age was 1 (range, 1 to 89; mean, 2.7); 96% of women filled fewer than 10 class D or X prescriptions in 2001. An additional 15 803 prescriptions for angiotensin-converting enzyme inhibitors were excluded from this analysis because they were not labeled class D or X if used in the first trimester, although more recent data indicate an increased risk for major congenital malformations with first-trimester use of angiotensin-converting enzyme inhibitors (13).

During the year, 9040 clinicians prescribed 1 or more class D or X medications. The median number of these potentially teratogenic medications prescribed by a clinician was 4 (range, 1 to 882; mean, 23). Internists and family practitioners prescribed the largest proportion (48%) of class D and X medications to women of childbearing age. Psychiatrists, dermatologists, obstetrician-gynecologists, and pediatricians prescribed 15%, 12%, 6%, and 3%, respectively.

Many women who filled class D (52% of prescriptions, 48% of women) or X (51% of prescriptions, 47% of women) medications in 2001 had no contraceptive method dispensed, had not been sterilized, and had no documentation of contraceptive counseling in the 2 years before filling a potentially teratogenic prescription.

Among class D or X medications other than isotretinoin, there was little variation in documentation of contraception by clinical indication. Prescriptions for statins were least likely to have documentation of contraception use, sterilization, or contraceptive counseling (Table 2).

Of women who were using contraception at the time they filled a class D or X prescription, the types most commonly used were oral contraceptive pills (used with 20% of class D and 21% of class X prescription) and surgical sterilization (used with 11% of class D and 15% of class X prescription). The contraceptives least commonly used by women in this sample were intrauterine devices (2.2% and 1.7%, respectively), medroxyprogesterone injections (2.4% and 1.9%, respectively), and contraceptive implants (0.3% and 0.2%, respectively). Women who filled a class D or X prescription were not more likely than women who filled a class A or B prescription to have recently filled a contraceptive prescription or to have previously been sterilized (37.0% vs. 39.4% of prescriptions). Women who filled a class D or X prescription had the same likelihood as women who filled class A or B prescriptions to have no documented receipt of contraceptive counseling (47.6% vs. 47.0% of women). However, women who filled only 1 prescription were more likely to have documentation of contraceptive counseling if the prescription was for a class D or X medication rather than a class A or B medication (53.2% vs. 48.4% of women).

Women who filled class D or X prescriptions were only slightly less likely than women who filled class A or B prescriptions to have a positive pregnancy test within 3 months after filling the prescription (Table 3). Among women who filled only 1 prescription, 1.64% of class D or

X prescriptions was followed by a positive pregnancy test, compared with 1.57% of class A or B prescriptions. Women who filled class D or X prescriptions and had documentation of any form of contraception were less likely than women who filled these prescriptions and had no documented use of contraception (but may have used condoms or natural family planning methods) have a positive pregnancy test result (0.8% vs. 1.1% of class D or X prescriptions filled). Prescriptions for class D or X medications filled by women who were using contraceptive methods of the highest efficacy (such as an intrauterine device, a contraceptive implant, or surgical sterilization) were least likely to have a positive pregnancy test within 3 months.

Discussion

Our examination of the prescription records of nearly half a million women of reproductive age showed that 1 of every 6 women (16%) filled a prescription for a class D or X medication at some point during 2001. Although these medications are potentially teratogenic, only half of prescriptions were accompanied by contraceptive counseling, and fewer than half were filled by women who had filled a contraceptive prescription or had been sterilized before they filled the potentially teratogenic prescription. Compared with prescriptions for class A and B medications, which are considered safer for use during pregnancy, prescriptions for class D and X medications were no more likely to be filled by women who had received contraceptive counseling, filled a contraceptive prescription, or been sterilized. There was little variation in documentation of contraceptive counseling by clinical indication, with the exception of prescriptions for isotretinoin. In addition, the proportion of prescriptions followed by documentation of a positive pregnancy test was similar among women who filled prescriptions for class A and B medications and those who filled prescriptions for class D and X medications.

Because provision of contraceptive counseling affects use of contraception (14), which in turn affects rates of unintended pregnancy (15), these findings suggest that policies that increase rates of contraceptive counseling and contraceptive use may be able to reduce the number of women who unintentionally become pregnant while using a class D or X medication. Our finding that prescriptions filled by women who used the most effective methods of contraception were least likely to have documentation of pregnancy within 3 months of filling a class D or X prescription may be a helpful finding for clinicians to emphasize when they talk with their patients about the risks and benefits of using potentially teratogenic medications. These findings may also be helpful for policymakers to consider when determining benefits to be included in health plans because coverage of contraceptive methods may affect women's choices about contraception (16) and associated rates of birth defects.

Our study supports previous work (2) in finding that women of childbearing age commonly use class D or X medications and (not uncommonly) become pregnant. Although we found that 1% of episodes in which women filled a class D or X prescription were followed by a positive pregnancy test recorded within 3 months, an estimated 6% of U.S. pregnancies are exposed to class D or X medications (3,4). Even though women using class D or X medications in this study were more likely to have received contraceptive counseling than women in a national study of use of potentially teratogenic medications (2), the fact that rates of pregnancy differed only slightly by pregnancy risk classification suggests that increasing use of more effective methods of contraception may be helpful in decreasing rates of unintended pregnancy among women using teratogenic medications.

While we recognize the shortcomings of the current FDA risk classification (17,18) and opinions differ about what level of teratogenic risk requires the provision of contraceptive counseling, we believe that clinicians should engage women in shared decision making when potentially teratogenic medications are prescribed. Given the large number of women in our

study, we had to rely on available electronic databases for information about contraceptive counseling, contraception use, and pregnancy test results. These sources of information have several limitations that may overestimate the need for contraception and underestimate the provision of contraceptive counseling. First, we did not have information about the women's sexual orientation, desire to conceive, level of sexual activity, fertility, or partner's fertility. Thus, we may have overestimated the need for contraception. Second, some women may have begun using an intrauterine device, had a contraceptive implant, or undergone surgical sterilization before joining Kaiser Permanente Northern California. However, 47% of the women had continuous membership with Kaiser Permanente Northern California for 5 years or more before entering this study (1996–2000), and 29% had continuous membership for 10 years or more (1991–2000). Third, when prescription episodes are the unit of analysis, the contraceptive practices of women who filled several prescriptions may be overrepresented. Fourth, some women in our study may have obtained contraception from an outside pharmacy or may have used condoms for contraception. This may lead us to underestimate the use of contraception. However, because an estimated 15% of women who use condoms (and 25% of women who use periodic abstinence) will become pregnant each year (15), and because the risk for contraceptive failure is cumulative over time (19), we believe that more effective methods of contraception should be considered by all women who are using class D and X medications and, in particular, by women who have a chronic disease for which these drugs are prescribed on a long-term basis. Fifth, given the availability of home pregnancy tests, our study probably underestimates the number of pregnancy tests that were performed. Finally, pregnancy within 3 months of filling a class D or X prescription is a surrogate outcome that probably overestimates use of a potentially teratogenic medication during pregnancy and subsequent birth of an infant affected by use of a teratogenic medication.

Future research should include more detailed assessments of use of medication in early pregnancy. In addition, studies should address whether differences in use of contraception among women prescribed teratogenic medications result in different pregnancy outcomes (including abortion, obstetric complications, and congenital abnormalities).

Given that women of reproductive age commonly fill prescriptions for class D or X medications and half of the pregnancies in the United States are unintended (20), efforts to ensure the safe use of these medications are needed. Clinician education about teratogenic risks and contraceptive options must precede effective patient education, but refinements of health care delivery systems at both the clinic and pharmacy level are also needed. Because birth defects occur in 1% to 3% of U.S. offspring (21), health plan administrators and clinicians in all specialties should examine whether women whose medical conditions may benefit from use of class D and X medications are fully involved in the decision-making process and receive adequate preconception and contraceptive counseling.

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Table 1Women Who Filled Prescriptions in a Health Maintenance Organization in 2001^{*}

Prescriptions Filled, <i>n</i>	Class D Drug, <i>n</i> (%)	Class X Drug, <i>n</i> (%)	Class D or X Drug, <i>n</i> (%)	Class A or B Drug, <i>n</i> (%)
1	37 368 (53.9)	7080 (52.0)	39 577 (51.2)	100 765 (38.6)
2	11 596 (16.7)	2305 (16.9)	13 150 (17.0)	57 143 (21.9)
3	6427 (9.3)	1478 (10.9)	7525 (9.7)	33 720 (12.9)
≥4	13 956 (20.1)	2760 (20.3)	17 126 (22.1)	69 638 (26.7)

^{*} Results determined by U.S. Food and Drug Administration pregnancy risk classification and number of prescriptions filled.

Table 2
Documentation of Use of Contraception and Receipt of Contraceptive Counseling When Filling Prescriptions*

Class or Type of Medication [†]	Women Who Filled Prescriptions, %	Annual Prescription Rate per 100 Women	Prescriptions Accompanied by Documentation of Contraception, % [‡]		Prescriptions Filled without Concurrent Documentation of Use of Contraception, %	Prescriptions Filled without Concurrent Documentation of Use of Contraception or Recent Contraceptive Counseling, %
			Most Effective Method	Highly Effective Method		
Potential teratogens						
Class D	14.2	36.4	13	22	0.7	52
Class X	2.8	6.7	17	23	0.5	51
Class D or X used for specific clinical indications						
Antibiotics	7.4	11.6	9	28	0.6	49
Anticonvulsants	1.4	5.1	13	18	0.7	58
Antineoplastic agents	0.1	0.9	15	13	0.8	61
Antithyroid agents	0.1	0.3	9	17	1.6	54
Atenolol	1.4	3.9	18	16	0.5	57
Benzodiazepines	4.8	12.0	17	21	0.9	51
Immunologic agents	0.0	0.4	11	20	0.5	60
Isotretinoin	0.4	0.9	4	48	0.2	38
Nicotine	0.3	0.5	15	19	0.6	55
Psychiatric agents	1.0	3.0	14	26	0.8	49
Statins	0.5	1.5	17	13	0.2	63
Warfarin	0.1	0.5	18	12	1.2	57
Class A or B	53.5	164.2	13	26	0.6	49

* Results determined by medication and U.S. Food and Drug Administration pregnancy risk classification.

[†] Class A and B medications have no evidence of fetal harm in humans. Class D and X medications are potentially teratogenic. Antibiotics include doxycycline, tetracycline, and tobramycin. Anticonvulsants include carbamazepine, phenobarbital, phenytoin, primidone, secobarbital, and valproate. Benzodiazepines include alprazolam, clonazepam, diazepam, lorazepam, and temazepam. Psychiatric medications include imipramine, lithium, and nortriptyline. Statins include atorvastatin, fluvastatin, lovastatin, pravastatin, and simvastatin.

[‡] The most effective contraceptives are intrauterine devices, contraceptive implants, and surgical sterilization. Highly effective contraceptives include contraceptive pills, patches, rings, and medroxyprogesterone injections. Moderately effective contraceptives include diaphragms and cervical caps.

Table 3
Prescriptions with Documentation of a Positive Pregnancy Test within 3 Months*

Medication Class	Women Age 15–44 y		Women Age 15–24 y		Women Age 25–34 y		Women Age 35–44 y	
	Class A or B Drug (n = 201 243)	Class D or X Drug (n = 77 378)	Class A or B Drug (n = 56 905)	Class D or X Drug (n = 18 557)	Class A or B Drug (n = 64 516)	Class D or X Drug (n = 21 415)	Class A or B Drug (n = 79 822)	Class D or X Drug (n = 37 406)
All prescriptions	11 451/801 354 (1.4)	2002/210 304 (1.0)	3546/165 180 (2.2)	581/41 635 (1.4)	5716/232 968 (2.5)	944/52 037 (1.8)	2189/403 206 (0.5)	477/116 632 (0.4)
Prescriptions filled with documented use of any contraceptive method	3108/315 918 (1.0)	612/77 871 (0.8)	1301/65 047 (2.0)	259/14 901 (1.7)	1436/107 281 (1.3)	254/23 426 (1.1)	371/143 590 (0.3)	99/39 544 (0.3)
Prescription filled while using a most effective contraceptive method [†]	316/100 357 (0.3)	59/29 202 (0.2)	55/2207 (2.5)	13/496 (2.6)	202/23 657 (0.9)	31/5980 (0.5)	59/74 493 (0.1)	15/22 726 (0.1)
Prescription filled while using a highly effective contraceptive method [†]	2667/210 445 (1.3)	516/47 253 (1.1)	1221/62 453 (2.0)	241/14 298 (1.7)	1160/81 982 (1.4)	202/16 986 (1.2)	286/66 010 (0.4)	73/15 969 (0.5)
Prescription filled while using a moderately effective contraceptive method [†]	125/5116 (2.4)	37/1416 (2.6)	25/387 (6.5)	5/107 (4.7)	74/1642 (4.5)	21/460 (4.6)	26/3087 (0.8)	11/849 (1.3)
Prescriptions filled without documented use of contraception	8343/485 436 (1.7)	1390/132 433 (1.0)	2245/100 133 (2.2)	322/26 734 (1.2)	4280/125 687 (3.4)	690/28 611 (2.4)	1818/259 616 (0.7)	378/77 088 (0.5)
With documentation of contraceptive counseling	3901/97 081 (4.0)	656/22 671 (2.9)	1327/27 241 (4.9)	179/6034 (3.0)	1904/37 538 (5.1)	331/7615 (4.4)	670/32 302 (2.1)	146/9022 (1.6)
No documented contraceptive counseling	4442/388 355 (1.1)	734/109 762 (0.7)	918/72 892 (1.3)	143/20 700 (0.7)	2376/88 149 (2.7)	359/20 996 (1.7)	1148/227 314 (0.5)	232/68 066 (0.3)
Prescriptions filled by women	5502/201 243 (2.7)	1488/77 378 (1.9)	1704/56 905 (3.0)	445/18 557 (2.4)	2869/64 516 (4.5)	717/21 415 (3.4)	929/79 822 (1.2)	326/37 406 (0.9)

* Results determined by U.S. Food and Drug Administration pregnancy medication class. Data are expressed as the number (percentage) of prescriptions. Class A and B medications have no evidence of fetal harm in humans. Class D and X medications are potentially teratogenic. A class D medication is a drug for which there is evidence of fetal risk but the potential benefits of the drug in pregnant women may be acceptable despite its potential risks. Class X medications are defined as a drug that is contraindicated in women who are or may become pregnant.

[†] The most effective contraceptives are intrauterine devices, contraceptive implants, and surgical sterilization. Highly effective contraceptives include contraceptive pills, patches, rings, and medroxyprogesterone injections. Moderately effective contraceptives include diaphragms and cervical caps.

Appendix Table

Class A, B, D, and X Medications Prescribed to Study Participants (Women of Reproductive Age) during 2001

Categorized as class A in first trimester of pregnancy

Ascorbic acid
 Cholecalciferol
 Dihydrotachysterol
 Ergocalciferol
 Folic acid
 Folic acid/multivitamins
 Levothyroxine sodium
 Liothyronine sodium
 Liotrix
 Magnesium gluconate
 Niacin
 Niacinamide
 Prenatal vitamins/iron/folic acid
 Pyridoxine hydrochloride
 Thiamine hydrochloride
 Thyroid hormone
 Vitamin A
 Vitamin E

Categorized as class B in first trimester of pregnancy

Acarbose
 Acebutolol hydrochloride
 Acetaminophen
 Acyclovir
 Acyclovir sodium
 Alosetron hydrochloride
 Amiloride hydrochloride
 Amoxicillin trihydrate
 Amoxicillin trihydrate/K clavulanate
 Amphotericin B
 Amphotericin B lipid complex
 Ampicillin sodium
 Ampicillin trihydrate
 Ampicillin/sulbactam
 Azatadine maleate
 Azelaic acid
 Azithromycin
 Balsalazide disodium
 Brimonidine tartrate
 Bupropion hydrochloride
 Buspirone hydrochloride

Butenafine hydrochloride
Cabergoline
Caffeine citrated solution
Carbenicillin indanyl sodium
Cefaclor
Cefadroxil hydrate
Cefazolin 50 mg/mL super eye drops
Cefazolin fortified 50 mg/mL eye drops
Cefazolin sodium
Cefdinir
Cefixime
Cefotetan disodium
Cefpodoxime proxetil
Ceftazidime
Ceftizoxime sodium
Ceftriaxone sodium
Cefuroxime axetil
Cephalexin MH
Cetirizine hydrochloride
Chlorhexidine gluconate
Chlorhexidine gluconate/isopropanol
Chlorpheniramine maleate
Chlorthalidone
Cholestyramine/aspartame
Cholestyramine/sucrose
Ciclopirox olamine
Ciclopirox
Cimetidine
Cimetidine hydrochloride
Clemastine fumarate
Clindamycin 1% in Cetaphil moisturizing lotion (Galderma Laboratories, Fort Worth, Texas)
Clindamycin 2% in 70% isopropyl alcohol
Clindamycin 2% in Cetaphil moisturizing lotion (Galderma Laboratories, Fort Worth, Texas)
Clindamycin 2% in clotrimazole vaginal cream
Clindamycin 2% in Ionax astringent (Healthpoint, Fort Worth, Texas)
Clindamycin 2% solution
Clindamycin hydrochloride
Clindamycin palmitate
Clindamycin phosphate
Clopidogrel bisulfate
Clotrimazole
Clotrimazole 3% topical solution
Clozapine
Colestipol hydrochloride

Cromolyn powder/acid mantle cream
Cromolyn sodium
Cyclobenzaprine hydrochloride
Cyproheptadine hydrochloride
Desmopressin acetate
Dexchlorpheniramine maleate
Diclofenac potassium
Diclofenac sodium
Dicloxacillin sodium
Dicyclomine hydrochloride
Didanosine
Diethylpropion hydrochloride
Diphenhydramine hydrochloride
Dipivefrin-Q6JX
Dipyridamole
Doxercalciferol
Enoxaparin sodium
Erythromycin base
Erythromycin base/ethyl alcohol
Erythromycin estolate
Erythromycin ethylsuccinate
Erythromycin stearate
Esomeprazole mag trihydrate
Etanercept
Ethacrynic acid
Ethambutol hydrochloride
Famciclovir
Famotidine
Fenoprofen calcium
Flavoxate hydrochloride
Flurbiprofen
Flurbiprofen sodium
Glatiramer acetate
Glucagon
Glucagon, human recombinant
Glycopyrrolate
Granisetron hydrochloride
Guanfacine hydrochloride
Hydrochlorothiazide
Hydrochlorothiazide/amiloride hydrochloride
Hydromorphone hydrochloride
Ibuprofen
Indapamide
Indomethacin

Infliximab
Insulin glargine, human recombinant analog
Insulin lispro
Insulin neutral protamine Hagedorn human recombinant
Insulin regular human recombinant
Insulin regular human recombinant buffered
Ipratropium bromide
Kaopectate/diphenhydramine EL 1:1
Ketoprofen
Lactulose
Lansoprazole
Levocarnitine
Lidocaine 4% nasal spray
Lidocaine 5% in silver sulfadiazine cream
Lidocaine 5% ointment/orabase 1:1
Lidocaine hydrochloride (anesthetic)
Lidocaine hydrochloride
Lidocaine
Lidocaine/prilocaine
Lindane
Loperamide hydrochloride
Loracarbef
Loratadine
Magnesium sulfate
Maprotiline hydrochloride
Meclizine hydrochloride
Meperidine hydrochloride
Meropenem
Mesalamine
Metformin hydrochloride
Methadone hydrochloride
Methyldopa
Metoclopramide hydrochloride
Metolazone
Metronidazole
Metronidazole/sodium chloride
Miglitol
Montelukast sodium
Nafcillin sodium
Naftifine hydrochloride
Naproxen
Naproxen sodium
Nedocromil sodium
Nelfinavir mesylate

Nitrofurantoin
Nitrofurantoin macrocrystal
Nitrofurantoin/nitrofurantoin macro
Nizatidine
Octreotide acetate
Ondansetron
Ondansetron hydrochloride
Orlistat
Oxiconazole nitrate
Oxybutynin chloride
Oxycodone hydrochloride
Oxycodone hydrochloride/acetaminophen
Pantoprazole sodium
Paregoric
Pemoline
Penciclovir
Penicillin G benzathine
Penicillin G potassium
Penicillin G procaine/penicillin G potassium
Penicillin G sodium
Penicillin V potassium
Pentosan polysulfate sodium
Pergolide mesylate
Permethrin
Phenazopyridine hydrochloride
Pindolol
Piperacillin sodium
Piperacillin sodium/tazobactam sodium
Praziquantel
Probenecid
Rabeprazole sodium
Ranitidine hydrochloride
Rifabutin
Ritonavir
Saquinavir
Sildenafil citrate
Silver sulfadiazine
Sotalol hydrochloride
Spectinomycin hydrochloride
Sucralfate
Sulfasalazine
Sulindac
Tamsulosin hydrochloride
Tenofovir disoproxil fumarate

Terbinafine hydrochloride
Terbutaline sulfate
Tiagabine hydrochloride
Ticlopidine hydrochloride
Torsemide
Tranexamic acid 4.8% solution
Trastuzumab
Ursodiol
Valacyclovir hydrochloride
Vancomycin 25 mg/mL eye drops
Vancomycin hydrochloride
Zafirlukast
Zolpidem tartrate

Categorized as class D in first trimester of pregnancy

Alprazolam
Amikacin sulfate
Amiodarone hydrochloride
Amitriptyline hydrochloride/chlordiazepoxide
Anastrozole
Arsenic trioxide
Aspirin/meprobamate
Atenolol
Azathioprine
Belladonna alkaloids/phenobarbital
Bleomycin sulfate
Busulfan
Cadexomer iodine
Capecitabine
Carbamazepine
Carboplatin
Chlorambucil
Chlordiazepoxide hydrochloride
Cisplatin
Cladribine
Clidinium bromide/chlordiazepoxide
Clonazepam
Clorazepate dipotassium
Colchicine
Colchicine/probenecid
Cyclophosphamide
Cytarabine
Dactinomycin
Daunorubicin hydrochloride
Demeclocycline hydrochloride

Dexamethasone/diphenhydramine/nystatin/tetracycline solution
Dexamethasone/diphenhydramine/tetracycline 1:1:1
Diazepam
Divalproex sodium
Docetaxel
Doxorubicin hydrochloride liposome
Doxorubicin hydrochloride
Doxycycline calcium
Doxycycline hyclate
Doxycycline monohydrate
Epirubicin hydrochloride
Etoposide
Exemestane
Flutamide
Gemcitabine hydrochloride
Gentamicin 14 mg/mL eye drops
Gentamicin fortified eye drops
Gentamicin in Ocean Nasal Spray (Fleming Pharmaceuticals, Fenton, Missouri)
Gentamicin sulfate
Gentamicin sulfate/sodium chloride
Gentamicin sulfate/prednisolone acetate
Hydroxyurea
Idarubicin hydrochloride
Ifosfamide
Imatinib mesylate
Imipramine hydrochloride
Imipramine pamoate
Irinotecan hydrochloride
Letrozole
Lithium carbonate
Lorazepam
Mechlorethamine 0.01% (10 mg %) in Aquaphor (Beiersdorf AG, Hamburg, Germany)
Mechlorethamine hydrochloride
Meclofenamate sodium
Melfalan
Mephobarbital
Meprobamate
Mercaptopurine
Methimazole
Midazolam hydrochloride
Minocycline hydrochloride
Mitoxantrone hydrochloride
Neomycin sulfate
Nicotine

Nortriptyline hydrochloride
Oxazepam
Paclitaxel, semisynthetic
Pamidronate disodium
Penicillamine
Pentobarbital sodium
Phenobarbital
Phenytoin
Phenytoin sodium extended
Potassium iodide (for oral use)
Potassium iodide/iodine
Povidone–iodine
Povidone–iodine swabs
Primidone
Procarbazine hydrochloride
Propylthiouracil
Secobarbital sodium
Tamoxifen citrate
Temozolomide
Tetracycline hydrochloride
Tetracycline, nystatin, hydrocortisone mouthwash
Tetracycline, nystatin, hydrocortisone powder, water
Thioguanine
Tobramycin fortified ophthalmic drops
Tobramycin sulfate
Tobramycin sulfate/dexamethasone
Tobramycin/sodium chloride
Toremifene citrate
Tretinoin
Tretinoin A 0.05% cream/hydrocortisone 1% cream
Tretinoin
Valproic acid
Vinblastine sulfate
Vincristine sulfate
Vinorelbine tartrate

Categorized as class X in first trimester of pregnancy

Acitretin
Atorvastatin calcium
Bexarotene
Cerivastatin sodium
Danazol
Diclofenac sodium/misoprostol
Dienestrol
Dihydroergotamine mesylate

Ergotamine tartrate
Ergotamine tartrate/caffeine
Ergotamine/belladonna/phenobarbital
Estazolam
Finasteride
Fluorouracil
Fluoxymesterone
Flurazepam hydrochloride
Fluvastatin sodium
Goserelin acetate
Isotretinoin
Leflunomide
Leuprolide acetate
Leuprolide acetate 40 µg/0.2 mL
Lovastatin
Methotrexate 2.5 mg/mL solution
Methotrexate sodium
Methotrexate sodium/PF
Methyltestosterone
Methyltestosterone (compounded)
Methyltestosterone/estrogens, Esteri-G1BX
Misoprostol
Mitomycin
Mitomycin 0.02% ophthalmic solution
Oxandrolone
Pravastatin sodium
Quazepam
Quinine sulfate
Raloxifene hydrochloride
Ribavirin
Ribavirin/interferon ALFA-2B, recombinant
Simvastatin
Tazarotene
Temazepam
Testosterone
Testosterone 1% in Lidex ointment (Medicis, Scottsdale, Arizona)
Testosterone 1% in White petrolatum (Penreco, Dickinson, Texas)
Testosterone 2% in Aquaphor (Beiersdorf AG, Hamburg, Germany)
Testosterone 2% in Eucerin cream (Beiersdorf AG, Hamburg, Germany)
Testosterone 2% in Velvachol cream (DPT Laboratories, San Antonio, Texas)
Testosterone 2% in White petrolatum (Penreco, Dickinson, Texas)
Testosterone 3% in Velvachol cream (DPT Laboratories, San Antonio, Texas)
Testosterone 3% in White petrolatum (Penreco, Dickinson, Texas)
Testosterone cypionate

Testosterone enanthate

Testosterone in Aquaphor (Beiersdorf AG, Hamburg, Germany)

Testosterone in triamcinolone ointment

Testosterone in Velvachol cream (DPT Laboratories, San Antonio, Texas)

Thalidomide

Triazolam

Warfarin sodium