

Medicare Private Plans Under Pressure to Improve

BY JOEL B. FINKELSTEIN

Contributing Writer

WASHINGTON If competition drives prices down, why does the government pay private insurers more per patient than the Medicare program spends on an average beneficiary?

That was the question from a growing number of people, said panelists at a press briefing on health care costs sponsored by the Center for Studying Health System

Change. "A lot of folks are suffering from amnesia about this whole issue. In 2003, we passed something called the Medicare Modernization Act. . . . It was about how are we going to solve the baby boomer problem, how are we going to bring Medicare costs under control," said Robert Laszewski, president of a health policy and marketplace consulting firm in Alexandria, Va.

At the time, the Republican-led Congress decided that the best way to bring

costs under control was to encourage more Medicare beneficiaries to join private plans. So, depending upon which type of plan they offer, managed care companies receive 10%-20% above what Medicare spends on the average beneficiary in the fee-for-service system. This induces private insurers to offer managed Medicare products and enable them to offer more benefits to attract beneficiaries into the private plans, according to the philosophy behind the legislation.

It's 4 years later, and some are wondering what they are buying with the millions of extra dollars flowing to private insurers. Physicians on the government's Medicare Physician Advisory Commission (MedPAC) have called on Congress to redirect those funds toward other priorities, such as fixing the sustainable growth rate formula.

However, it may be too early to pull the plug on this experiment, said Christine Arnold, a managing director at Morgan Stanley who covers the managed care industry. "The managed care companies that I speak to say that they can reduce medical costs 10% for a managed product versus an unmanaged product, but it takes 2-4 years."

It is not just in the Medicare program that cost-saving techniques are being questioned. Health savings accounts and other consumer-driven approaches are losing favor with the public. The number of U.S. workers who enrolled in consumer-directed plans grew by a meager 300,000 between 2005 and 2006, according to the Kaiser

Family Founda-

tion's annual survey of employer benefits. A survey by America's Health Insurance Plans, a trade organization, confirms that trend. After a few years in which enrollment in health savings account-affiliated, high-deductible plans doubled and then tripled, last year the number of people in the plans grew by less than a third.

Consumer-directed plans may be a good idea, but they're based on the false assumption that patients have the resources to make the right choices, said Douglas Simpson, the senior managed care analyst at Merrill Lynch & Co.

"We're incentivizing them with the benefit structure, but then we're really not giving them the tools to make better decisions. It's sort of like giving somebody \$100 to go out to dinner and then not putting the prices on the menu," Mr. Simpson said.

The cyclical nature of health care reform also is becoming more apparent, said Joshua Raskin, who covers the managed care industry as a senior vice president at Lehman Brothers Inc. During the late 1980s and early 1990s, health care premiums grew by double digits, resulting in political backlash. Hillary Clinton's universal care plan further popularized health maintenance organizations. "HMOs had this huge period of proliferation and you got the cost trending down in the mid-1990s to. . . really low single digits," said Mr. Raskin. Then, the economy picked back up—along with medical costs—and double-digit growth returned. Now, the discussion is again focusing on "more government intervention. It's 2007 and 2008, and guess what: Hillary Clinton is back and so is universal health care."

YAZ® (drospirenone and ethinyl estradiol) Tablets

Brief Summary of Prescribing Information

CONTRAINDICATIONS: YAZ® should not be used in women who have the following: •Renal insufficiency •Hepatic dysfunction •Adrenal insufficiency •Thrombopilethris or thromboembolic disorders •A past history of deep-vein thrombopilethris or thromboembolic disorders •Cerebral-vascular or coronary-artery disease (see Part 1 of History) •Valvular heart disease with thrombotic complications •Severe hypertension •Diabetes with vascular involvement •Headaches with focal neurological symptoms •Major surgery with prolonged immobilization •Known or suspected carcinoma of the breast •Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia •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 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.

YAZ contains 3 mg of the progestin drospirenone that has antimineralocorticoid activity, including the potential for hyperkalemia in high-risk patients, comparable to a 25 mg dose of spironolactone. YAZ should not be used in patients with conditions that predispose to hyperkalemia (i.e., renal insufficiency, hepatic dysfunction and adrenal insufficiency). Women receiving daily, long-term treatment for chronic conditions or diseases with medications that may increase serum potassium should have their serum potassium level checked during the first treatment cycle. Medications that may increase serum potassium include ACE inhibitors, angiotensin II receptor antagonists, potassium-sparing diuretics, potassium supplementation, hepatic enzyme antagonists, and NSAIDs. 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 without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity and diabetes. 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 hormonal estrogens and progestagens than those in common use today. The effect of long-term use of oral contraceptives with lower hormonal estrogens and progestagens remains to be determined. However, this package insert contains epidemiologic studies reported are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of a disease, namely, a ratio of the incidence of a disease among oral contraceptive users to that among nonusers. The relative risk does not provide information on the actual clinical occurrence 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. 1. THROMBOEMBOLIC DISORDERS AND OTHER VASCULAR PROBLEMS: a. Myocardial infarction: An increased risk of myocardial infarction has been attributed to oral contraceptive use. This risk is primarily in smokers or 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 associated with circulatory disease have been shown to increase substantially in smokers over the age of 35 and nonsmokers over the age of 40 among women who use oral contraceptives. Oral contraceptives may compound the effects of well-known risk factors, such as hypertension, diabetes, hyperlipidemias, age and obesity. In particular, some progestagens are known to decrease HDL cholesterol and cause glucose intolerance, while estrogens may create a state of hyperinsulinism. Oral contraceptives have been shown to increase blood pressure among users (see section 9 in WARNINGS). Similar effects on risk factors have been associated with an increased risk of heart disease. Oral contraceptives must be used with caution in women with cardiovascular disease risk factors. b. Thromboembolism: An increased risk of thromboembolic and thrombotic disease associated with the use of oral contraceptives is well established. Case control studies have found the relative risk of users compared to nonusers to be 3 for the first episode of superficial venous thrombosis, 4 to 11 for deep vein thrombosis or pulmonary embolism, and 1.5 to 6 for women with predisposing conditions for venous thromboembolic disease. Cohort studies have shown the relative risk to be somewhat lower, about 1 for new cases and about 1.5 for recurrent cases. Myocardial infarction has been reported in women taking oral contraceptives in a study where overall mortality was not increased among users. The relative risk of cerebrovascular events has been reported to be similar to that of nonusers. However, both studies were performed with oral contraceptive formulations containing 50 micrograms or higher of estrogens. 2. ESTIMATES OF MORTALITY FROM CONTRACEPTIVE USE: One study gathered data from a variety of sources which have estimated the mortality rate associated with different methods of contraception at different ages. These estimates include the combined risk of death associated with contraceptive methods plus the risk 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 do not smoke, mortality associated with all methods of birth control is below that associated with childbirth. 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—but not reported until 1983. However, current clinical practice involves the use of lower estrogen dose formulations combined with careful restriction of oral contraceptive use to women who do not have the various risk factors listed in this labeling. Because of these changes in practice and also, because of some limited new data which suggest that the risk of cardiovascular disease with the use of oral contraceptives may now be less than previously observed, the Fertility and Maternal Health Drugs Advisory Committee was asked to review the topic in 1989. The Committee concluded that although cardiovascular disease risks may be increased with oral contraceptive use after age 40 in healthy nonsmoking 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. Therefore, the Committee recommended that the benefits of oral contraceptive use by healthy nonsmoking women over 40 may outweigh the possible risks. Of course, women of all ages who take oral contraceptives should take the lowest possible dose formulation that is effective. 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. Although the risk of having breast cancer diagnosed may be slightly increased among current and recent users of combined oral contraceptives (RR=1.24), this excess risk decreases over time after combination oral contraceptive use and is not statistically significant after 10 years after cessation of oral contraceptive use. 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 is women who first used oral contraceptives before age 20, but because breast cancer is so rare at these young ages, the number of cases attributable to this early oral contraceptive use is extremely small. Breast cancers diagnosed in current or previous OC users tend to be less clinically advanced than in never users. Women who currently have or have had breast cancer should not use oral contraceptives because breast cancer is a hormonally-sensitive tumor. Some studies suggest that oral contraceptive use has not 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. 4. HEPATIC NEOPLASIA: Benign hepatic adenomas are associated with oral contraceptive use, although the incidence of benign tumors is rare in the United States. Indirect calculations have estimated the attributable risk to be in the range of 3.3 cases/100,000 for users, a risk that increases after four or more years of use. Rupture of rare, benign, hepatic adenomas may cause death through intra-abdominal hemorrhage. Studies from Britain have shown an increased risk of developing hepatocellular carcinoma in long-term (≥8 years) oral contraceptive users. However, these cancers are extremely rare in the U.S. and the attributable risk (the excess incidence) of liver cancers in oral contraceptive users approaches less than one per million users. 5. OCULAR LESIONS: There have been clinical case reports of retinal thrombosis associated with the use of oral contraceptives, which may lead to partial or complete loss of vision. Oral contraceptives should be discontinued if there is unexplained partial or complete loss of vision; onset of proptosis or diplopia; papilledema; or retinal vascular lesions. Appropriate diagnostic and therapeutic measures should be undertaken immediately. 6. ORAL CONTRACEPTIVE USE BEFORE OR APPROXIMATE EARLY PREGNANCY: Extensive epidemiological studies have revealed no increased risk of birth defects in women who have used oral contraceptives 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. The administration of oral contraceptives to induce withdrawal bleeding should not be used as a test for pregnancy. Oral contraceptives should not be used during pregnancy to treat threatened or habitual abortion. (See CONTRAINDICATIONS) It is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out. If the patient has not adhered to the prescribed dosing schedule, the possibility of pregnancy should be considered at the time of the first missed period. Oral contraceptive use should be discontinued if pregnancy is confirmed. 7. GALLBLADDER DISEASE: Earlier studies have reported an increased lifetime relative risk of gallbladder surgery in users of oral contraceptives and estrogens. More recent studies, however, have shown that the relative risk of developing gallbladder disease among oral contraceptive users may be minimal. The recent findings of minimal risk may be related to the use of oral contraceptives in formulations containing lower hormone doses of estrogen and progestogens. 8. CARBOHYDRATE AND LIPID METABOLIC EFFECTS: Oral contraceptives have been shown to cause glucose intolerance in a significant percentage of users. Oral contraceptives containing greater than 75 micrograms of estrogens cause hyperinsulinism, while lower doses of estrogen cause less glucose intolerance. Progestogens increase insulin secretion and create 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 women should be carefully observed while taking oral contraceptives. A small proportion of women will have persistent hypertriglyceridemia while on the pill. As discussed earlier (see WARNINGS 1a and 1b), changes in serum triglycerides and lipoprotein levels have been reported in oral contraceptive users. 9. ELEVATED BLOOD PRESSURE: 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 in older oral contraceptive users and with continued use. Data from the Royal College of General Practitioners and subsequent randomized trials have shown that the incidence of hypertension increases with increasing concentrations of progestogens. Women with a history of hypertension or hypertension-related diseases, or renal disease should be encouraged to use another method of contraception. If women with hypertension elect to use oral contraceptives, they should be monitored closely, and if significant elevation of blood pressure occurs, oral contraceptives should be discontinued. For most women, elevated blood pressure will return to normal after stopping oral contraceptives and there is no difference in the occurrence of hypertension among ever- and never-users. 10. HEADACHE: The onset or exacerbation of migraine or development of headache with a new pattern which is recurrent, persistent or severe requires discontinuation of oral contraceptives and evaluation of the cause. 11. BLEEDING IRREGULARITIES:

Breakthrough bleeding and spotting are sometimes encountered in patients on oral contraceptives, especially during the first three months of use. In some cases, a change in the bleeding pattern may occur. Such changes may be due to a change in the timing of the event of breakthrough bleeding, as in the case of an abnormal vaginal bleeding. If pathology has been excluded, time or change in other formulation may solve the problem. In the event of amenorrhea, pregnancy should be ruled out. Women who may encounter post-pill amenorrhea or oligomenorrhea, especially when such a condition was pre-existent. **PRECAUTIONS:** 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 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 if requested by the woman and judged appropriate by the clinician. The physical examination should include special reference 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. 3. LIPID DISORDERS: Women who are being treated for hyperlipidemias should be followed closely if they elect to use oral contraceptives. Some progestagens may elevate LDL levels and may render the control of hyperlipidemias more difficult. (See WARNINGS 1.d.) In patients with familial defects of lipoprotein metabolism receiving estrogen-containing preparations, there have been case reports of significant elevations of plasma triglycerides leading to pancreatitis. 4. LIVER FUNCTION: If jaundice develops in any woman taking oral contraceptives, the medication should be discontinued. Steroid hormones may be poorly metabolized in patients with impaired liver function. 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. 6. EMOTIONAL DISORDERS: 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. 7. CONTACT LENSES: Contact-lens wearers who develop visual changes or changes in lens tolerance should be assessed by an ophthalmologist. 8. DRUG INTERACTIONS: Effects of Other Drugs on Combined Hormonal Contraceptives: Rifampin: Rifampin, an inducer of estradiol and some progestins (e.g., norethindrone) is increased by rifampin. A reduction in contraceptive effectiveness and an increase in menstrual irregularities have been associated with concomitant use of rifampin. **Miconazole:** Miconazole-related changes in estradiol, progesterone, FSH and LH plasma levels, breakthrough bleeding, or contraceptive failure cannot be ruled out. **Anticoagulants:** Anticoagulants such as phenobarbital, phenytoin, and carbamazepine have been shown to increase the metabolism of ethinyl estradiol and/or some progestins, which could result in a reduction of contraceptive effectiveness. **Antibiotics:** Pregnancy while taking combined hormonal contraceptives has been reported when the combined hormonal contraceptives were administered with antimicrobials such as ampicillin, tetracycline, and griseofulvin. However, clinical pharmacokinetic studies have not demonstrated any consistent effects of antibiotics (other than rifampin—see above) on plasma concentrations of synthetic steroids. See also separate discussion on miconazole (above). **Atorvastatin:** Co-administration of atorvastatin and an oral contraceptive increased AUC values for norethindrone and ethinyl estradiol by approximately 30% and 20%, respectively. **St. John's Wort:** Herbal products containing St. John's Wort (hypericum perforatum) may induce hepatic enzymes (cytochrome P450) and p-glycoprotein transporter and may reduce the effectiveness of oral contraceptives and emergency contraceptive pills. This may also result in breakthrough bleeding. **Other:** Ascorbic acid and acetaminophen may increase plasma concentrations of some synthetic estrogens, possibly by inhibition of conjugation. **Effects of Drospirenone on Other Drugs: Metabolic Interactions:** Metabolism of DRSP or other drugs and its potential effects of DRSP on hepatic cytochrome P450 (CYP) enzymes have been investigated *in vitro* and *in vivo* studies (see **Metabolism** section of the full package insert). In *in vitro* studies DRSP did not affect turnover of model substrates of CYP1A2 and CYP2D6, but had an inhibitory influence on the turnover of model substrates of CYP1A1, CYP2C9, CYP2C19 and CYP3A4 with CYP2C19 being the most sensitive enzyme. The potential effect of DRSP on CYP2C19 activity was investigated in a clinical pharmacokinetic study using omeprazole as a marker substrate. In the study with 24 postmenopausal women [including 12 women with homozygous (wild type) CYP2C19 genotype and 12 women with heterozygous CYP2C19 genotype] the daily oral administration of 3 mg DRSP for 14 days did not affect the oral clearance of omeprazole (40 mg single oral dose) and the CYP2C19 product 5-hydroxy omeprazole. Furthermore, no significant effect of DRSP on the systemic clearance of the CYP3A4 product omeprazole sulfone was found. These results demonstrate that DRSP did not inhibit CYP2C19 and CYP3A4 *in vivo*. Two additional clinical drug-drug interaction studies using simvastatin and midazolam as marker substrates for CYP3A4 have each performed in 24 healthy postmenopausal women. The results of these studies demonstrated that pharmacokinetics of the CYP3A4 substrates were not influenced by steady state DRSP concentrations achieved after administration of 3 mg DRSP/day. **Interactions with Drugs that Have the Potential to Increase Serum Potassium:** There is a potential for an increase in serum potassium in women taking YAZ with other drugs (see **BOLDED WARNING**). Of note, potassium or chronic use of NSAID medication was not restricted in any of the clinical trials with YAZ. A causal association with the 3 mg DRSP/0.03 mg EE tablet is unknown. Twelve pregnancies had occurred with YAZ sex steroids and corticoids; however, free or biologically active levels remain unchanged. e. Triglycerides may be increased. f. Glucose tolerance may be decreased. 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 contraceptive dose, there was an increase in carcinomas of the harden gland in the group that received the high dose of drospirenone alone. In a similar study in rats given 10 mg/kg/day drospirenone alone or 0.3 + 0.03, 3 + 0.03 and 10 + 0.1 mg/kg/day drospirenone and ethinyl estradiol, 0.8 to 10 times the exposure of women taking a contraceptive dose, there was an increased incidence of benign and total (benign and malignant) adrenal gland pheochromocytomas in the group receiving the high dose of drospirenone. Drospirenone was not mutagenic in a number of *in vitro* (Ames, Chinese Hamster Lung gene mutation and chromosomal damage in human lymphocytes) and *in vivo* (mouse micronucleus) genotoxicity tests. Drospirenone increased unscheduled DNA synthesis in rat hepatocytes and formed adducts with rodent liver DNA but not with human liver DNA. (See **WARNINGS**). 11. PREGNANCY: Pregnancy category X. (See **CONTRAINDICATIONS and WARNINGS**) Estrogens and progestins should not be used during pregnancy. Fourteen pregnancies that occurred during exposure with 3 mg DRSP/0.03 mg EE tablets *in vitro* (none more than a single cycle of exposure) have been identified. One infant was born with esophageal atresia. A causal association with the 3 mg DRSP/0.03 mg EE tablet is unknown. Twelve pregnancies had occurred with YAZ sex steroids and corticoids; however, free or biologically active levels remain unchanged. e. Triglycerides may be increased. f. Glucose tolerance may be decreased. 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. 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