

# CMS Seeks to End Health Plan Marketing Abuse

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The Centers for Medicare and Medicaid Services, seeking to curtail marketing abuses within Medicare Advantage and Medicare Part D prescription drug plans, has proposed new regulations that would prohibit such tactics as door-to-door marketing and cold-calling of beneficiaries.

The proposed rules, which would in-

corporate into regulation several requirements that CMS already has imposed administratively, would tighten marketing standards and require independent insurance agents who sell Medicare Advantage and Part D products to be licensed by the state, the agency said.

The rules, which are subject to public comment, also seek to eliminate incentives for agents to "churn" beneficiaries, or persuade people to change plans, in order to gain enhanced commissions, said Abby

Block, director of the CMS Center for Beneficiary Choices, at a press briefing.

CMS plans to roll out the final rule before the fall open enrollment season.

CMS Acting Administrator Kerry Weems noted that the proposed regulations "go beyond what the insurance industry recently endorsed as necessary regulatory changes to the program."

However, the House Committee on Energy and Commerce, which has released a report on the Medicare Advantage pro-

gram, said that the proposed changes in marketing requirements "will do little to address the fundamental problems with Medicare Advantage plans."

According to Rep. Bart Stupak (D-Mich.), chairman of the committee's subcommittee on oversight and investigation, the committee's report "has verified countless stories of deceptive sales practices by insurance agents who prey on the elderly and disabled to sell them expensive and inappropriate private Medicare plans." He noted in a statement that the report "shows that steps taken by CMS will not be nearly enough to protect our most vulnerable citizens from deceptive sales practices."

The committee report recommended better sales agent training, strengthened state oversight of plan sales operations, standardization of plan benefit packages, and comprehensive tracking of beneficiary complaints.

The CMS proposal received mixed reviews from Medicare Advantage stakeholders. Karen Ignagni, president and CEO of America's Health Insurance Plans, said in a statement that the proposed regulations are "an important step to ensure beneficiaries can rely on the information being provided to make the Medicare coverage decisions that are right for them."

Robert Hayes, president of the consumer advocacy group the Medicare Rights Center, said in a statement that the proposed regulations "are inadequate to address the problems we see every day."

Specifically, the proposed plan marketing standards would prohibit cold-calling and expand the current prohibition on door-to-door solicitation to cover other unsolicited circumstances, such as sales activities at educational events like health information fairs and community meetings, or in areas such as waiting rooms where patients primarily intend to receive health care-related services, according to CMS. Any appointment with a beneficiary to market health care-related products would have to be limited to the scope that the beneficiary agreed to in advance.

The regulations also would require Medicare Advantage organizations to establish commission structures for sales agents and brokers that are level across all years and across all product types. Commission structures for prescription drug plans would have to be level across the sponsors' plans as well.

The rule also proposes new protections for beneficiaries enrolled in special needs plans (SNPs), a type of Medicare Advantage plan that provides coordinated care to individuals in certain institutions, such as nursing homes; those who are eligible for both Medicare and Medicaid; and those who have certain severe or disabling chronic conditions.

The proposed rules would require that 90% of new enrollees in SNPs be special needs individuals, would more clearly establish and clarify delivery of care standards for SNPs, and would protect beneficiaries enrolled in both Medicare and Medicaid from being billed for cost sharing that is not their responsibility.

CMS is accepting comments on the proposal until July 15.



## Brief Summary of Full Prescribing Information

### INDICATIONS AND USAGE

ORACEA is indicated for the treatment of only inflammatory lesions (papules and pustules) of rosacea in adult patients.

The dosage of ORACEA differs from that of doxycycline used to treat infections. To reduce the development of resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, ORACEA should be used only as indicated.

### CLINICAL PHARMACOLOGY

#### Pharmacokinetics

ORACEA capsules are not bioequivalent to other doxycycline products.

### CONTRAINDICATIONS

This drug is contraindicated in persons who have shown hypersensitivity to doxycycline or any of the other tetracyclines.

### WARNINGS

**Teratogenic effects:** 1) Doxycycline, like other tetracycline-class antibiotics, can cause fetal harm when administered to a pregnant woman. If any tetracycline is used during pregnancy or if the patient becomes pregnant while taking these drugs, the patient should be informed of the potential hazard to the fetus and treatment stopped immediately.

ORACEA should not be used during pregnancy (see **PRECAUTIONS: Pregnancy**).

2) The use of drugs of the tetracycline class during tooth development (last half of pregnancy, infancy, and childhood up to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term use of the drug but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used during tooth development unless other drugs are not likely to be effective or are contraindicated.

3) All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature human infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued.

Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development on the developing fetus. Evidence of embryotoxicity has been noted in animals treated early in pregnancy (see **PRECAUTIONS: Pregnancy** section).

**Gastrointestinal effects:** Pseudomembranous colitis has been reported with nearly all antibacterial agents and may range from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis". If a diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

**Metabolic effects:** The anti-anabolic action of the tetracyclines may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired function, higher serum levels of tetracycline-class antibiotics may lead to azotemia, hyperphosphatemia, and acidosis. If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulations of the drug and possible liver toxicity. Under such conditions, lower than usual total doses are indicated, and if therapy is prolonged, serum level determinations of the drug may be advisable.

**Photosensitivity:** Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Although this was not observed during the duration of the clinical studies with ORACEA, patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using ORACEA. If patients need to be outdoors while using ORACEA, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician.

### PRECAUTIONS

**General:** Safety of ORACEA beyond 9 months has not been established.

As with other antibiotic preparations, use of ORACEA may result in overgrowth of non-susceptible microorganisms, including fungi. If superinfection occurs, ORACEA should be discontinued and appropriate therapy instituted. Although not observed in clinical trials with ORACEA, the use of tetracyclines may increase the incidence of vaginal candidiasis.

ORACEA should be used with caution in patients with a history of or predisposition to candidiasis overgrowth. Bacterial resistance to tetracyclines may develop in patients using ORACEA. Because of the potential for drug-resistant bacteria to develop during the use of ORACEA, it should be used only as indicated.

**Autoimmune Syndromes:** Tetracyclines have been associated with the development of autoimmune syndromes. Symptoms may be manifested by fever, rash, arthralgia, and malaise. In symptomatic patients, liver function tests, ANA, CBC, and other appropriate tests should be performed to evaluate the patients. Use of all tetracycline-class drugs should be discontinued immediately.

**Tissue Hyperpigmentation:** Tetracycline class antibiotics are known to cause hyperpigmentation. Tetracycline therapy may induce hyperpigmentation in many organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves. Skin and oral pigmentation has been reported to occur independently of time or amount of drug administration, whereas other pigmentation has been reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as over sites of scars or injury.

**Pseudotumor cerebri:** Bulging fontanelles in infants and benign intracranial hypertension in adults have been reported in individuals receiving tetracyclines. These conditions disappeared when the drug was discontinued.

**Laboratory Tests:** Periodic laboratory evaluations of organ systems, including hematopoietic, renal and hepatic studies should be performed. Appropriate tests for autoimmune syndromes should be performed as indicated.

**Drug Interactions:** 1. Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage. 2. Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline-class drugs in conjunction with penicillin. 3. The concurrent use of tetracycline and methoxyflurane has been reported to result in fatal renal toxicity. 4. Absorption of tetracyclines is impaired by bismuth subsalicylate, proton pump inhibitors, antacids containing aluminum, calcium or magnesium and iron-containing preparations. 5. Doxycycline may interfere with the effectiveness of low dose oral contraceptives. To avoid contraceptive failure, females are advised to use a second form of contraceptive during treatment with doxycycline. 6. There have been reports of pseudotumor cerebri (benign intracranial hypertension) associated with the concomitant use of isotretinoin and tetracyclines. Since both oral retinoids, including isotretinoin and acitretin, and the tetracyclines, primarily minocycline, can cause increased intracranial pressure, the concurrent use of an oral retinoid and a tetracycline should be avoided.

### MICROBIOLOGY

The plasma concentrations of doxycycline achieved with ORACEA during administration (see **DOSE AND ADMINISTRATION**) are less than the concentration required to treat bacterial diseases. *In vivo* microbiological studies utilizing a similar drug exposure for up to 18 months demonstrated no detectable long-term effects on bacterial flora of the oral cavity, skin, intestinal tract, and vagina.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Doxycycline was assessed for potential to induce carcinogenesis in a study in which the compound was administered to Sprague-Dawley rats by gavage at dosages of 20, 75, and 200 mg/kg/day for two years. An increased incidence of uterine polyps was observed in female rats that received 200 mg/kg/day, a dosage that resulted in a systemic exposure to doxycycline approximately 12.2 times that observed in female humans who use ORACEA (exposure comparison based upon area under the curve (AUC) values). No impact upon tumor incidence was observed in male rats at 200 mg/kg/day, or in either gender at the other dosages studied. Evidence of oncogenic activity was obtained in studies with related compounds, i.e., oxytetracycline (adrenal and pituitary tumors) and minocycline (thyroid tumors).

Doxycycline demonstrated no potential to cause genetic toxicity in an *in vitro* point mutation study with mammalian cells (CHO/HGPRT forward mutation assay) or in an *in vivo* micronucleus assay conducted in CD-1 mice. However, data from an *in vitro* assay with CHO cells for potential to cause chromosomal aberrations suggest that doxycycline is a weak clastogen.

Oral administration of doxycycline to male and female Sprague-Dawley rats adversely affected fertility and reproductive performance, as evidenced by increased time for mating to occur, reduced sperm motility, velocity, and concentration, abnormal sperm morphology, and increased pre- and post-implantation losses. Doxycycline induced reproductive toxicity at all dosages that were examined in this study, as even the lowest dosage tested (50 mg/kg/day) induced a statistically significant reduction in sperm velocity. Note that 50 mg/kg/day is approximately 3.6 times the amount of doxycycline contained in the recommended daily dose of ORACEA for a 60-kg human when compared on the basis of AUC estimates. Although doxycycline impairs the fertility of rats when administered at sufficient dosage, the effect of ORACEA on human fertility is unknown.

**Pregnancy: Teratogenic Effects:** Pregnancy Category D. (see **WARNINGS** section). Results from animal studies indicate that doxycycline crosses the placenta and is found in fetal tissues.

**Nonteratogenic effects:** (see **WARNINGS** section).

**Labor and Delivery:** The effect of tetracyclines on labor and delivery is unknown.

**Nursing Mothers:** Tetracyclines are excreted in human milk. Because of the potential for serious adverse reactions in infants from doxycycline, ORACEA should not be used in mothers who breastfeed. (see **WARNINGS** section).

**Pediatric Use:** ORACEA should not be used in infants and children less than 8 years of age (see **WARNINGS** section). ORACEA has not been studied in children of any age with regard to safety or efficacy, therefore use in children is not recommended.

### ADVERSE REACTIONS

**Adverse Reactions in Clinical Trials of ORACEA:** In controlled clinical trials of adult patients with mild to moderate rosacea, 537 patients received ORACEA or placebo over a 16-week period. The most frequent adverse reactions occurring in these studies are listed in the table below.

Incidence (%) of Selected Adverse Reactions in Clinical Trials of ORACEA (n=269) vs. Placebo (n=268)	ORACEA	Placebo
Nasopharyngitis	13 (4.8)	9 (3.4)
Pharyngolaryngeal Pain	3 (1.1)	2 (0.7)
Sinusitis	7 (2.6)	2 (0.7)
Nasal Congestion	4 (1.5)	2 (0.7)
Fungal Infection	5 (1.9)	1 (0.4)
Influenza	5 (1.9)	3 (1.1)
Diarrhea	12 (4.5)	7 (2.6)
Abdominal Pain Upper	5 (1.9)	1 (0.4)
Abdominal Distention	3 (1.1)	1 (0.4)
Abdominal Pain	3 (1.1)	1 (0.4)
Stomach Discomfort	3 (1.1)	2 (0.7)

Note: Percentages based on total number of study participants in each treatment group.

**Adverse Reactions for Tetracyclines:** The following adverse reactions have been observed in patients receiving tetracyclines at higher, antimicrobial doses:

Gastrointestinal: anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, and inflammatory lesions (with vaginal candidiasis) in the anogenital region. Hepatotoxicity has been reported rarely. Rare instances of esophagitis and esophageal ulcerations have been reported in patients receiving the capsule forms of the drugs in the tetracycline class. Most of the patients experiencing esophagitis and/or esophageal ulceration took their medication immediately before lying down. (see **DOSE AND ADMINISTRATION** section).

Skin: maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Photosensitivity is discussed above. (see **WARNINGS** section).

**Renal toxicity:** Rise in BUN has been reported and is apparently dose-related. (see **WARNINGS** section).

Hypersensitivity reactions: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, serum sickness, pericarditis, and exacerbation of systemic lupus erythematosus.

Blood: Hemolytic anemia, thrombocytopenia, neutropenia, and eosinophilia have been reported.

### OVERDOSAGE

In case of overdosage, discontinue medication, treat symptomatically, and institute supportive measures. Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of overdose.

### DOSE AND ADMINISTRATION

**THE DOSE AND ADMINISTRATION OF ORACEA DIFFERS FROM THAT OF DOXYCYCLINE USED TO TREAT INFECTIONS. EXCEEDING THE RECOMMENDED DOSE MAY RESULT IN AN INCREASED INCIDENCE OF SIDE EFFECTS INCLUDING THE DEVELOPMENT OF RESISTANT MICROORGANISMS.**

One ORACEA Capsule (40 mg) should be taken once daily in the morning on an empty stomach, preferably at least one hour prior to or two hours after meals.

Efficacy beyond 16 weeks and safety beyond 9 months have not been established.

Administration of adequate amounts of fluid along with the capsules is recommended to wash down the capsule to reduce the risk of esophageal irritation and ulceration. (see **ADVERSE REACTIONS** section).

### HOW SUPPLIED

ORACEA (beige opaque capsule printed with GCP1 40) containing doxycycline, USP in an amount equivalent to 40 mg of anhydrous doxycycline. Bottle of 30 (NDC 64682-009-01).

**Storage:** All products are to be stored at controlled room temperatures of 15°C-30°C (59°F-86°F) and dispensed in light-resistant containers (USP). Keep out of reach of children.

Patent Information: U.S. Patents 5,789,395; 5,919,775; 7,232,572; 7,211,267 and patents pending.

ORACEA is a registered trademark of CollaGenex Pharmaceuticals, Inc.

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