

CMS Proposes to Switch to ICD-10 Codes by 2011

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Officials at the Centers for Medicare and Medicaid Services plan to replace the ICD-9-CM diagnosis and procedure code set with a significantly expanded set of codes—the ICD-10—by Oct. 1, 2011.

But physician groups are calling the agency's plan rushed and unworkable and want the agency to reconsider its compli-

ance date. In addition to the requirements for using the ICD-10 code sets, the CMS also is proposing to require entities covered under HIPAA to implement updated versions of electronic transmission standards—the Accredited Standards Committee X12 Version 5010 and the National Council for Prescription Drug Programs Version D.0. Both electronic standards have a compliance date of April 1, 2010. The X12 Version 5010 must be in place before the ICD-10 codes can be used.

The switch to ICD-10 has been under consideration by the Department of Health and Human Services since 1997. Size and specificity are two of the biggest drawbacks of the ICD-9-CM code set, according to the CMS.

The ICD-9-CM also fails to provide adequate clinical details, according to the CMS. "Because of the new and changing medical advancements during the past 20-plus years, the functionality of the ICD-9-CM code set has been exhausted," CMS offi-

cials wrote in the proposed regulation.

The CMS also is urging a switch to the ICD-10 code sets in an effort to keep in step with other countries. As of October 2002, 99 countries had adopted ICD-10 or a clinical modification for coding and reporting morbidity data. And the CMS contends that because it continues to use ICD-9-CM, it has problems identifying emerging recent global health threats.

Under the proposal, physicians, hospitals, health plans, and other covered health care entities would be required to use the ICD-10-CM for reporting diagnoses and the ICD-10-PCS for reporting procedures. The ICD-10 code sets offer significantly more codes, about 155,000 across the two sets, compared with about 17,000 for codes within the ICD-9-CM.

In addition to size, the ICD-10 code sets also provide greater specificity, such as being able to reflect the side of the body that is related to the diagnosis or procedure. The more detailed information available through the ICD-10 codes also will aid in the implementation of electronic health records and transmission of data for bio-surveillance or pay-for-performance programs, according to the CMS.

But physician groups say the CMS is asking physicians and other health care providers to do too much too fast.

The American Medical Association balked at the idea of implementation of both the updated X12 Version 5010 electronic transaction standard and the ICD-10 coding system in just 3 years. The X12 Version 5010 standard should first be piloted before physicians and others are asked to implement it, AMA said.

"This is a massive administrative undertaking for physicians and must be implemented in a time frame that allows for physician education, software vendor updates, coder training, and testing with payers—steps that cannot be rushed and are needed for a smooth transition," Dr. Joseph Heyman, AMA board chair, said in a statement.

The Medical Group Management Association also objected. While the MGMA supports the switch to the ICD-10 code sets, it said that 3 years is not enough time for the industry to implement the new system. Instead of a simultaneous implementation of the X12 Version 5010 standard and the ICD-10 code sets, the MGMA is asking the CMS to wait at least 3 years after the switch to X12 Version 5010 before implementing the ICD-10.

The switch to ICD-10 needs to be done separately because it will require significant changes from medical groups, according to the MGMA. Recent MGMA research indicates that most medical practices will have to purchase software upgrades for their practice management systems or buy all new software.

Officials at the American College of Physicians were still analyzing the CMS proposal at press time, but said they continue to have concerns about the switch to ICD-10. In a letter to the CMS in January 2007, the ACP said it opposes the change to ICD-10 for outpatient diagnosis coding and that such a switch would be expensive and time consuming for physicians. ■

Rx Only



Keep out of reach of children.

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 **DOSAGE 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 **DOSAGE 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.

DOSAGE AND ADMINISTRATION

THE DOSAGE OF ORACEA DIFFERS FROM THAT OF DOXYCYCLINE USED TO TREAT INFECTIONS. EXCEEDING THE RECOMMENDED DOSAGE 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 CGP1 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 tight, 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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