

Feds' Antitrust Efforts May Ease ACO Formation

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FROM A FEDERAL TRADE COMMISSION WORKSHOP

Many physicians have wondered how – and even if – they will be able to work together to form accountable care organizations without violating federal antitrust and fraud and abuse laws.

A federal regulatory meeting held earlier this fall offered possible answers to both questions. Federal regulators are considering exemptions to those laws that would allow providers who meet certain requirements to form ACOs.

"It is not easy to craft safe harbors that can replace an antitrust review that analyzes the specific facts of each case and market. But we're going to try to do this," said Jon Leibowitz, chairman of the Federal Trade Commission (FTC).

Similarly, Daniel Levinson, inspector general of the U.S. Department of Health and Human Services, noted that the Affordable Care Act gives the HHS secretary the authority to waive some fraud and abuse laws as needed to help ACO programs develop.

"We and our HHS colleagues are looking closely at how the secretary might exercise this authority most effectively,"

Mr. Levinson said, according to the meeting transcript.

The FTC, the HHS Office of Inspector General, and the Centers for Medicare and Medicaid Services conducted the workshop in Baltimore to hear the opinions of panelists and audience members on a variety of ACO issues.

However, much of the questioning focused on how antitrust and fraud and abuse exemptions could be applied to ACOs.

The Affordable Care Act promotes ACO creation to reduce health-care fragmentation, improve outcomes, and cut spending by, for instance, keeping patients out of hospitals when possible.

The goal is for providers to come together and contract with the CMS to integrate and manage the care of at least 5,000 patients, and to share part of the savings their efforts generate for Medicare, as long as quality parameters are met. Once formed, ACOs could pursue similar types of contracts with commercial insurance companies. The catch is that encouraging independent providers to jointly negotiate contracts and payment rates with health plans raises concerns about joint price fixing, reduced competition, and other antitrust matters.

Likewise, the shared-savings provision,

among others, raises antikickback, self-referral, and other fraud and abuse concerns, according to health care attorney Douglas Hastings, board chair of Epstein Becker & Green, Washington, and a meeting panelist who offered his insights during a later interview.

Regulators are interested in applying to ACOs antitrust protections that already exist for providers who are clinically integrated and jointly accept significant financial risk.

"In those cases, [collaboration is] not viewed as an antitrust matter, since they are behaving as an integrated organization," explained meeting panelist and health policy expert Harold Miller, executive director of the Center for Health Care Quality and Payment Reform, who also offered his insights during a later interview.

Defining the extent of integration required for protection, and the time frame to achieve it, remain key issues for regulators, as does the possible creation of additional antitrust safe harbors related to market share and other matters. Regulators also said that they want to foster multiple ACOs in a given market to increase competition.

Which providers would be covered under fraud and abuse waivers also remains

an issue, as well as whether waivers should apply only to shared savings payments or to other financial relationships ACOs create, Troy Barsky, director of the CMS Division of Technical Payment Policy, explained during the meeting.

Overall, the hope is to spur "coordination [and] cooperation among the people and the entities that provide health care," while at the same time ensure "appropriate corporate behaviors," said Dr. Donald Berwick, CMS administrator.

Proposed ACO regulations are expected from the CMS in late December.

In the meantime, Mr. Miller advised physicians, "If you want to be an ACO, you have to start looking at the data you have – or get access to data from payers, Medicare, and others – to identify opportunities for savings. Once you know where they are, figure out what programs to put in place to achieve those savings."

One option is to hire a nurse to help chronically ill patients manage their diseases, Mr. Miller said. That's been proven to help reduce emergency department visits and hospitalizations (Arch. Intern. Med. 2003;163:585-91).

The meeting's audio and transcript – as well as public comments on ACO concerns – are at www.ftc.gov/opp/workshops/aco/index.shtml. ■

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In the all-exposure population, the rate of malignancies remained consistent (1.10 events per 100 patient-years) with the rate observed in the 6-month controlled period [see Warnings and Precautions].

Other Adverse Reactions

Adverse reactions occurring in 2% or more of patients on 4 mg/kg or 8 mg/kg ACTEMRA plus DMARD, and at least 1% greater than that observed in patients on placebo plus DMARD, are summarized in Table 2.

Table 2 Adverse Reactions Occurring in at Least 2% or More of Patients on 4 mg/kg or 8 mg/kg ACTEMRA plus DMARD and at Least 1% Greater Than That Observed in Patients on Placebo plus DMARD

Preferred Term	6-Month Phase III Controlled Study Population				
	ACTEMRA 8 mg/kg Monotherapy N = 288 (%)	Methotrexate N = 284 (%)	ACTEMRA 4 mg/kg + DMARDs N = 774 (%)	ACTEMRA 8 mg/kg + DMARDs N = 1582 (%)	Placebo + DMARDs N = 1170 (%)
Upper Respiratory Tract Infection	7	5	6	8	6
Nasopharyngitis	7	6	4	6	4
Headache	7	2	6	5	3
Hypertension	6	2	4	4	3
ALT increased	6	4	3	3	1
Dizziness	3	1	2	3	2
Bronchitis	3	2	4	3	3
Rash	2	1	4	3	1
Mouth Ulceration	2	2	1	2	1
Abdominal Pain Upper	2	2	3	3	2
Gastritis	1	2	1	2	1
Transaminase increased	1	5	2	2	1

DRUG INTERACTIONS

Other Drugs for Treatment of Rheumatoid Arthritis

Population pharmacokinetic analyses did not detect any effect of methotrexate, nonsteroidal anti-inflammatory drugs or corticosteroids on tocilizumab clearance.

Concomitant administration of a single dose of 10 mg/kg ACTEMRA with 10-25 mg MTX once weekly had no clinically significant effect on MTX exposure.

ACTEMRA has not been studied in combination with biological DMARDs such as TNF antagonists [see Dosage and Administration].

Interactions with CYP450 Substrates

In vivo studies with omeprazole, metabolized by CYP2C19 and CYP3A4, and simvastatin, metabolized by CYP3A4, showed up to a 28% and 57% decrease in exposure one week following a single dose of ACTEMRA, respectively. The effect of tocilizumab on CYP enzymes may be clinically relevant for CYP450 substrates with narrow therapeutic index, where the dose is individually adjusted. Upon initiation or discontinuation of ACTEMRA, in patients being treated with these types of medicinal products, therapeutic monitoring of effect (eg, warfarin) or drug concentration (eg, cyclosporine or theophylline) should be performed and the individual dose of the medicinal product adjusted as needed. Prescribers should exercise caution when ACTEMRA is coadministered with CYP3A4 substrate drugs where decrease in effectiveness is undesirable, eg, oral contraceptives, lovastatin, atorvastatin, etc. The effect of tocilizumab on CYP450 enzyme activity may persist for several weeks after stopping therapy.

Live Vaccines

Live vaccines should not be given concurrently with ACTEMRA [see Warnings and Precautions].

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. ACTEMRA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

An embryo-fetal developmental toxicity study was performed in which pregnant cynomolgus monkeys were treated intravenously with tocilizumab (daily doses of 2, 10, or 50 mg/kg from gestation day 20-50) during organogenesis. Although there was no evidence for a teratogenic/dysmorphic effect at any dose, tocilizumab produced an increase in the incidence of

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abortion/embryo-fetal death at 10 mg/kg and 50 mg/kg doses (1.25 and 6.25 times the human dose of 8 mg/kg every 4 weeks based on a mg/kg comparison).

Nonteratogenic Effects.

Testing of a murine analogue of tocilizumab in mice did not yield any evidence of harm to offspring during the pre- and postnatal development phase when dosed at 50 mg/kg intravenously with treatment every three days from implantation until day 21 after delivery (weaning). There was no evidence for any functional impairment of the development and behavior, learning ability, immune competence and fertility of the offspring.

Pregnancy Registry:

To monitor the outcomes of pregnant women exposed to ACTEMRA, a pregnancy registry has been established. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.

Nursing Mothers

It is not known whether tocilizumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from ACTEMRA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness of ACTEMRA in pediatric patients have not been established.

Geriatric Use

Of the 2644 patients who received ACTEMRA in Studies I to V, a total of 435 rheumatoid arthritis patients were 65 years of age and older, including 50 patients 75 years and older. The frequency of serious infection among subjects treated with ACTEMRA 65 years of age and older was higher than those under the age of 65. As there is a higher incidence in infections in the elderly population in general, caution should be used when treating the elderly.

Hepatic Impairment

The safety and efficacy of ACTEMRA have not been studied in patients with hepatic impairment, including patients with positive HBV and HCV serology [see Warnings and Precautions].

Renal Impairment

No dose adjustment is required in patients with mild renal impairment. ACTEMRA has not been studied in patients with moderate to severe renal impairment.

OVERDOSAGE

There are limited data available on overdoses with ACTEMRA. One case of accidental overdose was reported in which a patient with multiple myeloma received a dose of 40 mg/kg. No adverse drug reactions were observed. No serious adverse drug reactions were observed in healthy volunteers who received single doses of up to 28 mg/kg, although all 5 patients at the highest dose of 28 mg/kg developed dose-limiting neutropenia.

In case of an overdose, it is recommended that the patient be monitored for signs and symptoms of adverse reactions. Patients who develop adverse reactions should receive appropriate symptomatic treatment.

PATIENT COUNSELING INFORMATION

Patient Counseling

Patients should be advised of the potential benefits and risks of ACTEMRA. Physicians should instruct their patients to read the Medication Guide before starting ACTEMRA therapy.

• Infections:

Inform patients that ACTEMRA may lower their resistance to infections. Instruct the patient of the importance of contacting their doctor immediately when symptoms suggesting infection appear in order to assure rapid evaluation and appropriate treatment.

• Gastrointestinal Perforation:

Inform patients that some patients who have been treated with ACTEMRA have had serious side effects in the stomach and intestines. Instruct the patient of the importance of contacting their doctor immediately when symptoms of severe, persistent abdominal pain appear to assure rapid evaluation and appropriate treatment.

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