IMPLEMENTING HEALTH REFORM

Closing the Doughnut Hole

One of the first provisions of the Patient Protection and Affordable Care Act to take effect is the $250 rebate for Medicare beneficiaries who fall into the Part D doughnut hole. The first rebate checks were mailed on June 10. The rebates are the first step in a multiyear effort to trim drug costs for seniors and other Medicare beneficiaries.

MARILYN TAVENNER

Next year, patient cost sharing for brand-name drugs will be cut in half, and the doughnut hole will be closed completely by 2020.

Just as checks started hitting seniors' mailboxes, the administration launched a $1 million radio ad campaign designed to help patients protect themselves from fraud, as criminals launch scams targeted at the new benefits.

Marilyn Tavenner, acting administrator at the Centers for Medicare and Medicaid Services, answered questions about how the new benefit will be implemented.

RHEUMATOLOGY NEWS: How many Medicare beneficiaries will fall into the doughnut hole this year? Will they all get checks this summer?

Ms. Tavenner: About 8 million Medicare beneficiaries are expected to reach the prescription drug coverage gap that we call the doughnut hole this year. Of those, 4 million will be eligible to get a tax-free, one-time rebate check. The remaining beneficiaries already receive assistance through Medicare Extra Help. Beneficiaries who hit this coverage gap do not need to fill out any form, or make any phone call, to receive this benefit under the Affordable Care Act. The one-time $250 rebate checks will be mailed automatically to seniors' homes from Medicare when they enter the doughnut hole. The first rebate checks were sent in June, and checks will be sent each month throughout this year as more beneficiaries enter the doughnut hole.

RN: Will the $250 rebate have a significant impact on patients' out-of-pocket drug costs this year?

Ms. Tavenner: The $250 rebate is immediate relief that marks the first step in completely eliminating the doughnut hole. This year's rebate will help put money back in the pockets of seniors who are too often forced to choose between paying for their groceries or for their medications. Next year, seniors who reach the coverage gap will get a 50% discount on brand-name drugs that will help reduce their costs. Also, under the new law, the actual coverage gap will get smaller and smaller every year, until it completely disappears in 2020.

RN: Physicians in all specialties spend a lot of time helping patients find affordable medications. How will these changes decrease the burden on doctors?

Ms. Tavenner: Physicians are on the front lines in helping seniors obtain medications that are not only successful in treating the patient, but are also affordable. By closing the coverage gap and making care more affordable, Medicare beneficiaries will be able to get the care they need and deserve. And starting next year, patients with Medicare can get free preventive care services like colorectal cancer screening and mammograms. Medicare also will cover an annual physical, where they can work with their physician to develop a personal prevention plan based on current health needs.

RN: How can physicians help their patients to take advantage of this benefit?

Ms. Tavenner: Doctors can educate patients about the benefits of the Affordable Care Act. If patients have questions on their rebate checks, they can call 1-800-Medicare or visit www.medicare.gov. Updates on the health reform law as it is implemented will be posted on www.healthreform.gov. Along with the additional benefits provided by the Affordable Care Act come increased threats of fraud. That's precisely why we're working with the Department of Justice to crack down on scam artists who are trying to procure personal information from Medicare beneficiaries by promising them rebate checks and other benefits under the law.

Patients should never give their Medicare ID number to anyone promising benefits or discounts under the new law. For fraud-fighting tips, please visit www.stopmedicarefraud.gov. ■

ACTEMRA® (tocilizumab)

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

6-Month Phase III Controlled Study Population					
Preferred Term	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/dysmorphogenic effect at any dose, tocilizumab produced an increase in the incidence of 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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