

Wanted: Docs to Help Craft Pay for Performance

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CHICAGO — Physicians need to help design the pay-for-performance programs now being initiated by Medicare and other payers or they may not like the results, Dr. Trent Haywood said at the annual meeting of the American Association of Clinical Endocrinologists.

“What it comes down to ... is there’s a certain level of fear, a certain uneasiness”

about the program among doctors, said Dr. Haywood, who is deputy chief clinical officer at the Centers for Medicare and Medicaid Services. “The thing is for clinicians to work with us and get on board. We don’t want to design a program and not have clinician input.”

Medicare currently has several pilot programs under which physician and hospital pay is based in part on patient outcomes and quality of care. Demonstrations include a project with 10 large multispecial-

ty practices nationwide, and an oncology project in which physicians are paid to report their use of guidelines as well as outcome measures for their patients.

Dr. John Rowe, executive chairman of Aetna, made a similar comment at the Society of Hospital Medicine meeting in Washington. “My fear is that the pay-for-performance train is leaving the station, and the doctors aren’t on it,” he said. “When I talk to people who buy Aetna’s services [such as large employers], they get

it. Corporate America is adopting the concept of pay for performance before the details are worked out, and the details have to be worked out by physicians.”

But physicians have reservations about the pay-for-performance concept. Dr. John Nelson, an American Medical Association trustee and panelist at the AACE meeting, said Medicare’s pay-for-performance program would be a great opportunity for physicians to serve patients, but only “if it improves quality, if it’s voluntary, and if the data are accurate, clinically meaningful, and relevant.”

However, another panelist had other ideas. Twila J. Brase, president of the Citizens’ Council on Health Care, a St. Paul, Minn., group that advocates competition in health care, said that pay for performance was based on what she called the “faulty premise” of evidence-based medicine. While the original idea behind evidence-based medicine was good, “it is being perverted to allow rationing of care,” she said. Because of its insistence on having all physicians practice in the same way, “evidence-based medicine will make every doctor a managed care doctor. It will lead to budget-based care, not customized care.”

Rather than participating in pay-for-performance programs, Ms. Brase urged doctors to stop participating in Medicare and private insurance programs and instead have patients pay cash for each visit. She called Medicare and private insurance “the real culprits” in the health care cost spiral.

“Evidence-based medicine isn’t about evidence. It’s not even about science. It’s about control. It’s meant to centralize power and control outside the exam room, and if you let pay for performance and evidence-based medicine become the standard way that you do business, the only way you’ll make a decent dollar working at your profession is to follow the directives of people who don’t know what they’re talking about,” she said to loud applause.

Dr. Haywood seemed taken aback by Ms. Brase’s comments. “This is the first time I’ve ever been on a panel where someone advocated the abolishment of Medicare and Medicaid,” he said. “It’s a shock to me.”

But he agreed with Ms. Brase that consumers need more information to make better health care choices. “I do believe we’re going to be providing information to consumers so that they can make some of those decisions, and hopefully that leads to better quality.”

One audience member wanted to know how CMS would deal with patients who, for one reason or another, don’t meet the outcome goals. “How will CMS deal with ... that 10% of the population who, come hell or high water, will never have a [hemoglobin] A_{1c} of 6.5%, for a variety of reasons?” she asked.

Dr. Haywood said that physician input would be helpful in trying to answer that question. In the meantime, he said, CMS is considering the idea that some patients will automatically get excluded because “they’ve reached the therapeutic goal for a variety of reasons and won’t fall into the denominator for that particular measure.” ■

BOTOX® COSMETIC (Botulinum Toxin Type A) Purified Neurotoxin Complex

INDICATIONS AND USAGE

BOTOX® COSMETIC is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients ≤ 65 years of age.

CONTRAINDICATIONS

BOTOX® COSMETIC is contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any ingredient in the formulation.

WARNINGS

BOTOX® and **BOTOX® COSMETIC** contain the same active ingredient in the same formulation. Therefore, adverse events observed with the use of **BOTOX®** also have the potential to be associated with the use of **BOTOX® COSMETIC**.

Do not exceed the recommended dosage and frequency of administration of **BOTOX® COSMETIC**. Risks resulting from administration at higher dosages are not known.

Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been rarely reported. These reactions include anaphylaxis, urticaria, soft tissue edema, and dyspnea. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently the causal agent cannot be reliably determined. If such a reaction occurs further injection of **BOTOX® COSMETIC** should be discontinued and appropriate medical therapy immediately instituted.

Pre-Existing Neuromuscular Disorders

Caution should be exercised when administering **BOTOX® COSMETIC** to individuals with peripheral motor neuropathic diseases (e.g., amyotrophic lateral sclerosis, or motor neuropathy) or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome). Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise from typical doses of **BOTOX® COSMETIC**. Published medical literature has reported rare cases of administration of a botulinum toxin to patients with known or unrecognized neuromuscular disorders where the patients have shown extreme sensitivity to the recognized effects of typical clinical doses. In some of these cases, dysphagia has lasted several months and required placement of a gastric feeding tube.

Dysphagia

Dysphagia is a commonly reported adverse event following treatment of cervical dystonia patients with all botulinum toxins. In these patients, there are reports of rare cases of dysphagia severe enough to warrant the insertion of a gastric feeding tube. There is also a case report where a patient developed aspiration pneumonia and died subsequent to the finding of dysphagia.

Cardiovascular System

There have also been rare reports following administration of **BOTOX®** of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease.

Human Albumin

This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

PRECAUTIONS

General:

The safe and effective use of **BOTOX® COSMETIC** depends upon proper storage of the product, selection of the correct dose, and proper reconstitution and administration techniques. Physicians administering **BOTOX® COSMETIC** must understand the relevant neuromuscular and/or orbital anatomy of the area involved, as well as any alterations to the anatomy due to prior surgical procedures and avoid injection into vulnerable anatomic areas. Caution should be used when **BOTOX® COSMETIC** treatment is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle(s).

Reduced blinking from **BOTOX® COSMETIC** injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve disorders. In the use of **BOTOX®** for the treatment of blepharospasm, one case of corneal perforation in an aphakic eye requiring corneal grafting has occurred because of this effect. Careful testing of corneal sensation in eyes previously operated upon, avoidance of injection into the lower lid area to avoid ectropion, and vigorous treatment of any epithelial defect should be employed. This may require protective drops, ointment, therapeutic soft contact lenses, or closure of the eye by patching or other means.

Inducing paralysis in one or more extraocular muscles may produce spatial disorientation, double vision or past pointing. Covering the affected eye may alleviate these symptoms.

Caution should be used when **BOTOX® COSMETIC** treatment is used in patients who have an inflammatory skin problem at the injection site, marked facial asymmetry, ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin or the inability to substantially lessen glabellar lines by physically spreading them apart as these patients were excluded from the Phase 3 safety and efficacy trials.

Needle-related pain and/or anxiety may result in vasovagal responses, (including e.g., syncope, hypotension) which may require appropriate medical therapy.

Injection intervals of **BOTOX® COSMETIC** should be no more frequent than every three months and should be performed using the lowest effective dose (See Adverse Reactions, Immunogenicity).

Information for Patients

Patients or caregivers should be advised to seek immediate medical attention if swallowing, speech or respiratory disorders arise.

Drug Interactions

Co-administration of **BOTOX® COSMETIC** and aminoglycosides¹ or other agents interfering with neuromuscular transmission (e.g., curare-like nondepolarizing blockers, lincosamides, polymyxins, quinidine, magnesium sulfate, anticholinesterases, succinylcholine chloride) should only be performed with caution as the effect of the toxin may be potentiated.

The effect of administering different botulinum neurotoxin serotypes at the same time or within several months of each other is unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin.

Pregnancy: Pregnancy Category C

Administration of **BOTOX® COSMETIC** is not recommended during pregnancy. There are no adequate and well-controlled studies of **BOTOX® COSMETIC** in pregnant women. When pregnant mice and rats were injected intramuscularly during the period of organogenesis, the developmental NOEL (No Observed Effect Level) of **BOTOX® COSMETIC** was 4 U/kg. Higher doses (8 or 16 U/kg) were associated with reductions in fetal body weights and/or delayed ossification.

In a range finding study in rabbits, daily injection of 0.125 U/kg/day (days 6 to 18 of gestation) and 2 U/kg (days 6 and 13 of gestation) produced severe maternal toxicity, abortions and/or fetal malformations. Higher doses resulted in death of the dams. The rabbit appears to be a very sensitive species to **BOTOX® COSMETIC**.

If the patient becomes pregnant after the administration of this drug, the patient should be apprised of the potential risks, including abortion or fetal malformations that have been observed in rabbits.

Carcinogenesis, Mutagenesis, Impairment of fertility

Long term studies in animals have not been performed to evaluate carcinogenic potential of **BOTOX® COSMETIC**.

The reproductive NOEL following intramuscular injection of 0, 4, 8, and 16 U/kg was 4 U/kg in male rats and 8 U/kg in female rats. Higher doses were associated with dose-dependent reductions in fertility in male rats (where limb weakness resulted in the inability to mate), and

testicular atrophy or an altered estrous cycle in female rats. There were no adverse effects on the viability of the embryos.

Nursing mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **BOTOX® COSMETIC** is administered to a nursing woman.

Pediatric use: Use of **BOTOX® COSMETIC** is not recommended in children.

Geriatric use

The two clinical studies of **BOTOX® COSMETIC** did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. However, the responder rates appeared to be higher for patients younger than age 65 than for patients 65 years or older. (See: CLINICAL STUDIES)

There were too few patients (N=3) over the age of 75 to allow any meaningful comparisons.

ADVERSE REACTIONS

General:

BOTOX® and **BOTOX® COSMETIC** contain the same active ingredient in the same formulation. Therefore, adverse events observed with the use of **BOTOX®** also have the potential to be associated with the use of **BOTOX® COSMETIC**.

The most serious adverse events reported after treatment with botulinum toxin include rare spontaneous reports of death, sometimes associated with anaphylaxis, dysphagia, pneumonia, and/or other significant debility. There have also been rare reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease. (See: WARNINGS). New onset or recurrent seizures have also been reported, typically in patients who are predisposed to experiencing these events. The exact relationship of these events to the botulinum toxin injection has not been established. Additionally, a report of acute angle closure glaucoma one day after receiving an injection of botulinum toxin for blepharospasm was received, with recovery four months later after laser iridotomy and trabeculectomy. Focal facial paralysis, syncope and exacerbation of myasthenia gravis have also been reported after treatment of blepharospasm.

In general, adverse events occur within the first week following injection of **BOTOX® COSMETIC** and while generally transient may have a duration of several months or longer. Localized pain, infection, inflammation, tenderness, swelling, erythema and/or bleeding/bruising may be associated with the injection.

Glabellar Lines

In clinical trials of **BOTOX® COSMETIC** the most frequently reported adverse events following injection of **BOTOX® COSMETIC** were headache*, respiratory infection*, flu syndrome*, blepharoptosis and nausea.

Less frequently occurring (<3%) adverse reactions included pain in the face, erythema at the injection site*, paresthesia* and muscle weakness. While local weakness of the injected muscle(s) is representative of the expected pharmacological action of botulinum toxin, weakness of adjacent muscles may occur as a result of the spread of toxin. These events are thought to be associated with the injection and occurred within the first week. The events were generally transient but may last several months or longer.

(* incidence not different from Placebo)

The data described in Table 4 reflect exposure to **BOTOX® COSMETIC** in 405 subjects aged 18 to 75 who were evaluated in the randomized, placebo-controlled clinical studies to assess the use of **BOTOX® COSMETIC** in the improvement of the appearance of glabellar lines (See: CLINICAL STUDIES). Adverse events of any cause were reported for 44% of the **BOTOX® COSMETIC** treated subjects and 42% of the placebo treated subjects. The incidence of blepharoptosis was higher in the **BOTOX® COSMETIC** treated arm than in placebo (3% vs. 0).

In the open-label, repeat injection study, blepharoptosis was reported for 2% (8/373) of subjects in the first treatment cycle and 1% (4/343) of subjects in the second treatment cycle. Adverse events of any type were reported for 49% (183/373) of subjects overall. The most frequently reported of these adverse events in the open-label study included respiratory infection, headache, flu syndrome, blepharoptosis, pain and nausea.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not be predictive of rates observed in practice.

TABLE 4.

Adverse Events by Body System	Percent of Patients Reporting Adverse Events	
	BOTOX® Cosmetic (N=405) %	Placebo (N=130) %
Overall	44	42
Body as a Whole		
Pain in Face	2	1
Skin and Appendages		
Skin Tightness	1	0
Digestive System		
Nausea	3	2
Dyspepsia	1	0
Tooth Disorder	1	0
Special Senses		
Blepharoptosis	3	0
Musculoskeletal System		
Muscle Weakness	2	0
Cardiovascular		
Hypertension	1	0

Adverse Events Reported at Higher Frequency (>1%) in the **BOTOX® COSMETIC** Group Compared to the Placebo Group

Immunogenicity

Treatment with **BOTOX® COSMETIC** may result in the formation of neutralizing antibodies that may reduce the effectiveness of subsequent treatments with **BOTOX® COSMETIC** by inactivating the biological activity of the toxin. The rate of formation of neutralizing antibodies in patients receiving **BOTOX® COSMETIC** has not been well studied.

The critical factors for neutralizing antibody formation have not been well characterized. The results from some studies suggest that botulinum toxin injections at more frequent intervals or at higher doses may lead to greater incidence of antibody formation. The potential for antibody formation may be minimized by injecting the lowest effective dose given at the longest feasible intervals between injections.

Rx Only

*Marks owned by Allergan, Inc.

Based on package insert 71711US13S revised January 2005

Manufactured by: Allergan Pharmaceuticals Ireland
a subsidiary of: Allergan, Inc., 2525 Dupont Dr., Irvine, CA 92612

Reference:

1. Wang YC, Burr DH, Korthals GJ, Sugiyama H. Acute toxicity of aminoglycoside antibiotics as an aid in detecting botulism. *Appl Environ Microbiol* 1984; 48:951-955.