



## THE ALLIANCE FOR PATIENT ACCESS

### Principles of Evidence-Based Medical Policy making

#### Summary

1. *Evidence-based medical policy making should be based upon an up-to-date, scientifically valid, and comprehensive review of the evidence of the effectiveness and safety of each option considered under a policy.*
2. *Reviews of evidence supporting a medical policy should clearly identify the strengths and limitations of the scientific evidence for each option discussed under a policy.*
3. *Reviews of evidence supporting a medical policy should clearly distinguish between clinical evidence of effectiveness and safety versus economic information about the value of each option discussed under a policy.*
4. *When applying scientific evidence from clinical studies to an individual patient, one must consider how the individual's characteristics compare to those of the populations included in the clinical studies.*
5. *Individual patient management must be left to the judgment of the treating provider and the informed choice of the patient.*

#### Principle 1:

**Evidence-based medical policy making should be based upon an up-to-date, scientifically valid, and comprehensive review of the evidence of the effectiveness and safety of each option considered under a policy.**

With the range of options for diagnosing and treating medical conditions increasing at a rapid pace and with the cost of those options pressing against limited budgets, professional societies, health plans and payers, employers, and patient and consumer groups are developing evidence-based medical policies aimed at promoting medical decision making to achieve improved health outcomes within acceptable budget limits. For such evidence-based policies to be successful, these must be grounded in evidence that is (1) up-to-date, (2) scientifically valid and (3) comprehensive. If evidence supporting a policy is out-of-date, the policy will not be accepted by providers or patients who will be familiar with newer technologies or more recent data not considered in the policy. Therefore, policies should be reviewed on a periodic basis to make sure that they reflect current evidence. If the type of evidence supporting a policy is not consistent with current standards of accepted evidence, then providers will not accept the evidence as being valid or relevant to their decision making. If the evidence is not comprehensive—i.e., important options are not considered or the evidence base excludes important data for one option but not another—providers and patients will infer that the policy is not relevant to their decision making.

**Principle 2:**

**Reviews of evidence supporting a medical policy should clearly identify the strengths and limitations of the scientific evidence for each option discussed under a policy.**

A medical policy will be acceptable to providers and patients only insofar as the evidence supporting the policy can withstand careful scrutiny of its timeliness, comprehensiveness and its validity. Medical policies should be accompanied by written documentation of the evidence considered in developing the policy. Such written documentation should clearly describe (1) the criteria used to identify the evidence to be considered, (2) the range of studies/papers reviewed, (3) the criteria for including or excluding evidence from the assessment of effectiveness and safety (or other relevant outcomes), (4) the application of those criteria to the evidence identified, (5) the effectiveness and safety (or other relevant outcomes) reported in the studies included, and (6) the strengths and limitations of each study. If the evidence supporting one treatment option is substantially different in scientific quality from the evidence supporting another treatment option, this should be made clear in the written statement supporting a medical policy. Option A cannot meaningfully be compared with option B if the quality of the scientific evidence supporting the two is vastly different. The lack of data to evaluate the safety and effectiveness of an option should be acknowledged expressly. The absence of head-to-head data among products should not be considered evidence of no difference between the products—absence of data is just that—no evidence.

**Principle 3:**

**Reviews of evidence supporting a medical policy should clearly distinguish between clinical evidence of effectiveness and safety (or other clinical outcomes) versus economic information about the value of each option discussed under a policy.**

With increased pressure on healthcare budgets, many medical policies consider not only scientific evidence of effectiveness and safety (or other clinical outcomes) but also consider the economic impact of the options considered. Costs and clinical outcomes may be combined in summary measures, such as cost-effectiveness ratios, cost-utility ratios or net cost-benefit values. Regardless how economic data are reported in an evaluation supporting a medical policy, it is critical that medical policy making clearly distinguish between what has been shown to be effective and safe—as a matter of science—versus the economic impact of treatment options and value-for-money preferences. An option that is the most effective and safe among alternatives may or may not be the most costly option. The effectiveness and safety of that option as a scientific matter is unchanged by its cost—cost enters into the analysis only in terms of value-for-money. Even when an option is excluded from coverage by a health benefits plan based upon the plan's assessment of high incremental cost for the clinical improvement that may be achieved, some patients may be willing to pay the incremental cost to receive the marginal benefit. Those patients should be given accurate information about the relative clinical outcomes of the various options separate from information about the costs of those options.

**Principle 4:**

**When applying scientific evidence from clinical studies to an individual patient, one must consider how the individual's characteristics compare to those of the populations included in the clinical studies.**

Scientific evidence comprises studies that enroll populations of patients. Results are generally presented comparing means or mean differences between groups. While these analyses can be highly informative, they do not necessarily predict the outcome of individual patients. Many factors may contribute to the

effectiveness or failure of a therapy, including genetic makeup, concomitant medications, comorbid conditions, diet, age and other features. Analysis of study results among prospectively identified subsets may help identify which patients within a larger group may obtain more versus less benefit from therapy, but even then, subset analyses may not predict outcomes in individual patients.

**Principle 5:**

**Individual patient management must be left to the judgment of the treating provider and the informed choice of the patient.**

Medical policies may be used for many purposes—e.g., to help inform decision making, for payer coverage decisions, as evidence of standards of medical practice. However, medical policies must not be self-executing determinants of patient care. Individual treatment decisions must remain a matter of provider judgment and patient choice considering evidence of the effectiveness and safety of treatment options, the relationship between study populations and individual patient characteristics, the providers' experience with the various options and professional judgment and individual patient values and preferences. Medical policies can be critical to inform decision making, but ultimately, the decision as to which treatment option a patient will receive must be left to the judgment of the provider and the informed choice of the patient.

**Case Study: Low vs High Osmolar Contrast Media**

There are two main classes of iodinated radiographic contrast media used in contrast-enhanced procedures, such as contrast CT scans, intravenous urography, venography and angiography: older, high osmolality contrast media (HOCM) and newer, low osmolality contrast media (LOCM). Clinical studies performed in the 1980's showed that LOCM were safer than HOCM<sup>(1),(2),(3)</sup> in reducing the risk of major and minor adverse events. The studies showed that the choice of agent was a major determinant of risk of adverse event—so-called “high risk” patients receiving LOCM were at lower risk of adverse event than “low risk” patients receiving HOCM. However, because LOCM were more than 10-times the cost of HOCM, several professional societies and payers developed policies recommending or covering LOCM only for patients meeting certain high risk criteria.

Even though a clinical study comparing LOCM vs HOCM showed that age >60 was a risk factor for adverse events<sup>(4)</sup>, Medicare developed and maintained a policy limiting coverage to patients meeting other high risk criteria—ignoring the age criterion altogether<sup>(5)</sup>.

The American College of Cardiology developed a policy in which the College concluded: “*There are no conclusive data to support the universal use of nonionic contrast agents in routine cardiac catheterization, in view of the increased cost.*”<sup>(6)</sup> How could cost affect the scientific assessment as to whether or not the clinical evidence supported the universal use of LOCM?

Over time, with more agents and certain changes in market dynamics, the cost differential between LOCM and HOCM narrowed substantially, and effective 2005, Medicare agreed to pay for LOCM in all patients in whom the agents are ordered.

This case study involved several examples of medical policy making that considered only part of the evidence base—not the whole evidence base. Medicare ignored the risk factor of age because it would have required universal coverage of LOCM at a time when Medicare was concerned about the potential cost implications of such a policy. The ACC policy statement mixed scientific conclusions with cost conclusions, possibly because the committee was concerned about issuing a statement that could be used as evidence to require universal use of LOCM at a time when payers were covering LOCM only for patients meeting certain high risk criteria. Ultimately, medical policy making evolved to reflect the scientific evidence supporting universal use of LOCM—but only after market dynamics resulted in a more favorable cost-effectiveness assessment.

1. Palmer FJ. Australas Radiol. 1988 Nov;32(4):426-428.
2. Wolf GL, Arenson RL, Cross AP. AJR Am J Roentgenol. 1989 May;152(5):939-944.
3. Katayama H, Yamaguchi K, Kozuka T, et al. Radiology. 1990 Jun;175(3):621-628.
4. Steinberg EP, Moore RD, Powe NR, et al. N Engl J Med. 1992;326(7):425-430.
5. See, e.g., 42 C.F.R. § 414.38 (1996).
6. Ritchie JL, Nissen SE, Doubles JSJr, et al. American College of Cardiology Cardiovascular Imaging Committee. J Am Coll Cardiol. 1993;21(1):269-273.

**Case study: Medicare policy on neurotoxins**

Botulinum neurotoxins are derived from the bacterium Clostridium botulinum and block the release of acetyl choline from cholinergic nerve terminals. Botulinum neurotoxins are among the most potent neurotoxins on Earth. Two botulinum neurotoxins have been approved for clinical use in the U.S.: (1) BOTOX<sup>®</sup> (botulinum toxin type A [Allergan]), and (2) Myobloc<sup>®</sup> (botulinum toxin type B [Solstice]). Although both the type A and type B neurotoxins block release of acetyl choline, the specific mechanisms of action are different. The FDA-approved indications differ between the two agents: BOTOX<sup>®</sup> has been approved by FDA for treatment of blepharospasm, strabismus, cervical dystonia, severe primary axillary hyperhidrosis and glabellar lines (the last as BOTOX<sup>®</sup> Cosmetic);<sup>(1),(2)</sup> Myobloc<sup>®</sup> has been approved by FDA for treatment of cervical dystonia.<sup>(3)</sup> Beyond the FDA-approved uses, uses supported by citations in drug compendia (USP-DI, AHFS and DrugDex) differ between the two agents. Dosing is also very different between the two agents—the average dose in clinical trials among patients with cervical dystonia treated with BOTOX<sup>®</sup> was 236 units; the recommended initial dosage of Myobloc<sup>®</sup> in cervical dystonia is 2,500 to 5,000 units.

Most Medicare contractors have developed coverage policies that address covered and non-covered uses of botulinum toxins. A case in point is CIGNA Government Services, which is the Medicare Part B carrier for Idaho, North Carolina, and Tennessee. In 2006, CIGNA released an LCD which described the two neurotoxins as follows: *“Botulinum toxin type B received FDA approval in December 2000 for, ‘the treatment of patients with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.’ Botulinum type B has not received approval for other indications. In considering the history of botulinum toxin type A (Botox<sup>®</sup>) success in treatment was achieved in multiple off label uses. Its success in the treatment of over-active muscles from blepharospasm, cervical dystonia, spasmodic dysphonia, writer’s cramp and spasticity came from the FDA approved and off-label uses. For purposes of this policy, Botulinum toxin type B (Myobloc<sup>™</sup>) will be covered for the same indications as botulinum toxin type A (Botox<sup>®</sup>). While recognizing that these two agents are not identical, and that therapeutic and adverse event profiles may differ slightly, practitioners may make the decision as to which agent to use in beneficiary care.”*<sup>(4)</sup>

Local providers presented evidence to the carrier about the differences between the neurotoxins and the importance of clearly presenting the evidence supporting each agent while leaving ultimate decision making to the treating provider. Based upon this presentation of evidence, CIGNA added the following note to clarify the differences between the neurotoxins consistent with the evidence: *“PLEASE NOTE: There are several botulinum toxins, currently A through G. Only A & B are now FDA-approved and commercially available. This policy deals ONLY with botulinum toxin A (Botox) and botulinum toxin B (Myobloc). These share certain properties, and some FDA-approvals, as well as certain off-label uses that are addressed in this LCD. However, these two agents are NOT identical, and have differing therapeutic and adverse event profiles. Further, units and dosing are not equivalent, so they are not directly interchangeable with one another. It is expected that providers familiar with and experienced in use of these agents will utilize evidence-based medicine to select the appropriate drug and dose regimen for each patient, condition and use. The choice of which agent to use is up to the practitioner.”*<sup>(5)</sup>

This case study shows the successful application of evidence-based principles to payer policy making. Policy statements that were not consistent with evidence were revised to reflect up-to-date, reliable evidence and to make it explicit that the decision about which therapy a patient should receive should be left to the judgment of the treating provider.

1. Package labeling BOTOX<sup>®</sup> (botulinum toxin type A). Allergan. October 2006.
2. Package labeling BOTOX<sup>®</sup> Cosmetic (botulinum toxin type A). Allergan. January 2005.
3. Package labeling Myobloc<sup>®</sup> (botulinum toxin type B). Solstice. November 2004.
4. CIGNA Government Services. Botulinum toxin. 96-009-15 (effective October 1, 2006).
5. CIGNA Government Services. Botulinum toxin. 96-009-15 LCD 13109 (effective January 23, 2007).