Safe and Effective Versus Reasonable and Necessary: Is the Deck Stacked Against Medical Devices?

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BACKGROUND

In the United States (US), differences in the level of clinical evidence required for premarket FDA approval (PMA) between drugs and medical devices has sometimes led to a higher level of scrutiny by health insurance providers in deciding whether to cover new medical devices.

Overview of the FDA Approval Process for Medical Devices

A 510(K) is a premarket submission made to the FDA to demonstrate that a medical device is at least as safe and effective as (i.e., substantially equivalent to) a legally marketed device that is not subject to PMA.[1]

PMA is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices (i.e., those that support or sustain human life; are of substantial importance in preventing impairment of human health; or which present a potential, unreasonable risk of illness or injury). Therefore, these medical devices require a PMA application under section 515 of the Federal Food, Drug, and Cosmetic Act, in order to obtain marketing clearance.[2]

PMA is the most stringent type of medical device marketing application required by the FDA. PMA approval is based on a determination by the FDA that the PMA contains sufficient valid scientific evidence to assure that the medical device is safe and effective for its intended use(s).[2]

OBJECTIVE

Our objective was to review coverage decisions for medical devices and reasons for noncoverage to determine whether payers are expecting more drug-like evidence.

METHODS

We reviewed Washington (WA) state health technology assessment (HTA) decisions for therapeutics from 2007 through 2012 (http://www.hta.hca.wa.gov/assessments.html). Reasons for noncoverage decisions were identified. As available, information regarding studies required for marketing clearance for products was retrieved from PMAs located on the FDA's Web site (www.accessdata.fda.gov).

RESULTS

We identified 22 therapeutic HTA reviews. Ten reviews resulted in coverage decisions. Twelve reviews included some level of noncoverage for the product or procedure (Table 1). For all noncoverage decisions, the reason was stated as insufficient evidence (i.e., a perceived lack of clinical efficacy evidence); further explanations were given regarding the level of insufficient evidence.

The WA state HTA review of the implantable infusion pump for the treatment of chronic noncancer pain suggested a lack of efficacy evidence. We reviewed the FDA PMA application to determine types of evidence required for marketing (Number P990034B, Medtronic Inc.).[3]

The 2008 WA state HTA decision against implantable infusion pumps for the treatment of chronic noncancer pain was based partly on the fact that *"[t]he only kind of evidence about whether implantable infusion pumps are effective for patients with chronic noncancer pain comes from uncontrolled case series, which are less rigorous clinical studies than controlled trials and therefore may yield less reliable conclusions."*[4] This statement is in contrast to what the FDA requires as evidence of safety and efficacy of implantable infusion pumps prior to marketing. Table 2 presents the contrast in requirements for demonstrating "safe and effective" versus "reasonable and necessary" for implantable infusion pumps.

Table 1. Summary of WA State HTA Therapeutic Technology Reviews: Noncoverage Decisions (2007-2012)

Technology (Decision Date)	Reason for Noncoverage
Pediatric bariatric surgery (8/24/2007)	Not covered for those aged < 18 years
	• Effectiveness – Scientific evidence confirmed that the laparoscopic adjustable gastric banding (LAGB) and Roux-en-Y gastric bypass (RYGB) bariatric procedures are effective at inducing clinically significant weight loss – Scientific evidence confirmed that the LAGB and RYGB bariatric procedures improve at least some medical comorbidity, but a majority of the committee was not confident in the evidence – Scientific evidence did not confirm that the LAGB and RYGB bariatric procedures improve psychological comorbidity
	• Safety – Scientific evidence did not confirm that the LAGB and RYGB bariatric procedures are safe in patients aged < 18 years – Compelling concerns included the lack of evidence on the impact of performing the surgery on patients who have not yet reached full maturity, small but significant surgical complications, and concern over the ability of the patient to legally consent as well as adequately appreciate the long-term impacts
Implantable infusion pumps (8/15/2008)	Not covered for treatment of chronic noncancer pain
	• The best available evidence on infusion pumps has been collected and summarized; however, the overall quality of this evidence is low, methodologically challenged, and not robust
	• Evidence on infusion pumps did not demonstrate net health benefit, because weak or unproven evidence of some effectiveness for certain patients was undermined by significant evidence of serious harms and adverse events associated with the implantation of infusion pumps
	• Infusion pumps were not proven to be equally or more safe and effective
Arthroscopic knee surgery (8/15/2008)	Not covered for osteoarthritis of the knee
	• In many technologies reviewed, trial design resulted in a lack of evidence on whether a treatment works
	• The committee concluded that the current evidence on knee arthroscopy demonstrates that there is not a net health benefit, because there were serious harms and the surgical intervention produced no better outcomes than placebo
Vagal nerve stimulation (VNS) (8/28/2009)	Not covered for depression
	• The committee concluded that the comprehensive efficacy, safety, and cost-effectiveness evidence reviewed shows that VNS technology is unproven compared with alternative management for depression
Electrical neural stimulation (ENS) (10/30/2009)	• Despite identification of over 80 RCTs, the evidence was insufficient to make conclusions about efficacy or effectiveness of ENS, mostly due to the low or very low quality of the studies (small numbers; lack of blinding; intermediate or insufficient outcomes; variable devices, indications, and settings used; inadequate descriptions and controls; inadequate measurements; and conflicting results)
Spinal cord stimulators (SCS) (8/20/2010)	Not covered for chronic neuropathic pain
	• Comprehensive evidence indicated that SCS is less safe than alternative treatments, is an invasive procedure, and has many adverse events
	• The comprehensive evidence about SCS does not prove effectiveness (studies had serious limitations in design, low patient sample sizes, and weak or inadequate comparators)
Knee joint replacement or knee arthroplasty (10/22/2010)	Not covered for multi-compartmental arthroplasty
	• Effectiveness – Knee pain, function, and revision: 1 small retrospective cohort study with very little evidence compared bi-unicompartmental knee arthroplasty with total knee arthroplasty (TKA); no difference was found in functional scores at a minimum of 4-year follow-up, and no revisions were recorded in either group – Two large registry studies comparing revision between bicompartmental knee arthroplasty and tricompartmental TKA found similar revision rates and 2- to 4-year implant survival
	• Safety – One small cohort study reported 2 cases (9%) of intraoperative fracture of the tibial spine in the bi-unicompartmental knee arthroplasty group
Vertebroplasty, kyphoplasty, and sacroplasty (12/10/2010)	• Effectiveness – The overall strength of evidence about effectiveness of vertebroplasty to reduce/relieve pain and improve patient function or quality of life is low; any effect estimate is uncertain and may change with additional research – The low strength of evidence and lack of ability to estimate effect based on evidence is due to the limitations of the studies and their differing outcomes (some studies showed benefit and others did not) – The overall strength of evidence about effectiveness of kyphoplasty to relieve/reduce pain is very low; it is uncertain whether kyphoplasty improves patient functioning and quality of life – There is no evidence of efficacy for sacroplasty
	• Safety – The overall strength of safety evidence is low for vertebroplasty and kyphoplasty and very low for sacroplasty, and evidence-based estimates of effect are uncertain – While rates of serious complications are low for vertebroplasty and kyphoplasty, there are few studies with long-term (> 5-year) follow-up, and comparative studies, especially RCTs, may have too few patients to detect rarer but serious outcomes
Femoroacetabular impingement (FAI) syndrome (9/16/2011)	• Effectiveness – No evidence indicates that 1 specific treatment resulted in better outcomes than another (surgery vs. no surgery, labral debridement vs. refixation, osteoplasty vs. no osteoplasty) – No long-term (≥ 10 years) data are available to assess long-term effectiveness of FAI surgery – There are no published data to test the hypothesis that FAI surgery prevents or delays hip osteoarthritis or the need for total hip arthroplasty.
	• Safety – 6 comparative studies, 31 case series, and 3 case reports reported complications following surgical treatment for FAI in nonathletes or recreational athletes – Neurological complications occurred in 22% of 258 patients undergoing a mini-open procedure
Osteochondral allograft and autograft transplantation (11/18/2011)	Not covered for joints other than the knee
	• Effectiveness – There were substantial differences in patient populations, lesion sizes, comparators, and outcome measures used across studies, making it difficult to draw overall conclusions – All studies are likely affected by confounding by indication; given the high potential for bias in these studies, no firm conclusions can be drawn
	• Safety – Reporting of procedural and longer-term outcomes was inconsistent, even among the RCTs – Differences across studies in patient characteristics and (for comparative studies) comparative procedures, coupled with small numbers of patients in some studies, create misleading percentages for various complications
Microprocessor-controlled lower limb prosthetics (11/18/2011)	Not covered for feet and ankle
	• There is insufficient evidence to evaluate efficacy, effectiveness, safety, subgroups, or economic considerations for microprocessor-controlled prosthetic feet
Bone morphogenic proteins (rhBMP) for use in spinal fusion (3/16/2012)	Not covered for protein-7 (rhBMP-7)
	• rhBMP-7 (OP-1) on-label use: No studies – Although OP-1 received a humanitarian device exemption from the FDA (H020008) for "use as an alternative to autograft in compromised patients [i.e., osteoporotic, smokers, diabetics] requiring revision posterolateral (intertransverse) lumbar spinal fusion, for whom autologous bone and bone marrow harvest are not feasible or are not expected to promote fusion," the pilot and pivotal trials evaluated primary (not revision) posterolateral fusion patients; therefore, these trials are not in accordance with on-label use of OP-1
	• Safety – In most of the data for safety outcomes, the level of evidence is low or insufficient

RCT = randomized controlled trial.

Table 2. Safe and Effective Versus Reasonable and Necessary: Implantable Infusion Pumps

Safe and Effective Excerpts from PMA P990034b[3]	Reasonable and Necessary Excerpts From WA HTA decision[4]
"The non-clinical and clinical testing performed demonstrate a reasonable assurance that the system is safe and effective when used in accordance with product labeling for: 1. The chronic intrathecal infusion of preservative free morphine sulfate sterile solution in the treatment of chronic intractable pain, and 2. The chronic intravascular infusion of floxuridine (FUDR) for the treatment of primary or metastatic cancer." [p 28]	"Based on the deliberations of key health outcomes, the committee decided that evidence on infusion pumps did not demonstrate net health benefit because weak or unproven evidence of some effectiveness for certain patients was undermined by significant evidence of serious harms and adverse events associated with the implantation of infusion pumps. The committee found that infusion pumps were not proven to be equally or more safe or effective, and the cost, while not a significant factor for this decision was likely equivalent. Based on these evidentiary findings, the committee voted 8 to 2 for noncoverage." [p 7]

Such statements demonstrate the disparity between FDA approval of medical devices and payer expectations for efficacy evidence to support coverage decisions.

DISCUSSION

- For Class III medical devices, the FDA determines approval for marketing based on information contained in the PMA, which must include sufficient valid scientific evidence to ensure that the medical device is safe and effective for its intended use. The FDA defines valid scientific evidence as "evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use."[5]
- For drugs, safety and efficacy evidence is considered prelaunch and is typically generated from large RCTs, usually placebo-controlled trials and generally two parallel trials.[6]
- Study designs that the FDA considers scientifically valid to provide information regarding safety and effectiveness of medical devices typically are not perceived as sufficiently valid by payers who evaluate whether the product is reasonable and necessary.
- Drugs may face similar challenges; however, the evidence requirements from the FDA (for safety and efficacy) are typically perceived as valid by payers (reasonable and necessary). For drugs, determination of reasonable and necessary translates into coverage level decisions and tier placement (e.g., tier 1, tier 3), rather than a coverage/noncoverage decision as with medical devices.
- The reasonable and necessary standard is intended to be different from the FDA's standard for approving a product's marketing. CMS uses the standard to determine coverage for FDA-approved products, including off-label uses.
- There will be little controversy around approving the use of a medical device if there is high-quality evidence demonstrating that it clearly saves lives and results in net cost savings for the health care system. However, when preliminary data suggest that an expensive medical device improves short-term quality of life or other intermediate outcomes but long-term outcomes are unknown, coverage decisions are difficult.
- Different groups may reach different decisions based on the same evidence, because they emphasize different aspects of the evidence.[7]

CONCLUSIONS

No roadmap exists for determination of reasonable and necessary levels of evidence for decisions on coverage of medical devices. FDA and payer evidence requirements are not aligned. Moving forward, evidence-generation efforts for medical devices will, in most cases, have to exceed FDA requirements in order for payer evidence needs to be met. The focus on value is only accelerating.

REFERENCES

Please see handout.

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