

**Coverage, Cost-Control Mechanisms, and Financial Risk-Sharing Alternatives of
High-Cost Health Care Technologies**

for

California Institute for Regenerative Medicine

by

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Executive Summary*

The development of new stem cell-based therapies could significantly improve and extend the lives of people with currently incurable medical conditions, such as diabetes, macular degeneration, osteoarthritis, and spinal cord injuries. However, there is concern that these therapies may not be affordable and accessible because of the high research and development costs, coupled with the uncertainty as to whether health plans will cover these therapies. This may result in these therapies not being developed at a rate that corresponds to their economic benefit. This report describes (1) the processes that public and private health plans use to determine whether to cover a new treatment; (2) examples of high-cost treatments that are currently covered by health plans; (3) the current thinking on how coverage decisions would be made for new stem cell-based therapies, and how costs would be controlled; and (4) preliminary financial risk-sharing ideas to improve the likelihood that these therapies would be covered by health plans. This report is based on a literature review and on interviews with officials from Medicare, Medicaid, private health plans, biotech companies, a venture capital firm, a law firm, and universities (see Appendix III for number of interviewees by organizational type). Although the interviewees provided key insights, they are not necessarily representative of their organizational type, because of the limited number of officials interviewed.

Medicare, Medicaid, and private plans each have formal processes and criteria that are used to determine whether a new medical technology will become a covered benefit, and whether there will be coverage restrictions. When insurers evaluate a new

* Citations are included in the main report; they are excluded from the Executive Summary.

treatment, the primary criteria are clinical effectiveness and safety. The cost of the treatment typically does not directly affect a coverage decision, but a higher-cost treatment receives a more stringent medical review, and if it becomes a covered treatment, the insurer may require higher patient cost sharing and impose administrative requirements, which reduce affordability and access.

Many precedents exist for health plans covering expensive treatments, including organ transplants, cord blood transplant therapies, and drugs. Organ transplant costs range from kidney (\$259,000) to heart (\$787,700) to intestine (\$1,121,800). A cord blood bone marrow transplant to treat sickle cell disease costs approximately \$250,000 to \$500,000. Cerezyme, a drug used to treat Gaucher disease, costs \$145,000 to \$290,000 per year. These and other expensive treatments have been used only to treat a small patient population, so the effect at the insurance plan level has been minimal. Further, although insurers decide what care is needed based on medical necessity, these high costs are politically easier to justify because the treatments extend an individual's life, rather than only improving the quality of life.

Insurers currently think that they will use existing processes to make coverage decisions for new stem cell-based therapies, meaning that the therapies will be evaluated primarily for clinical effectiveness and safety. However, this conclusion is tentative because they have not formally considered new stem cell-based therapies, because clinical effectiveness and safety have not been proven, and the cost per patient and the total cost impact cannot yet be precisely estimated. Insurers acknowledge that costs may receive greater consideration in the future, because of the potential for national health reform, and the pressure to reduce the rate of healthcare expenditure increases. As with

other high-cost treatments, insurers plan to manage these cost increases through higher premiums; although the premiums would be reduced if the curative treatments generate long-term cost savings. Insurers will control costs from these therapies using managed care, cost sharing, benefit limitations, and coverage exclusions. Furthermore, Medicare and Medicaid programs will control costs using lower reimbursement rates as compared to private plans.

To improve the likelihood that new stem cell-based therapies will be covered by health plans, financial risk-sharing mechanisms may need to be formulated. The three primary financial issues include the total costs of the therapy, the uncertainty about the level of future health care cost savings that result from therapy, and whether the payer for the therapy will be the beneficiary of any future savings. The cost impact of the therapy is likely to be high, because of a therapy's high cost per patient, and the potentially large number of individuals who might benefit from the therapy. This expense would put additional stress on the Medicare and Medicaid budgets, cause private insurance health premiums to increase, and create an incentive for private plans to avoid covering individuals eligible for a therapy. The financial impact could be lessened if the therapies generate health care cost savings by curing diseases and disabilities that are expensive to treat. When the therapies are introduced, the financial uncertainty of these savings will be the highest. Stem-cell firms may need to bear some of this financial risk, as is being done by multiple sclerosis drug manufacturers in the United Kingdom. Because private plans experience approximately 20 percent annual enrollee turnover, this gives them an incentive to avoid covering an individual eligible for a therapy, not only because of the high cost of the therapy, but also because future healthcare savings might benefit a

different insurer. Risk adjustment and reinsurance programs, which compensate an insurer for covering an individual with above-average risk or high health care expenses, or both, could be used to mitigate this incentive.

In summary, new stem cell-based therapies are likely to be expensive, but Medicare, Medicaid, and private health plans currently intend to use their existing coverage-decision processes, which focus on clinical effectiveness and safety. Costs may receive greater consideration if health reform is passed. Health insurance premiums may increase to cover the costs of these therapies, particularly in the early years, when potential future health care savings are more uncertain, but premiums may decrease in the long run if the therapies cure medical conditions. The therapy costs will be tightly managed through a combination of managed care, cost sharing, benefit limitations, and coverage exclusions. Designing financial mechanisms to share financial risk will reduce the incentive of private insurers to avoid covering individuals eligible for these therapies. This will increase the new therapies' affordability and access, and will help ensure that investors who fund therapy development will be compensated, resulting in a development rate that more closely corresponds to the therapies' benefits.

I. Introduction

New stem cell-based therapies offer the promise of a cure for many diseases and disabilities, because stem cells have the potential to become a multitude of specialized cells that can be used to repair or replace defective or damaged organs. These therapies have the potential to significantly improve and extend the lives of people with currently incurable medical conditions, such as diabetes, macular degeneration, osteoarthritis, and spinal cord injuries. Adult and umbilical cord stem cells currently are used to treat leukemia, lymphoma, and sickle cell disease.

However, there is concern that new stem cell-based therapies may not be affordable and accessible because of the high research and development costs, coupled with the uncertainty as to whether health plans will cover these therapies. This may result in these therapies not being developed at a rate that corresponds to their economic benefit. This report describes (1) the processes that public and private health plans use to determine whether to cover a new treatment; (2) examples of high-cost treatments that are currently covered by health plans; (3) the current thinking on how coverage decisions would be made for new stem cell-based therapies, and how costs would be controlled; and (4) preliminary financial risk-sharing ideas to improve the likelihood that these therapies would be covered by health plans. This report is based on a literature review and on interviews with officials from Medicare, Medicaid, private health plans, biotech companies, a venture capital firm, a law firm, and universities (see Appendix III for number of interviewees by organizational type). Although the interviewees provided key insights, they are not necessarily representative of their organizational type, because of the limited number of officials interviewed.

II. Coverage Decision Processes

New technology coverage decision processes for Medicare, Medicaid, and private health plans primarily evaluate the clinical effectiveness and safety of the treatment. The cost of the treatment typically does not directly affect a coverage decision, but a higher-cost treatment receives a more stringent medical review, and if it becomes a covered treatment, the insurer may require higher patient cost sharing and impose administrative requirements (e.g., prior authorization), which reduce affordability and access.

The different ways costs can enter into a coverage decision are important to understand, because the consideration of costs may become more prevalent in the United States if national health reform is passed, and because costs are used to direct coverage decisions in other countries. In general, there are four types of treatment comparisons. These comparisons differ on two key variables: first, whether the new treatment is being compared to no treatment, or being compared to an existing treatment; and second, whether costs are considered (Figure 1). The first type compares the new treatment to no treatment (or a placebo). It determines whether the treatment is safe (the clinical benefits outweigh the risks), and does not consider costs. The U.S. Food and Drug Administration (FDA) uses this method to approve new drugs and devices. The second type, known as comparative effectiveness, compares the new treatment to existing treatments for the same condition; again, costs are not considered.

Figure 1: Treatment Comparison Types

| | | Costs Considered | | |
|---------------------------------|--------------------|---|---|--|
| | | <u>No</u> | <u>Yes</u> | |
| | | | Comparison Treatments Have Clinically Equivalent Outcomes | Comparison Treatments Have Clinically Different Outcomes |
| Clinical Standard of Comparison | No Treatment | I. Clinical Effectiveness (e.g., FDA) | Not Applicable* | IV. Cost Effectiveness (e.g., NICE) |
| | Existing Treatment | II. Comparative Effectiveness (e.g., AHRQ Center for CER)** | III. Cost Comparison (e.g., insurer's tier-based formulary) | IV. Cost Effectiveness (e.g., NICE) |

*Not Applicable: this box is not applicable because if a treatment is not clinically more effective than not being treated, then when costs are considered, the treatment would be considered inferior.

**AHRQ Center for CER: Agency for Healthcare Research and Quality Center for Comparative Effectiveness Research

Unlike the first two comparison types, the third and fourth comparison types consider costs, with treatments that result in clinically equivalent and clinically different outcomes, respectively. The third comparison type, in which treatments result in clinically equivalent outcomes, the cost comparison dominates. Medicare, Medicaid, and private plans generally cover all FDA-approved drugs, so when two drugs result in clinically equivalent outcomes, insurers may require higher cost sharing (known as tier-based formularies) and additional administrative approval (e.g., prior authorization) for the more expensive drug. With the exception of drugs, treatments rarely result in clinically equivalent outcomes, thus the role for this comparison type is limited.

The fourth comparison type, which evaluates treatments with clinically different outcomes, is more complex. Each treatment's effectiveness needs to be evaluated within a cost effectiveness framework using a common measure, such as the cost per quality-adjusted life-year (QALY), a measure that is used in Europe, but is not formally used in

the United States. While this type of cost effectiveness analysis could be done for an individual, it is more often done in countries with single-payer plans that have a budget ceiling on total health expenditures. For example, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom adopted a cost effectiveness threshold range of between £20,000 and £30,000 (or \$33,000 to \$50,000) per QALY to make its coverage recommendations to the National Health Service.¹

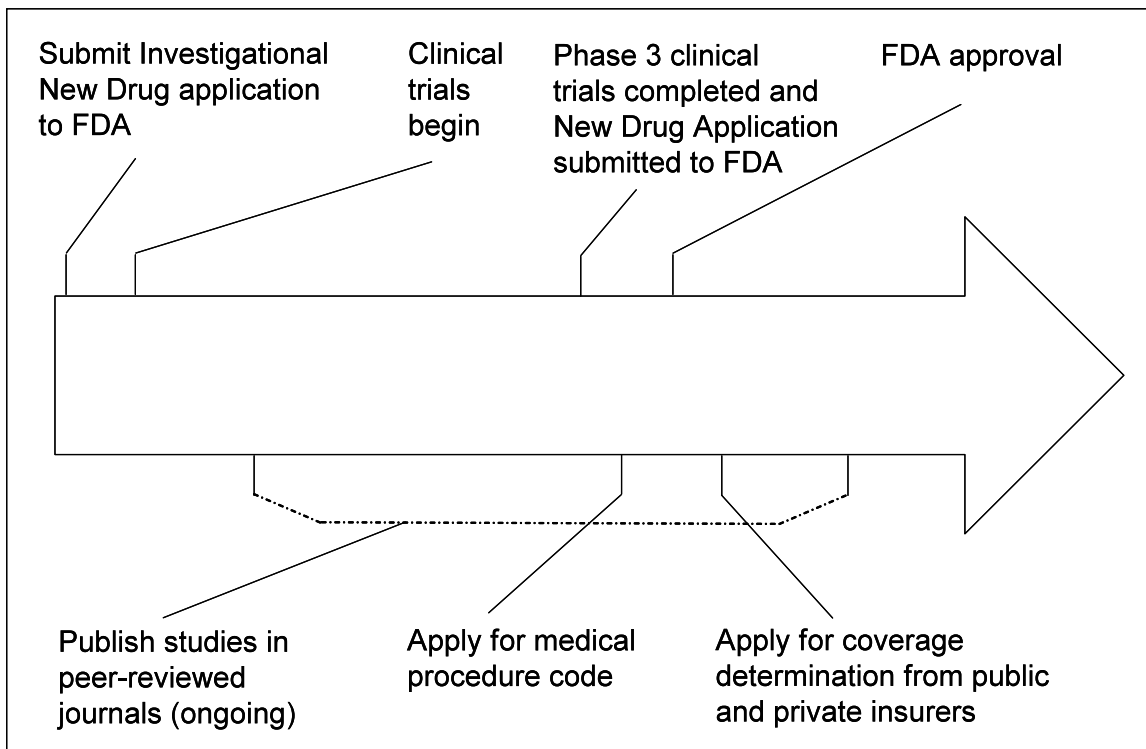
Cost effectiveness analysis in the United States has been largely unpopular, both politically and culturally,² primarily because of concerns that it may lead to rationing of health care. For example, both the Advanced Medical Technology Association (AdvaMed) and Pharmaceutical Research and Manufacturers of America (PhRMA) emphasize that medical devices and pharmaceuticals should be evaluated primarily on clinical outcomes, not cost effectiveness.^{3,4} However, comparative effectiveness is gaining traction in the national health reform debate. The American Recovery and Reinvestment Act of 2009 created the Federal Coordinating Council for Comparative Effectiveness Research, and included \$1.1 billion for comparative effectiveness research.⁵

Treatment Approval and Medical Procedure Coding Process

The process for a new drug to become FDA approved, and become a covered benefit by insurance plans is outlined in Figure 2. To begin clinical trials, an Investigation New Drug application needs to be approved by the FDA. The clinical trial results are submitted to the FDA, and published in peer-reviewed journals. In addition, the FDA may require follow-up research, known as post-marketing study commitments, to continue after initial approval.

To speed up the approval process for serious and life-threatening illnesses, the FDA in 1992 implemented a new regulatory process, “Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses,” known as Accelerated Approval.⁶ A new drug may be tentatively approved, based on its demonstrated effectiveness on a surrogate endpoint, which is a biological marker that is “reasonably likely...to predict clinical benefit” (e.g., in oncology, a reduction in the size of a tumor). Accelerated Approval may be applicable to some types of new stem cell-based therapies, given that they would be used to treat serious and life-threatening illnesses.

Figure 2: Process to Obtain Coverage for a New Treatment



Obtaining a medical procedure code is important for reimbursement purposes, and this process begins prior to FDA approval. The Healthcare Common Procedure Coding System (HCPCS), developed and maintained by the Centers for Medicare & Medicaid Services (CMS), is the major medical procedure code system used for billing in the

United States. Level I HCPCS codes are identical to the Current Procedural Terminology (CPT®), which is owned and maintained by the American Medical Association (AMA). Level II HCPCS codes include products, services, and supplies not identified in the CPT®, including drugs and biologics that are not self-administered, which receive a Level II HCPCS J code.⁷ CMS annually updates the Level II HCPCS codes, which are publicly available.⁸ Applicants for new Level II HCPCS codes that include claims of significant therapeutic distinction must submit information to substantiate those claims.⁹ FDA approval must be obtained by March 31 of the year the Level II HCPCS application is submitted. Until a new code is issued, a temporary code is sometimes used.

Once firms obtain FDA approval for a new drug or treatment, they apply for coverage to public and private insurers. In general, public and private health plans do not cover treatments prior to FDA approval, because the treatment is considered experimental. Initially, coverage decisions are sometimes made on a case-by-case basis. Once a new drug is established as the standard of care, systematic coverage becomes available for either all individuals, or a patient population with particular indications.

Medicare Coverage Decision Process

Medicare is the largest single payer of health care services in the United States, with 44 million beneficiaries and a budget of \$420 billion in FY2009.¹⁰ While Congress has the authority to change Medicare benefit categories, CMS makes the decision whether to approve new treatments,^{11,12} and these decisions also influence private health plans' coverage decisions, because of Medicare's size.¹³ CMS decisions are based on the statutory requirement to cover treatments that are "reasonable and necessary" from a

clinical perspective; neither comparative effectiveness nor cost effectiveness is currently an explicit criterion.^{14,15,16}

CMS and its regional claim-processing contractors have the authority to develop coverage determinations. CMS makes National Coverage Determinations (NCDs) that apply nationally; regional claims contractors make Local Coverage Determinations (LCDs) that only apply to the local region. Because only 10-12 NCDs are made each year, they are reserved for items or services that will (1) result in significant clinical consequences for the beneficiaries; (2) divide the medical community based on the treatment's merits; or (3) significantly impact the Medicare system (see Appendix I for the list of NCDs in 2008-2009).¹⁷ Overall, the vast majority of coverage decisions are LCDs;¹⁸ however, because of the political and financial significance of new stem cell-based therapies, an NCD would likely be issued.

In 2006, CMS issued the guidance document, *National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development*, which describes an NCD with ongoing data collection as a condition of coverage.¹⁹ This program applies to items and services for which a coverage determination cannot be made, because of a lack of evidence, but the item or service has promising potential based on the existing evidence. Coverage with Evidence Development (CED) may be applicable to new stem cell-based therapies that are currently in clinical trials. Since its inception, six CEDs have been approved (see Appendix II for the list of CEDs).²⁰

Medi-Cal Coverage Decision Processes

Medicaid is a joint federal-state program. The federal government mandates that states cover broad categories of benefits, such as inpatient hospitalization and physician

services, but each state determines whether particular items and services are covered within these categories. For example, optional Medicaid coverage areas include chiropractic, podiatry, and audiology services.²¹

Because state Medicaid policies vary, we chose to describe California's Medi-Cal coverage determination policy, because CIRM is located in California, and because of the large size of Medi-Cal. Medi-Cal generally covers items and services that are a "medical necessity," as described in the California Welfare and Institutions Code (sections 14131-14138). Medi-Cal uses a process similar to Medicare's to evaluate the clinical effectiveness and safety of a new treatment. Items and services are considered for evaluation based on several sources, such as favorable coverage determinations by Medicare or private health plans, and when new CPT® or HCPCS codes are issued. Requiring prior authorization is one example used to control costs. Furthermore, when prior authorization is required, it may only be granted for the lowest-cost treatment that meets the person's medical needs (California Code of Regulations, Title 22, §51003). Medi-Cal covers all FDA-approved drugs, regardless of cost. For example, it covers Herceptin, which is used to treat HER 2+, node positive breast cancer at a cost of \$50,000 per year.^{22,23}

Private Health Plan Coverage Decision Processes

Private health plans have more discretion on what to cover, as compared to Medicare and Medicaid. Private insurers make coverage decisions based on whether the item or service is medically necessary, using technology assessment committees as well as pharmacy and therapeutics committees. These committees focus on evaluating the clinical effectiveness and safety of the new technology; other parts of the insurer's

organization consider costs, and most also use comparative treatment effectiveness versus cost effectiveness analysis.²⁴

To assess a new technology's clinical effectiveness and safety, health plans do internal assessments (e.g., Kaiser Permanente's Interregional New Technologies Committee), or contract with organizations to do technology assessments, such as Blue Cross Blue Shield Association's (BCBSA) Technology Evaluation Center (TEC) and California Technology Assessment Forum. For example, BCBSA TEC determines whether a technology meets its technology assessment criteria. These are: (1) the technology must have received final approval from the appropriate governmental regulatory bodies, such as FDA; (2) the scientific evidence must allow conclusions to be drawn concerning the technology's effect on health outcomes; (3) the technology's beneficial effects must outweigh any harmful effects; (4) the technology must be as beneficial as any established alternatives; and (5) the health improvement must be attainable outside investigational settings.²⁵ However, each BCBSA member plan makes its own coverage decisions.

The cost of the treatment is evaluated separately, and its impact will mostly affect the degree that financial and administrative cost control mechanisms will be implemented (see Table 1 in Section IV).

III. Expensive Covered Treatments

Health plans cover some very expensive treatments, and these precedents offer lessons that are applicable to new stem cell-based therapies gaining coverage. Some of these covered treatments include organ transplants, cord blood transplant therapies, drugs, and mental health services. Although health plans cover these treatments, they

have imposed cost control mechanisms (which will be described in the next section of this report).

Organ transplants have similar attributes to new stem cell-based therapies. Their clinical effectiveness and safety take a long time to establish; both treatments are expensive; and both involve immune-response concerns. Organ transplant costs range from kidney (\$259,000) to heart (\$787,700) to intestine (\$1,121,800).²⁶ The first successful human heart transplant was in the late 1960s,^{27,28} but because the clinical effectiveness and safety of the transplant took time to establish, insurers did not systemically cover heart transplants until several years later. Private insurers were among the first to cover heart transplants, specifically Massachusetts Blue Cross and Blue Shield in 1983, and Blue Shield of California in 1984.²⁹ Medicare started covering heart transplants in 1987. Prior to this, most transplants coverage decisions were made on a case-by-case basis.

Congress also has passed legislation to cover a particular transplant and disease. In 1972, for example, the End Stage Renal Disease (ESRD) Program extended Medicare coverage to people with ESRD.³⁰ It covered kidney transplants and provided coverage for dialysis treatment while the patient waited for a kidney donor.

While Medicare covers most organ transplants, it requires that the clinical benefits outweigh the clinical risks. For example, because of the risks of a pancreas-only transplant, Medicare only covers this transplant for patients who have a history of medically uncontrollable labile (brittle) insulin-dependent diabetes mellitus.³¹

The process that Children's Hospital & Research Center Oakland (CHO), of California, undertook to obtain coverage for bone marrow transplants using cord blood

for sickle cell disease provides another interesting coverage example. In 2000, CHO did its first bone marrow transplant, using cord blood from a relative, for treatment of sickle cell disease. The treatment, which costs approximately \$250,000 to \$500,000, required a multi-year process to gain coverage.³² CHO applied to CMS for a new Level II HCPCS code by submitting evidence and peer-reviewed journal articles indicating the clinical effectiveness and safety of the treatment.³³ CHO then sought approval from insurers on a case-by-case basis. Once the treatment was deemed the standard of care, private plans began to cover this treatment systematically.

In general, before a treatment can become a standard of care, two large randomized controlled trials are required.³⁴ Medi-Cal was one of the last insurers to provide coverage of this procedure, and its reimbursement rates do not cover the full costs. By 2008, most plans covered cord blood transplants for the treatment of sickle cell disease.

As with expensive procedures, expensive drugs also have become covered benefits. Once drugs gain FDA approval, drug manufacturers simultaneously approach Medicare, Medicaid, and private insurers to gain coverage. For example, Cerezyme, manufactured by Genzyme, is used to treat Gaucher disease, a rare metabolic disorder that affects the body's organs and tissues, and can cause extreme disability or death.³⁵ The disease affects approximately 6,000 people worldwide.³⁶ Cerezyme was used to treat 4,500 Gaucher disease patients in 2005, at an annual cost of \$145,000 to \$290,000 per patient.³⁷ Examples of high cost cancer drugs include Genentech's Herceptin (trastuzumab) and Avastin. Herceptin is used to treat HER 2+, node positive breast cancer, costs \$50,000 per year, and improves survival by one year.³⁸ Avastin is used to

treat colorectal cancer; Genentech, its manufacturer, capped the costs at \$55,000 per year for patients below a certain income threshold.³⁹

The above expensive treatments and drugs only applied to a small percentage of the patient population (well below 1 percent) within a given health plan, so their effect was minimal. However, if new stem cell-based therapies benefit a large patient population, their effect on a health plan's costs could be substantial. Further, although insurers decide what care is needed based on medical necessity, these high costs are politically easier to justify, because the treatments extend an individual's life, rather than only improving the quality of life.

IV. Current Thinking on Coverage Decisions and Cost Control Mechanisms

The research costs to bring a drug to market are between \$500 million and \$2 billion.⁴⁰ Once the drug is developed, the manufacturing and delivery costs are typically smaller in comparison, and average about 25 percent of revenues.⁴¹ For new stem cell-based therapies, the research costs will be high for some types of stem cells and for some indications, possibly higher than many drugs. Furthermore, the manufacturing and delivery costs will likely be higher than drugs, because stem cell-based therapies consist of living cells that may need to be individualized, and delivered in a hospital or clinic setting requiring professional healthcare staff.

Although new stem cell-based therapies will be expensive, insurers currently think that they will use existing processes to make coverage decisions for these therapies, meaning that the therapies will be evaluated primarily for clinical effectiveness and safety. However, this conclusion is tentative because they have not formally considered

new stem cell-based therapies, because clinical effectiveness and safety have not been proven, and the cost per patient and the total cost impact cannot yet be precisely estimated.

Insurers acknowledge that costs may receive greater consideration in the future, because of the potential for national health reform and increased pressure to reduce the growth rate of health care expenditures. As with other high-cost treatments, insurers plan to manage these cost increases through higher premiums; the premiums would be reduced if the curative treatments generate long-term cost savings. Insurers will control costs from these therapies using managed care, cost sharing, benefit limitations, and coverage exclusions. Table 1 provides a summary of the cost control mechanisms used by Medicare, Medicaid, and private health insurers.

Table 1: Cost Control Mechanisms

| Cost Control Mechanism | Medicare | Medicaid | Private Plans |
|------------------------|----------|----------|---------------|
| <u>Financial</u> | | | |
| Cost sharing | x | x | x |
| Tier-based formularies | x | x | x |
| Annual benefit cap | | | x |
| Lifetime benefit cap | | | x |
| Reimbursement rates | x | x | |
| <u>Administrative</u> | | | |
| Prior authorization | x | x | x |
| Step therapies | x | x | x |
| Quantity limitations | x | x | x |
| Coverage exclusions | x | x | x |

The financial mechanisms to control costs include cost sharing, tier-based formularies, annual and lifetime benefit caps, and reimbursement rates. Patient cost sharing includes deductibles, co-payments, and co-insurance. Tier-based formularies incorporate different levels of cost sharing, based on the tier that the drug is classified. Drugs in the higher tiers typically cost the insurer more (e.g., branded versus generic),

and a portion of the cost difference is passed on to patients. The portion passed on to patients is typically capped, known as the maximum out-of-pocket level. An annual benefit cap is the maximum amount in benefits that an insurer will pay for a patient in a given year, and a lifetime benefit cap is the maximum lifetime amount. The reimbursement rate paid to physicians, hospitals, device manufacturers, and pharmaceutical firms varies across Medicare, Medicaid, and private plans. Plans that have substantial market power can negotiate reimbursement rates that are lower than the long-run cost to produce the item or service. Medicare and Medicaid typically have lower reimbursement rates as compared to private insurers.

The administrative mechanisms to control costs include prior authorization, step therapies, quantity limitations, and coverage exclusions. An insurer may require prior authorization for treatments or drugs that are expensive, to better ensure they are given to the patient population that is indicated for the treatment or drug. A step therapy is a process where a less expensive drug is tried first to determine if it produces the desired clinical outcomes, prior to switching to a more expensive drug. Quantity limitations restrict the number of services per time period, such as limits on mental health visits. Coverage exclusions might include exclusions for mental health services, dental care, in vitro fertilization, and cosmetic surgery solely for beautification.

Medicare Cost Control Mechanisms

Although comparative effectiveness is not used in Medicare coverage decisions, it does influence the terms under which drugs are available to beneficiaries enrolled in Medicare Part D, the program's drug benefits plan, which is obtained through private insurers. In this plan, insurers are permitted to include incentive-based tier formularies, as

long as the actuarial drug benefit is the same as the standard benefit. Insurers also may require prior authorization, step therapy, and quantity limit restrictions.⁴² The costs to the patient can be substantial. A study of tiering for biologic disease-modifying antirheumatic drugs estimated annual out-of-pocket payments at more than \$4,000 per patient,⁴³ which significantly affects their affordability and access. Furthermore, while Medicare covers most organ transplants, it will only cover up to 36 months of immunosuppressive medications.⁴⁴

New stem cell-based therapy likely would be covered by Medicare Part A if the treatment is provided in a hospital, or by Medicare Part B if the therapy needs to be delivered by a physician intravenously or intramuscularly.⁴⁵ Medicare statutes can limit its ability reduce costs. In *Hays v. Leavitt* (2008), for example, the U.S. District Court for the District of Columbia ruled that Medicare does not have the authority to change a drug's reimbursement level covered under Part B to a level that is based on what it pays for other medically equivalent drugs.⁴⁶ The case involved DuoNeb, an inhalation drug that combined albuterol sulfate and ipratropium bromide into a single dose to treat chronic obstructive pulmonary disease. Medicare changed its policy to reimburse DuoNeb based on the lower reimbursement rate of separate doses of the two drugs. The court ruled that Medicare did not have the authority to change a covered drug's reimbursement rate, which is set by statute at 106 percent of the average sales price.

Medi-Cal Cost Control Mechanisms

Medi-Cal considers comparative effectiveness of drugs and treatments, and will only cover the lowest cost treatment for a given health outcome. Medi-Cal also uses managed care, which may use the cost control mechanisms in Table 1. Because Medi-Cal

primarily serves a low-income population, the cost control mechanisms are more administrative than financial, which might result in the beneficiary not obtaining needed care. Therefore, Medi-Cal may require physicians to obtain prior authorization for a given treatment. Medi-Cal also saves costs by having lower reimbursement rates than Medicare and private plans. Due to California's current budget crisis, effective July 1, 2009, Medi-Cal no longer covers a number of services, including dentistry, speech therapy, podiatry, and chiropractic.⁴⁷ Because new stem cell-based therapies will be expensive, they may be subject to cuts in difficult budget periods, unless it is clear that costs could be recouped because of future healthcare savings due to the curative nature of the treatment.

Private Health Plan Cost Control Mechanisms

Technology assessment committees as well as pharmacy and therapeutics committees evaluate the clinical effectiveness and safety of a new drug or treatment and do not consider cost. The cost of the treatment is evaluated separately, and costs are mitigated through higher premiums and through the use of managed care, cost sharing, benefit limitations, and coverage exclusions. As part of managed care, insurers may require prior authorization for expensive treatments to ensure that the treatment is approved for the patient. For example, guidelines from the major oncology professional associations recommend the use of Herceptin only for individuals who overexpress the HER2 gene.⁴⁸ UnitedHealthcare found that up to 20 percent of women taking Herceptin did not have the required gene screening test, or if they did have a screening test, they did not meet the target threshold indicated for Herceptin use.⁴⁹ Prior authorization would likely be required for expensive new stem cell-based therapy.

Cost sharing includes deductibles, co-payments, and co-insurance, and can be implemented based on preferred provider networks and tiered formularies. Insurer contracts typically have maximum lifetime benefit caps, and may have reduced caps for particular treatments, such as organ transplants.⁵⁰ For biologics, some insurers have created a fourth tier within their formularies that replaces co-payments with high co-insurance (20-40 percent), and which includes pharmacy-specific deductibles and higher annual limits on patient payments.⁵¹ Researchers have found that mental health and substance abuse benefits rarely have maximum lifetime benefit limits, but most had annual limitations on the number of days or visits, or had high cost sharing for these services as compared to other services.⁵²

Insurers also have excluded coverage for mental health services, dental care, in vitro fertilization, and cosmetic surgery solely for beautification.⁵³ However, regulation has limited insurers' ability to exclude or limit coverage. States have mandated that benefits cover various treatments, such as chiropractic care, drug abuse treatment, and fertility treatment. Regulation limits insurers from having different coverage limits for mental health services as compared to all medical/surgical services (e.g., state laws and the Mental Health Parity Act of 1996), or which limits costing sharing differences between mental health and all medical/surgical services (e.g., Mental Health Parity and Addiction Equity Act of 2008).

Several studies have found that coverage decisions vary across plans for new treatments. For example, one study found that coverage for 15 laser therapies significantly varied across plans; indemnity plans were more likely to offer coverage than HMOs, and for-profit plans were more likely to offer coverage than non-profit plans.⁵⁴

Another study found significant coverage variation among private and government health plans for breast and ovarian cancer prophylactic surgery.⁵⁵ When plans covered these surgeries, it was for patient populations who had a strong family history of the specific cancer, or a genetic predisposition.

V. Preliminary Discussion of Financial Risk-Sharing Mechanisms

For a new stem cell-based therapy to be affordable and accessible, health plans need to not only cover the therapy, but also offer coverage to individuals who would benefit from the therapy, and not deny coverage because of pre-existing conditions. To improve the potential for coverage, financial risk-sharing mechanisms may need to be formulated. The three primary financial issues that could limit the therapies from being covered include the total costs of the therapy, the uncertainty about the level of future health care cost savings that result from therapy, and whether the payer for the therapy will be the beneficiary of any future savings. The cost impact of a new therapy could be significant if both the cost per patient is high, and the number of individuals who would benefit from the therapy is high. This expense would put additional stress on the Medicare and Medicaid budgets, cause private insurance health premiums to increase, and create an incentive for private plans to avoid covering individuals eligible for a therapy. The financial impact could be lessened if the therapies generate health care cost savings by curing diseases and disabilities that are expensive to treat. However, because private plans experience approximately 20 percent annual enrollee turnover,⁵⁶ the bulk of these savings might not be realized by the insurance plan that paid for a given therapy. In addition to the potential direct health care cost savings, there may be indirect cost

savings, because diseases and disabilities often result in reduced productivity, missed work, and premature mortality. For example, the direct health care cost attributable to diabetes was estimated to be \$116 billion (or \$6,649 per diabetic) in 2007 in the United States, while the indirect cost was estimated at \$58 billion.⁵⁷

The following risk-sharing mechanisms are designed to either allocate the risk to the entities that can best estimate it, or to reduce the risk. When the therapies are introduced, the financial uncertainty of the potential health care cost savings will be the highest. Stem-cell firms may need to bear some of this financial risk, because they best understand the potential of their therapies. For example, cost savings levels could be guaranteed by stem cell firms, using a similar approach to multiple sclerosis drug manufacturers in the United Kingdom.⁵⁸ After NICE refused to recommend glatiramer and beta-interferon for patients with multiple sclerosis, because of the drugs' high cost per QALY, the Department of Health and drug manufacturers reached an agreement whereby the National Health Services would cover the drugs as part of a 10-year study, and the drug manufacturers would reimburse the Department of Health if the drugs were found to be less effective than £36,000 per QALY.⁵⁹ As compared to the Department of Health, the drug manufacturers better understood the cost effectiveness of their drugs, and had the capacity to bear some of the financial risk.

The main concern of a private insurer is that an individual who is eligible for a new stem cell-based therapy enrolls in its plan, and the plan immediately incurs a large expense, with no clear path for reaping potential future cost savings because of high enrollee turnover. To reduce the financial risk, a reinsurance fund could be created. Health plans could draw from the fund to pay for stem cell-based therapy claims. This

fund could be subsidized by the government, as is the case with state reinsurance plans.⁶⁰ For example, the State of New York subsidizes Healthy New York, a health insurance plan program created in 2000. The reinsurance program pays 90 percent of claims between \$5,000 and \$75,000, which totaled \$62 million in 2006.⁶¹ Reinsurance funds would reduce the incentive for health plans to avoid covering individuals who might be eligible for the therapy.

Reinsurance can be considered a special case of more general risk adjustment programs. A risk adjustment program could subsidize enrollees based on prospective risk factors (e.g., diagnoses), retrospective health care expenses, or a combination of both. A number of insurers already use risk adjustment programs. For example, Medicare uses patient diagnosis information to adjust premium payments to Medicare Advantage plans, as a way to reduce problems associated with adverse selection.⁶² The Medicare risk-adjustment scheme has facilitated the development of special needs plans, such as plans for HIV patients. Because premiums are adjusted to compensate for the additional expected health care costs, these plans have less of an incentive to avoid covering these individuals, or dropping coverage for individuals who are currently covered. Many European countries use risk adjustment, with The Netherlands being one of the most advanced.⁶³

VI. Conclusion

New stem cell-based therapies are likely to be expensive, but they have the potential to significantly extend and improve the lives of people with incurable medical conditions. Medicare, Medicaid, and private health plans will initially use their existing coverage-decision processes to evaluate these new therapies; these processes focus on

clinical effectiveness and safety. Costs may receive greater consideration if health reform is passed. Although treatment costs do not currently influence coverage decisions directly, costs do affect the stringency of medical review, the level of patient cost-sharing, and administrative requirements. Both public and private insurers will use cost control mechanisms such as managed care, cost sharing, benefit limitations, and coverage exclusions, to reduce the economic impact of these new therapies. In addition, public and private plans will cover their increased costs through tax revenues or premium increases, but the cost impact may be mitigated from health care cost savings generated from the therapy.

To improve the likelihood that new stem cell-based therapies will be covered by health plans, financial risk-sharing mechanisms may need to be formulated. These may include stem-cell firms bearing some financial risk, particularly regarding the uncertainty as to whether the therapies will result in future health care cost savings because of potential to cure diseases and disabilities. Risk-adjustment and reinsurance programs, which compensate an insurer for covering an individual with above-average risk or high expenses, or both, could be used to reduce private insurers' incentive to avoid covering individuals who might benefit from an expensive therapy. In turn, this will increase the new therapies' affordability and access, and will help ensure that investors who fund therapy development will be compensated, resulting in a development rate that more closely corresponds to the therapies' benefits.

Appendix I: List of Medicare NCDs for 2008-2009

Medicare National Coverage Decisions (NCDs) for 2009 and 2008 are listed below; each NCD listed contains a hyperlink to the NCD. The list includes NCDs that approved coverage for particular patient indications, and also includes NCDs that denied coverage for the given coverage request. These NCDs as well as additional NCDs can be found by year, beginning in 1985, on the following CMS website:

http://www.cms.hhs.gov/mcd/national_by_year_criteria.asp.

2009 NCDs

1. [Bariatric Surgery for Treatment of Morbid Obesity](#)
2. [Colorectal Cancer Screening Tests](#)
3. [Heartsbreath Test for Heart Transplant Rejection](#)
4. [PET Scans and Positron Emission Tomography \(FDG\) for Oncologic Conditions:](#)
 - a. [PET \(FDG\) for All Other Cancer Indications Not Previously Specified](#)
 - b. [PET \(FDG\) for Brain, Cervical, Ovarian, Pancreatic, Small Cell Lung, and Testicular Cancers](#)
 - c. [PET \(FDG\) for Breast Cancer](#)
 - d. [PET \(FDG\) for Colorectal Cancer](#)
 - e. [PET \(FDG\) for Dementia and Neurodegenerative Diseases](#)
 - f. [PET \(FDG\) for Esophageal Cancer](#)
 - g. [PET \(FDG\) for Head and Neck Cancers](#)
 - h. [PET \(FDG\) for Lung Cancer](#)
 - i. [PET \(FDG\) for Lymphoma](#)
 - j. [PET \(FDG\) for Melanoma](#)
 - k. [PET \(FDG\) for Soft Tissue Sarcoma](#)
 - l. [PET \(FDG\) for Thyroid Cancer](#)
 - m. [PET for Perfusion of the Heart](#)

5. [Sleep Testing for Obstructive Sleep Apnea \(OSA\)](#)
6. [Surgery for Diabetes](#)
7. [Surgical or Other Invasive Procedure Performed on the Wrong Body Part](#)
8. [Surgical or Other Invasive Procedure Performed on the Wrong Patient](#)
9. [Wrong Surgical or Other Invasive Procedure Performed on a Patient](#)

2008 NCDs

1. [Artificial Hearts and Related Devices](#)
2. [Blood-Derived Products for Chronic Non-Healing Wounds](#)
3. [Computed Tomography](#)
4. [Continuous Positive Airway Pressure \(CPAP\) Therapy For Obstructive Sleep Apnea \(OSA\)](#)
5. [Erythropoiesis Stimulating Agents \(ESAs\) in Cancer and Related Neoplastic Conditions](#)
6. [Heart Transplants](#)
7. [Home Prothrombin Time INR Monitoring for Anticoagulation Management](#)
8. [Microvolt T-Wave Alternans \(MTWA\)](#)
9. [Percutaneous Transluminal Angioplasty \(PTA\)](#)
10. [PET for Infection and Inflammation](#)
11. [Thermal Intradiscal Procedures \(TIPs\)](#)

Appendix II: List of Medicare’s National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development

The six Medicare NCDs with Data Collection as a Condition of Coverage (Coverage with Evidence Development) are listed below. Each NCD listed contains a hyperlink to the NCD.

1. [Cochlear Implantation](#)
2. [Chemotherapy for Colorectal Cancer](#)
3. [PET \(FDG\) for Brain, Cervical, Ovarian, Pancreatic, Small Cell Lung, and Testicular Cancers](#)
4. [Implantable Cardioverter Defibrillators \(ICDs\)](#)
5. [PET \(FDG\) for Dementia and Neurodegenerative Diseases](#)
6. [Home Use of Oxygen](#)

Source: http://www.cms.hhs.gov/CoverageGenInfo/03_CED.asp, accessed October 2, 2009.

Appendix III: Number of Interviewees by Organizational Type

This appendix summarizes the 16 interviews we conducted for this report. The majority of the interviews were conducted by telephone; two were conducted via email. For each interview, we told the interviewee that his/her responses would not be attributed to him/her. In order to maintain that confidentiality, the list below includes the number of interviews we conducted by organizational type.

- A. Stem cell company, adult or cord blood (2 separate interviews from 1 company)
- B. Stem cell company, embryonic (1)
- C. Biotech company with high-cost treatment (1)
- D. Company with wide-spread experimental cell transplant therapy (1)
- E. Medicare (2)
- F. Medicaid (Medi-Cal and New York Medicaid) (2)
- G. Private insurers (2)
- H. Venture capitalist (1)
- I. University (2)
- J. Law firm (1)
- K. Other (1)

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