

ALLIANCE FOR REGENERATIVE MEDICINE REIMBURSEMENT PORTFOLIO

OVERVIEW

While FDA approval is critical to market entry, market success only comes when health plans cover the product and pay a reasonable rate for its use. Understanding the importance of the coverage and reimbursement processes used by public and private health plans is just as important as understanding the basic science behind a new regenerative medicine technology. In fact, the realities of insurance payment can, and should, have an important impact on how a company develops a new therapy, from the earliest conceptual days.

An important goal of the Alliance for Regenerative Medicine (ARM) is to provide the membership the tools they need to succeed in the marketplace. Market success is critical to further development of the entire field. These reimbursement briefs are intended to alert the membership to key issues related to health insurance coverage and payment that need attention earlier, not later, in the development process. While not specific to any one type of regenerative medicine product, ARM hopes that these briefs provide the membership with some early warnings about pitfalls that can be avoided by proper planning and action. Many of the corporate members may not have in-house experts in these areas; however, there are consultants who can help management, scientists and investors work through the tasks that are essential to adequate insurance reimbursement.

Regenerative medicine, like all other therapies that are included as health insurance benefits, will be covered by public health plans (primarily Medicare and Medicaid) and private insurance (Blue Cross Blue Shield, Aetna, Cigna, etc.). Each health plan has its own specific characteristics that could affect payment for regenerative medicine therapies, but there are a number of similarities.

One of the major differences between private and public health insurance is that public plans are created by statute and have publicly available regulations and other guidance. As such, the benefit categories in public plans are usually quite specific in their definition and scope, which can affect the way a regenerative medicine therapy is covered and reimbursed. The primary distinction in the private sector is that private plans are not bound by the statutory definitions (although they are not immune from state and federal regulation), and can be more flexible in their benefit design,

but may be more opaque in their decision making than public health insurance programs.

Private health plans are also designed around the kinds of patients they cover. For example, OB and pediatrics care will be covered under virtually any private health plan, but not Medicare. Alternatively, Medicare covers individuals with disability and people suffering end stage renal disease (ESRD). Private health plan coverage is more limited in these areas. In addition, durable medical equipment benefits tend to be more generous in Medicare than in private plans.

An important distinction is that Medicare benefits are consistent and portable. A beneficiary enrolled in regular Medicare will have the same kinds of benefits, deductible and copayments, regardless of where they live, even if they move from one state to another. A person with private health insurance may have to find a new plan if they change jobs or move from one state to another. Private health plans contract with employers, unions and other group purchasers. They may offer a variety of different products according to the nature of the contract that is negotiated. Two companies in the same building may both offer Blue Cross Blue Shield to their employees, but the two plans could look quite different in terms of benefits, costs and other variable. Corporate purchases of health insurance also regularly switch plans from one company to another. This can mean a shift in benefits and change in health providers as different physicians and hospitals are in different networks. This variation is not found in Medicare.

An important similarity is that private health plans often borrow policies from Medicare and Medicaid and have many requirements in common. This facilitates coding, coverage and payment activities that regenerative medicine companies need to pursue. For example, product codes, such as HCPCS codes, are universally adopted by the public and private health plans. All health plans use CPT codes to describe physician services. Private health plans often use Medicare payment rates as the starting point for negotiating their own payments, but are often more generous in their payments than Medicare might be. The kind of medical data needed for coverage decisions by public and private insurance are usually comparable, although statutory standards that are an integral part of public plans can impact coverage decisions in ways that are not seen in private health insurance.

There are several ways Medicare can pay for a drug, biological or device—Part A, hospital inpatient service; Part B, hospital outpatient service, ambulatory surgical center (ASC) or physician office; Part C, Medicare Advantage plan (Medicare managed care); and Part D, Medicare prescription drug benefit. Payment may also be done in conjunction with skilled nursing services, rehabilitation care or home health care, but these are less common settings. Since regenerative medicine can be delivered to a patient in any number of ways, such as injection, infusion, or pill, manufacturers need a basic understanding of each of these reimbursement systems. Private health plans may simply cover regenerative medicine under their medical benefits structure or their prescription drug plan, depending on the application. The segmentation found in Medicare is often not a part of private health insurance.

Regenerative medicine is a new technology, but still has to fall within a defined Medicare benefit and the parameters of one of these Medicare segments in order to be covered for payment. Private health plans reflect many Medicare policies, but the key in the private sector is whether a particular regenerative medicine falls under the medical benefit or the prescription drug benefit. Medicaid is a hybrid state-federal system, with increasing reliance on managed care and strict formularies.

The briefs will not look at every aspect of Medicare, Medicaid or private health plans but will scan the major points that can affect a regenerative therapy and show how various company decisions can affect the way health insurance covers and pays for a particular regenerative medicine product. Since drugs, biologicals, medical devices and combination therapies are treated differently in each segment, decisions made early in the design of the product can impact where it will eventually

fall in the insurance spectrum and the steps that must be completed for successful reimbursement. Each paper on the different segments will describe the key issues for a regenerative medicine product as it works its way through the particular rules of each segment.

Since no health plan will pay for a product or service that is not covered by the plan, a brief analysis of the coverage process for public and private health plans is included.

Separate briefs summarize the path to obtaining a CPT code (physician procedure code) and a HCPCS code (product code), key elements for payment by any health plan. The briefs on inpatient and outpatient hospital payments cover the systems (DRGs and APCs) used to bundle services for payment purposes. Codes are an essential element for successful claims processing in public and private health plans.

Coding and coverage decisions usually precede reimbursement and these briefs will explain the timetables and the relationships between each element.

The first ten briefs examine payment policy as it is currently functioning in public health plans. However, there are numerous pilot projects looking at different ways to organize the financing and delivery of health services. These include bundled payments for hospital services, accountable care organizations (ACOs) and other efforts to improve quality and control spending. A separate brief will discuss the implications of these emerging policies on regenerative medicine.

These documents are not definitive analyses of all aspects of reimbursement issues. The specific facts for each product will dictate the applicability of various rules and policies, and a final reimbursement strategy is only possible when built around the particular needs of an individual product. However, each brief should identify the key issues and problem areas that companies will want to address as they begin planning their market strategies. Companies should consider engaging expert guidance when applying these general payment policies to the specific issues of their individual regenerative medicine product.

TABLE OF CONTENTS

1. CPT CODE AND RELATIVE VALUE DEVELOPMENT PROCESSES
2. HEALTHCARE COMMON PROCEDURE CODING SYSTEM (HCPCS) LEVEL II CODES AND CODING PROCEDURES
3. MEDICARE COVERAGE POLICY
4. MEDICARE PAYMENT IN THE INPATIENT HOSPITAL SETTING (PART A)
5. MEDICARE PAYMENT IN THE HOSPITAL OUTPATIENT DEPARTMENT (PART B)
6. MEDICARE PAYMENT IN THE AMBULATORY SURGICAL CENTER (ASC)
7. MEDICARE PAYMENT FOR PHYSICIANS AND OTHER HEALTH PROFESSIONALS AND PHYSICIAN ADMINISTERED DRUGS (PART B)
8. MEDICARE ADVANTAGE MANAGED CARE PAYMENT POLICY (PART C)
9. MEDICARE PAYMENT FOR PRESCRIPTION DRUGS (PART D)
10. MEDICAID
11. HEALTHCARE REFORM—IMPLICATIONS FOR REGENERATIVE MEDICINE

1. CPT CODE AND RELATIVE VALUE DEVELOPMENT PROCESSES

BACKGROUND

CPT stands for “Current Procedural Terminology”, and the codes are the descriptions of medical procedures used in billing and data collection. The relative value development process translates the CPT code into a payment amount used by Medicare and widely adopted by private health plans. CPT codes and relative values are basic to physician payment, and adequate payment is important to ensuring the use of products and services by physicians. The main issue for regenerative medicine will be whether existing codes and payments are adequate for the work that the physician must perform to administer the regenerative medicine product. If not, then application for new code(s) and payment(s) will be necessary to build the market for the product.

Both processes are run by the American Medical Association and involve all of the medical specialty societies. Representatives of medical societies review all code applications and make recommendations to the CPT Editorial Panel. The Editorial Panel considers all coding requests and makes the final decisions. The CPT list is updated annually, with new codes becoming effective on January 1 of the year after the new code is adopted. Anyone can request a new code and meetings are public. However, the entire process is controlled by organized medicine, which means that companies must maintain good relationships with the coding committees, leaders and staff in the various medical specialty societies.

There are three categories of CPT codes. Category I codes identify procedures and services generally accepted by the medical profession and commonly reimbursed by health plans. Category II CPT codes facilitate data collection on positive health outcomes and quality patient care. They are usually not used for payment purposes. Category III codes are tracking codes for new and emerging technologies, used only for procedures deemed experimental and generally not eligible for insurance payment. Companies seeking new CPT codes will want to focus on Category I as those codes are the only ones with assured payment. Categories II and III are not helpful to market and financial success.

Coding applications require a clinical vignette that describes the typical patient who would receive the procedure(s)/ service(s) including diagnosis and relevant conditions. This same vignette is used during the development of work values by the AMA/Specialty Society Relative Value Scale Update Committee (RUC). A carefully drafted vignette can be a great advantage to the company, while a poorly written one can lead to inadequate codes and payment.

Medicare pays for physicians’ services using a standardized fee schedule based on a resource-based relative value scale (RBRVS). In the RBRVS system, payments for services are determined by the resource costs needed to provide them. The cost of providing each service is divided into three components: physician work, practice expense and professional liability insurance (PLI). Payments are calculated by multiplying the combined relative values of a service by a conversion factor (a monetary amount that is determined by the Centers for Medicare and Medicaid Services).

Annual updates to the physician work relative values are based on recommendations from a committee involving the AMA and national medical specialty societies. The AMA/ Specialty Society RVS Update Committee (RUC) was formed in 1991 to make recommendations to CMS on the relative values to be assigned to new or revised CPT codes. Changes in CPT necessitate annual updates to the RBRVS for the new and revised codes. The role of the companies is usually behind the scenes and focuses most heavily on the practice expense portion of the relative value units.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

A key variable is the amount of payment that will be available to physicians and institutions. CPT codes, and relative values, are particularly important for payments to physicians in any setting, and for determining payments in hospital outpatient departments and ambulatory surgery centers (ASCs). These different fee schedules use the CPT codes as the starting point for identifying the professional service and the institutional costs associated with providing the service.

Key elements are the time it takes to perform the service and the amount of work the physician is required to do to complete the service. For example, a lengthy cardiovascular surgical procedure will be assigned greater value than a simple office based diagnostic service. A new regenerative medicine therapy may require more complex physician work and take extra time than the older service it is replacing. Thus the existing code and payment would be inadequate for the new service. In such a case, a new CPT code and new relative values would be essential parts of the payment structure.

Both the CPT and relative value processes are uniquely driven by the American Medical Association and the various medical specialty societies. While anyone can submit an application for a new CPT code, the manufacturer's journey should start with a conversation with the physician and staff coding experts at the AMA and especially at the medical specialty society representing the clinicians who would use the new product. The support of the specialty society is critical to success. Its absence is a guarantee of failure.

Once the company secures the support of the relevant specialty societies, an application can be submitted to the CPT Editorial Panel. The panel is made up of a subset of all the interested physician specialties and is staffed by the American Medical Association. The Editorial Panel meets three times a year and considers applications and comments from representatives of medical societies. While meetings are public, deliberations are not and the CPT compendium is updated only once a year. Given the CPT calendar, meetings in 2013 are devoted to changes that will be effective in January 2015.

The rigidity of this schedule, which is available on the AMA website, is a factor that has to be considered as companies plan their market launch. Timing of FDA action is critical as CPT will not consider a new code for a product that does not have FDA approval. FDA timing can be difficult to predict, but companies should be prepared to apply for any needed CPT codes as soon as the FDA acts. This means that the

manufacturer has to have everything ready for the application process well in advance of the actual date of application. Otherwise, valuable time can be lost.

The details of the application will vary according to product characteristics and intended use. However, there are a number of general criteria that all applications for Category I codes must meet. They are as follows:

- The proposed descriptor is unique, well-defined, and describes a procedure or service which is clearly identified and distinguished from existing procedures and services already in CPT.
- The descriptor structure, guidelines and instructions are consistent with current Editorial Panel standards for maintenance of the code set.
- The proposed descriptor for the procedure or service is neither a fragmentation of an existing procedure or service nor currently reportable as a complete service by one or more existing codes (with the exclusion of unlisted codes). However, procedures and services frequently performed together may require new or revised codes.
- The structure and content of the proposed code descriptor accurately reflects the procedure or service as typically performed. If always or frequently performed with one or more other procedures or services, the descriptor structure and content will reflect the typical combination or complete procedure or service.
- The descriptor for the procedure or service is not proposed as a means to report extraordinary circumstances related to the performance of a procedure or service already described in the CPT code set.
- All devices and drugs necessary for performance of the procedure or service have received FDA clearance or approval when such is required for performance of the procedure or service.
- The procedure or service is performed by many physicians or other qualified health care professionals across the United States.
- The procedure or service is performed with frequency consistent with the intended clinical use (i.e., a service for a common condition should have high volume, whereas a service commonly performed for a rare condition may have low volume).

- The procedure or service is consistent with current medical practice.
- The clinical efficacy of the procedure or service is documented in literature that meets the requirements set forth in the CPT code change application. Good scientific data published in peer reviewed journals (preferably US) is critical to a successful application and also plays a major role in the ultimate coverage decision made by health plans.

Once a new CPT code has been approved, it automatically moves into the relative value process. As noted this process is also staffed by the AMA and controlled by that organization and the medical specialty societies. The manufacturer has even less of a role than during the CPT application review process. The meeting schedule for the AMA's Relative Value Update Committee (RUC) is also available on the AMA website and is closely tied to the CPT schedule.

While the CPT Editorial Panel is the final decider on the coding applications, the RUC is advisory to the Centers for Medicare and Medicaid Services (CMS). CMS makes the final decisions on all relative values and updates them at the beginning of the calendar year. Because the RUC only considers final recommendations from the CPT Editorial Panel, before they are released to the public, these decisions also don't take effect until later. Thus 2013, and early 2014, RUC meetings are considering changes that will go into effect in the 2015 physician fee schedule.

The RUC prepares recommendations for CMS on two parts of the physician fee schedule—physician work and direct costs of services (practice expenses). Physician work data are captured through specialized surveys conducted by relevant medical specialty societies. Some of the practice expense information comes from the manufacturer and the rest is derived from the RUC process. These recommendations are confidential and submitted to CMS on an annual basis. CMS reviews them, adds a factor for indirect costs and the costs of professional liability insurance and releases the proposed new values for public comment in the Federal Register.

A typical timetable for CPT and RUC review spans at least one year, and can be longer. To illustrate, assume that a company has determined that a new CPT code is needed for its product/service and has secured the support of the relevant medical specialty societies. FDA clearance/approval is final in October 2014. This means that the earliest date a new code and payment rate can become effective will be January 1, 2016. In order to meet the CPT and RUC imposed deadlines, the CPT application must be submitted no later than November 5, 2014. The CPT Editorial Panel will meet to consider the application on February 5-7, 2015. If the application is approved, it will go before the RUC at the April 23-26, 2015 meeting. Quite a bit of work is required before that meeting to develop the data that will support the relative value requests.

If the RUC approves the relative value request (often there are modifications to the request made by the specialty society that are negotiated as part of the RUC process), it will forward the approved recommendations to CMS. Once CMS review is complete the new relative values will be published in the Federal Register during the summer of 2015 as part of the annual proposed rule on the physician fee schedule changes that will take effect in 2016. The final rule is released no later than November 1, 2015. The new CPT codes and their relative values will become effective for payment on January 1, 2016. New codes are often considered "interim" and subject to further comment during 2016. These comments could lead to modifications in the 2017 fee schedule.

The Medicare values are, as noted, frequently used by private health plans as a basis for their own price setting, so these processes should not be taken lightly by any regenerative medicine company. Success requires cooperation with the physician community, strong scientific data that is published, and considerable early planning well in advance of FDA's final action in order to meet all of the timing requirements imposed by the CPT and RUC processes.

2. HEALTHCARE COMMON PROCEDURE CODING SYSTEM (HCPCS) LEVEL II CODES AND CODING PROCEDURES

BACKGROUND

The HCPCS is divided into two principal subsystems, referred to as Level I and Level II of the HCPCS. Level I of the HCPCS is comprised of the numeric CPT codes, used to identify the services of physicians and other health professionals.

Level II of the HCPCS is a standardized alphanumeric coding system that is used primarily to identify products, supplies, and services not included in the CPT codes, such as certain drugs, ambulance services and durable medical equipment, prosthetics, orthotics and supplies (DMEPOS) when used outside a physician's office.

Within CMS there is a HCPCS Workgroup comprised of representatives of the major components of CMS, as well as other consultants from pertinent Federal agencies. The workgroup is responsible for developing and updating the HCPCS Level II codes. These codes are widely used by public and private health plans for billing purposes. The descriptors of the codes identify a category of like items or services and typically do not identify specific products or brand/trade names. HCPCS codes are used to identify regenerative medicine products so they can be properly reimbursed by public and private health plans.

There are several types of HCPCS Level II codes.

National permanent HCPCS Level II codes are maintained by the CMS HCPCS Workgroup. These codes are for the use of all private and public health insurers. Permanent national codes are only updated once a year, on January 1.

National codes also include "miscellaneous/not otherwise classified" codes. These codes are used when a supplier is submitting a bill for an item or service and there is no existing national code that adequately describes the item or service being billed. Miscellaneous codes are to be avoided where possible, as claims processing is often slow and denials are frequent.

Temporary codes are for the purpose of meeting, within a short time frame, the national program operational needs of a particular insurer that are not addressed by an already

existing national code. Decisions regarding the number and type of temporary codes and how they are used are also made by the CMS HCPCS Workgroup. Breakthrough regenerative medicine products should seek one of these codes to accelerate market entry and payment since they can be implemented quickly, thus avoiding the one year delay that normally occurs when a new code is issued. A permanent code will be issued by CMS, usually in the next HCPCS cycle.

Anyone can submit a request for modifying the HCPCS Level II national code set. The HCPCS coding review process is an ongoing continuous process. Requests may be submitted at any time throughout the year. Requests that are received and complete by January 4 of the current year will be considered for inclusion in the next annual update (January 1st of the following year). Requests received on or after January 5, and requests received earlier that require additional evaluation, will be included in a later HCPCS update.

A new or modified code is not established for an item unless the FDA allows the item to be marketed. FDA approval documentation is required to be submitted with the coding request application for all non-drug items. For drugs, FDA approval documentation will be accepted up to March 31 following the application deadline as long as the application is otherwise complete and submitted by the deadline.

All applications are reviewed by CMS staff and a draft recommendation is prepared. These drafts are released in advance of the series of public meetings held to review the applications and draft recommendations. Interested parties are offered the opportunity for public comment. These meetings are held in the May-June timeframe each year. Typically the agenda for a meeting is devoted to a single topic, like drugs or durable medical equipment.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

Even if a company determines that a new CPT code is not necessary for claims processing involving the regenerative medicine product, virtually every product will need a unique HCPCS Level II code for proper identification and payment. While obtaining a HCPCS code is less complicated than the CPT process, the potential for delay of market entry is very real.

Timing is critical since the application must be received by CMS in early January of the year that the new code will be considered. If that deadline is missed, the application goes over to the next cycle. For example, an application received by January 4, 2012 would have been considered during the 2012 cycle and, if approved, would have been effective January 1, 2013. Had the application been submitted in March 2012, it is almost certain that it would not be considered until 2013. If approved in the 2013 cycle, the code would become effective January 1, 2014.

This means that regenerative medicine companies must really be prepared to submit their HCPCS applications no later than the end of the year prior to the year of consideration. While the data that must be submitted with an application are straightforward, nonetheless they must be well organized and make a persuasive case for approval.

Before submitting applications, CMS recommends that manufacturers contact medical directors at public and private health plans to see if these individuals believe a new code is necessary or if an existing code is adequate. The manufacturer should gather this information well before the application deadline in order to make a good decision about proceeding with a request for a new HCPCS code. Even if a company is already convinced a new code is required, this exercise is useful and can support the request for the new code.

As a general rule, companies will want to get a new code for a new product in order to differentiate it from competitive products and to have a basis for trying to establish higher reimbursement. If a new product gets bundled under an existing code, the payment for all products under the code will be the same.

Since manufacturers are dependent on the FDA schedule for review and approval, it is helpful to get an early determination from CMS that the product fits the drug exception to submission of all information by early January. If CMS agrees that the exception applies, this gives the company a little flexibility in the application process. The application for a HCPCS code for a drug can be submitted even if FDA approval is not complete. If the FDA does not act by March 31, CMS delays the application until the next cycle.

A company is free to market its product once the FDA has acted positively, but if there is no HCPCS code in place, the billing entity will have to use a miscellaneous code in its claim for payment. These claims are the last to be processed and are frequently denied. An appeal is then necessary. While appeals are often successful, they carry some processing costs for the billing entity and the delays in payment can be quite frustrating to providers.

3. MEDICARE COVERAGE POLICY

BACKGROUND

Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category). In the absence of a defined benefit category, a product or service cannot be covered by Medicare. National coverage determinations (NCDs) are made through an evidence-based process, with opportunities for public participation. In some cases, CMS' own research is supplemented by an outside technology assessment and/or consultation with the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC). In the absence of a national coverage policy, an item or service may be covered at the discretion of the Medicare contractors based on a local coverage determination (LCD). The vast majority of coverage decisions are made at the local contractor level.

Anyone can request a coverage determination or agency personnel can initiate such an action. Whether the process is a national coverage determination or a local coverage decision, there are specific timeframes and opportunities for public input that must be observed.

All national and local coverage decisions, including pending actions, are publicly available on the CMS website.

The coverage process in Medicare does not look at product cost, which can be advantageous to regenerative medicine therapies that may be costly. Rather the focus is on clinical outcome, which should be a strong point for regenerative medicine. The quality of the scientific data that have been published is critical to successful coverage. Several organizations, such as the Blue Cross Blue Shield Association, have developed criteria to measure the strength of the evidence presented. While details may differ, their basic standards are all very similar. Anyone seeking Medicare coverage can turn to one of these policies to help evaluate the strength of the information that will be provided and get a good idea of how the data will be received. Coverage teams expect the highest levels of data, particularly when products are new and expensive.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

Among the many hurdles that stand between product development and marketing success, health insurance coverage can be one of the most difficult to overcome. The key element to success in the coverage process is the strength of the published data about the effectiveness of the treatment. This means that regenerative medicine manufacturers are going to have to compile data that answer the coverage questions that all insurance medical directors ask. This often goes beyond the data needs imposed by the FDA.

In planning a coverage strategy, companies should begin discussions with CMS coverage staff early in the FDA process, to determine what information CMS will need to respond

favorably and in a timely manner. Since regenerative medicine is a new technological field, it will be important to support any claims with thorough studies that have been published in peer reviewed journals. Medicare and other health plans will be skeptical of "breakthrough" claims that have only weak or limited support in the literature. The planning for coverage, whether Medicare or any other health plan, needs to begin early. Often a study for FDA can be modified to include data collection that will be valuable in the coverage process.

Since there is a preference for studies that have been published in the peer reviewed medical and scientific literature, companies need to consider the time it takes to move a study through the peer review and publication process. This time is part of the overall calendar of events that lead to eventual market entry and success.

It is very important to keep in mind that coverage looks at clinical outcomes in patients. This may be different from benchmarks that the FDA establishes for review and approval of products. The durability of the clinical result is also very important. Health plans often want to see patients followed for a longer time than the FDA may require. In the case of Medicare, it is also important that the published studies include data from Medicare beneficiaries. Studies that do not include Medicare beneficiaries are of little interest or value to the Medicare coverage process.

A strategic decision that needs to be made early is whether to seek a national coverage decision right away or to secure positive coverage action by the local Medicare Administrative Contractors, one at a time. The local process tends to be less rigorous than a national coverage decision, although any local medical director can move consideration to the national office if there is controversy about the new therapy or service. It can be helpful to talk early in the product development process with one or more local medical directors to get their views on whether the therapy in question is one they feel is appropriate for local or national coverage action.

Medicare approval is helpful to coverage by private health plans, but is not a guarantee that the private sector will quickly adopt a Medicare policy. Similarly, private health insurance coverage can be a positive influence on Medicare, but CMS is not obligated to accept the actions of any other health plan and may insist on using its own process in addition.

In preparing to run the coverage gauntlet, regenerative medicine companies need to focus early on the clinical benefit to the patient, establish a strong data base of well accepted clinical information and do as much as possible to coordinate the activities at FDA with those at Medicare to avoid delays in the various approvals that are required before a new product can be successful in the market.

4. MEDICARE PAYMENT IN THE INPATIENT HOSPITAL SETTING (PART A)

BACKGROUND

Hospital inpatient services provided in the traditional fee-for-service program are paid on the basis of predetermined payment rates under the acute inpatient prospective payment system (IPPS). This is a bundled payment which is considered payment in full to the hospital. The IPPS pays per discharge rates that begin with two national base payment rates—covering operating and capital expenses—which are then adjusted to account for two factors that affect hospitals' costs of furnishing care:

- the patient's condition and related treatment strategy, and
- market conditions in the facility's location.

A major drawback for new therapies like regenerative medicine is that the data CMS uses to calculate rates is often one to two years old, meaning that data about new products are often missing from the formula.

To account for the patient's needs, Medicare assigns discharges to 751 severity adjusted diagnosis related groups (MS-DRGs), which group patients with similar clinical problems that are expected to require similar amounts of hospital resources. Each MS-DRG has a relative weight that reflects the expected relative costliness of inpatient treatment for patients in that group. The payment rates are adjusted to reflect local market conditions. In addition, the operating and capital payment rates are increased for facilities that operate an approved resident training program or that treat a disproportionate share of low-income patients. Outlier payments are added for cases that are extraordinarily costly.

Discharge destination and use of a specific drug are occasionally used along with principal diagnosis and procedures in structuring base DRGs.

CMS annually reviews the MS-DRG definitions to ensure that each group continues to include cases with clinically similar conditions requiring comparable amounts of inpatient resources. When the review shows that subsets of clinically similar cases within an MS-DRG consume significantly different amounts of resources, CMS often reassigns them to a different MS-DRG with comparable resource use, or creates a new MS-DRG.

Hospitals with cases treated using certain cost-increasing technologies can receive temporary (two - three years) add-on payments for new technologies. This may be an option for some regenerative medicine products with an important inpatient market segment.

Some cases are extraordinarily costly, producing losses that may be too large for hospitals to offset. Medicare makes extra payments for these so-called outlier cases. The limits on this process, however, may mean that it is not very helpful to new, expensive regenerative medicines.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

Many of the indications now being tested by regenerative medicine companies, such as stroke and cardiovascular conditions, will involve complex patients being treated in the hospital inpatient setting. Medicare's bundled payments for inpatient care can limit the resources available, causing hospitals to be reluctant to embrace expensive technologies and therapies. This price sensitivity needs to be considered by the manufacturer early in the development process. It will be important to demonstrate substantial clinical advantage for the new products, perhaps even showing that use of regenerative medicine displaces older therapies thus freeing up resources to pay for the newer products.

Upon introduction, a new product may be considered for the new technology payments. Manufacturers should review all of the CMS requirements for the program to see if their product can qualify. The additional payment could be very helpful in the initial launch period and manufacturers should consider the requirements early in their product design process to see if it can be possible to qualify.

Companies also need to analyze existing DRG payments for relevant diagnoses before product launch. It may be possible to persuade CMS to make a DRG assignment that provides better reimbursement to the hospital. Demonstrating strong scientific support for the effectiveness and uniqueness of the therapy, along with good cost effectiveness data, will be key to convincing CMS to act on a request for assignment to specific DRG.

Regardless of the success of any of these efforts, new DRG assignment or new technology, inpatient payments are always bundled in Medicare and the pressure on costs is constant. Market return expectations need to be realistic given the structure and relative inflexibility of hospital payment under Medicare.

5. MEDICARE PAYMENT IN THE HOSPITAL OUTPATIENT DEPARTMENT (PART B)

BACKGROUND

Services in the hospital outpatient department are paid based on prospectively determined, bundled payments much like those for inpatient services. The outpatient prospective payment system (OPPS) sets payments for individual services using a set of relative weights, a conversion factor, and adjustments for geographic differences in input prices. Hospitals also can receive additional payments in the form of outlier adjustments for extraordinarily high-cost services, and pass-through payments for some new technologies. The new technology payment systems in the outpatient department are more robust than those available for inpatient care.

The unit of payment under the OPPS is the individual service as identified by CPT code. CMS classifies services into ambulatory payment classifications (APCs) on the basis of clinical and cost similarity. All services within an APC have the same payment rate. In addition, CMS assigns some new services to “new technology” APCs based only on similarity of resource use. Services remain in these APCs for two to three years, while CMS collects the data necessary to develop payment rates for them.

Within each APC, CMS packages integral services and items with the primary service. CMS pays separately for corneal tissue acquisition costs; blood and blood products; and many drugs.

CMS determines the payment rate for each service by multiplying the relative weight for the service’s APC by a dollar conversion factor. The relative weight for an APC measures the resource requirements of the service and is based on the median cost of services in that APC.

One exception to CMS’s method for setting payment rates is the new technology APCs.

Each new technology APC encompasses a cost range, the lowest being for services that cost \$0 to \$10, the highest for services that cost \$9,500 to \$10,000.

In addition to new technology APCs, pass-through payments are another way that the OPPS accounts for new technologies. In contrast to new technology APCs—which are payments for individual services—pass-through payments are for specific drugs, biologicals, and devices.

Drugs and biologicals whose costs exceed a threshold (\$80 per day in 2013) have separate APCs.

Drugs and biologicals that are eligible for separate payment in the outpatient department are normally paid on the basis of average sales price (ASP), plus a six percent handling fee. This is the same system used in the ambulatory surgical center and the physician office. Since the ASP methodology is so widely used by Medicare, it is important that regenerative medicine companies understand how it works and the implications for product development and marketing.

A manufacturer’s ASP must be calculated by the manufacturer every calendar quarter and submitted to the Center for Medicare and Medicaid Services within 30 days of the close of the quarter. For each drug, CMS calculates a weighted average sales price using the data submitted by manufacturers, and then determines the Medicare payment of 106 percent of ASP.

CMS continues to expand the list of drugs and biologicals that are packaged into the APC and to broaden the use of the ASP for those products that are paid separately in the hospital outpatient department.

In cases where the ASP of a new drug during the first quarter of sales is unavailable, payment may be set at 106 percent of the wholesale acquisition cost (WAC), which is the manufacturer’s list price to wholesalers. If the WAC is not yet available for the new drug, payment is based on the invoice price.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

Changing medical practice and technology have made the hospital outpatient department (HOPD) an increasingly important site of hospital service. This means that many of the patients who are candidates for regenerative medicine could be treated in the HOPD exclusively or for part of their therapy. Although Medicare payments in this setting are bundled and pressures to reduce costs are always present, there are several factors that make the HOPD an attractive option for manufacturers of regenerative medicine.

First, there are separate APCs for drugs and biologicals whose costs exceed a threshold, which in 2013 is \$80 per day. CMS reviews the threshold amount each year and has continually adjusted it upward over the life of the PPS system.

Anticipating that regenerative medicine treatments may be expensive, this aspect of the HOPD system may be attractive if outpatient care is appropriate for the patient.

Second, the system has two avenues for separate payment for new technologies and services—pass through payments and new technology APCs. Regenerative medicine therapies that can qualify for these exceptions when they enter the market could benefit from more generous payments in the first two or three years of active sales. At the conclusion of this time, CMS usually bundles the drug, device or therapy into an appropriate APC based on hospital cost data or assigns expensive drugs and biologicals to their own APC if they exceed the cost threshold discussed in the previous paragraph. Nevertheless, these avenues for new products and services can be advantageous for establishing market position and companies should be prepared to seek appropriate assignment by CMS as soon as possible after getting the green light from FDA.

As noted above, the payment rate for separately payable drugs and biologicals is ASP, plus six percent. A company's financial expectations should always incorporate this system for separately paid products used in the hospital outpatient department, ambulatory surgical center or physician office.

Regenerative medicine companies may consider the outpatient department to be a preferred treatment locale for these and other reasons. Planning for this decision should begin early in the product development process so that the company can take full advantage of any opportunities the HOPD payment system may offer. While it is likely that at least some patients will still be admitted as inpatients when they receive the regenerative medicine treatment, the HOPD payment system may influence the design of products, selection of patients or timing of treatments in order to allow companies to take full advantage of any opportunities the HOPD may offer.

6. MEDICARE PAYMENT IN THE AMBULATORY SURGICAL CENTER (ASC)

BACKGROUND

Since 1982, Medicare has covered surgical procedures provided in freestanding or hospital-based ambulatory surgical centers (ASCs). These facilities provide outpatient surgical services to patients who do not require an overnight stay after surgery. In 2011, there were 5,344 Medicare-certified ASCs. Medicare covers about 3600 surgical procedures in the ASC, and the most common ones are cataract removal with lens insertion, upper gastrointestinal endoscopy, colonoscopy, and other eye procedures.

Since ASCs were first covered by Medicare, they have enjoyed robust growth in numbers. That trend has slowed since 2010, largely due to a new payment system that went into effect in 2008, the general slowdown in health spending and the increasing trend of hospital employment of physicians. According to the Medicare Payment Advisory Commission (MedPAC), Medicare payment rates for most ambulatory surgical services have become much higher in hospital outpatient departments (HOPDs) than in ASCs—for 2013, the Medicare rates are 78 percent higher in HOPDs than in ASCs. Although Medicare is an important part of the ASC sector, on average Medicare spending accounts for only about 17 percent of an ASC's overall revenue. However, many private health plans base their payments on a percentage of the Medicare rate. Medicare regulations, known as conditions of coverage, specify standards for administration of anesthesia, quality evaluation, operating and recovery rooms, medical staff, nursing services, and other areas. These requirements are also usually a condition of private payment.

Medicare pays for all procedures that do not pose a significant safety risk when performed in an ASC and do not require an overnight stay. CMS updates the list of approved procedures annually. Private health plans have comparable coverage of surgical procedures in the ASC.

Until 2008, ASCs functioned under their own Medicare fee schedule. However, since then ASC payments have been tied to the structure used in the hospital outpatient department prospective payment system (OPPS). The ASC payment system is also partially linked to the physician fee schedule. The most significant changes in the 2008 revisions included a substantial increase in the number of surgical procedures covered under the ASC payment system, allowing ASCs to bill separately for certain ancillary services, and large changes in payment rates for many procedures.

Like the OPPS, the ASC payment system sets payments for procedures using a set of relative weights, a conversion factor (or base payment amount), and adjustments for geographic differences in input prices. Beneficiaries are responsible for paying 20 percent of the ASC payment rate. The patient out of pocket amount is usually smaller in the ASC than in the HOPD for the same procedure.

Payment rates for most services covered under both systems are less in ASCs for a number of reasons. First, the relative weights are lower in the ASC system. Second, the ASC conversion factor (\$42.92 in 2013) is lower than the OPPS conversion factor (\$71.31 in 2013). CMS also uses a different method to determine payment rates for procedures that are predominantly performed in physicians' offices and that were first covered under the ASC payment system in 2008 or later. Payment for these "office-based" procedures is the lesser of the amount derived from the standard ASC method or the in-office practice expense portion of the physician fee schedule.

The ASC payment system generally parallels the OPSS in terms of which ancillary services are paid separately and which ones are packaged into the payment of the associated surgical procedure. ASCs receive separate payment for the following ancillary services:

- radiology services that are integral to a covered surgical procedure if separate payment is made for the radiology service in the OPSS;
- brachytherapy sources implanted during a surgical procedure;
- all pass-through and non-pass-through drugs that are paid for separately under the OPSS when provided as part of a covered surgical procedure; and
- devices with pass-through status under the OPSS.

ASCs and HOPDs receive the same amount for drugs that are paid for separately under the OPSS and for pass-through devices, usually 106% of the average sales price (ASP). ASP is determined by CMS based on information submitted by

manufacturers. It is the common basis for Medicare payment of most drugs and biologics in the outpatient setting, other than those products covered under Part D, the prescription drug benefit for Medicare.

The unit of payment for the ASC is the individual surgical procedure. Each of the approximately 3,500 procedures approved for payment in an ASC is classified into an ambulatory payment classification (APC) group on the basis of clinical and cost similarity. There are several hundred APCs. All services within an APC have the same payment rate. The ASC system uses the same APCs as the OPSS. Both payment systems are adjusted annually.

As in the OPSS, ASC payment rates are adjusted when multiple surgical procedures are performed during the same operative session. In this case, the ASC receives full payment only for the procedure with the highest payment rate; payments for the other procedures are reduced to one-half of their usual rates.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

At this juncture, it is not clear how frequently or widely regenerative medicine therapies will be used in the ASC. The coverage of services is narrower than the hospital outpatient department and the overall payment structure is substantially less than payments in the HOPD or hospital inpatient setting. Payment for regenerative medicine will only be allowed in the ASC if the product is used in conjunction with an approved ASC service. Also, the ASC typically treats more healthy patients. Various studies have shown that the more complicated the patient, the more likely the case will be done in a hospital, with its broad array of services and support systems. Given the nature of the indications being studied for many regenerative medicine products, such as heart disease or stroke, many patients may not be suitable candidates for procedures in the ASC environment.

However, there are now products in use for wound care and similar conditions that may be very useful in the ASC and contribute significantly to the success of the surgical

treatment. As the technology advances, other uses appropriate to the ASC may emerge. Procedures in ophthalmology and gastroenterology dominate the Medicare services provided in the ASC. Companies targeting conditions in those two areas may find the ASC a congenial setting. Other specialty areas are less common in the ASC so regenerative medicine indications in orthopedics, cardiovascular surgery, or urology may not find the necessary procedure volume for market success in that environment.

Companies should evaluate the potential for the ASC as a service venue, but be mindful of the many limits imposed on that setting by regulators that may narrow the market opportunity, absent a major technological or regulatory change impacting the potential for ASC services.

7. MEDICARE PAYMENT FOR PHYSICIANS AND OTHER HEALTH PROFESSIONALS AND PHYSICIAN ADMINISTERED DRUGS (PART B)

BACKGROUND

Physician services include office visits, surgical procedures, and a broad range of other diagnostic and therapeutic services. These services are furnished in all settings, including physicians' offices, hospitals, ambulatory surgical centers, skilled nursing facilities and other post-acute care settings, hospices, outpatient dialysis facilities, clinical laboratories and beneficiaries' homes. The Medicare definition of "physician" is expansive, including MDs, DOs, dentists, podiatrists, optometrists and chiropractors for services within their defined scope of practice. Under certain circumstances, Medicare will also pay for the services of nurse practitioners and physician assistants.

Medicare pays for physician services based on a list of services (identified by CPT codes) and their payment rates, called the physician fee schedule. In determining payment rates for each service on the fee schedule, CMS considers the amount of work required to provide a service, expenses related to maintaining a practice, and liability insurance costs. The values given to these three types of resources are adjusted by variations in the input prices in different markets, and then a total is multiplied by a standard dollar amount, called the fee schedule's conversion factor (\$34.02 in 2013), to arrive at the payment. For most services, Medicare pays 80 percent of the total, with the patient responsible for the remaining 20 percent. Most beneficiaries have some type of supplemental insurance that covers some or all of the 20 percent copayment.

The payment rate varies by setting, on the assumption that a physician's practice costs are borne by his/her office when performed there and by another party, such as a hospital, when provided in a different setting. The practice expense portion of the payment is thus usually reduced when the physician provides a service outside of the office.

Under the physician fee schedule, the unit of payment is generally the individual service, such as an office visit or a

diagnostic procedure. These products, however, range from narrow services (an injection) to broader bundles of services associated with surgical procedures, which include the surgery and related pre-operative and post-operative visits. All services—surgical and non-surgical—are classified and reported to CMS using CPT codes.

These practice expenses do not include the cost of drugs administered in the physician's office, which are paid under Part B, not the prescription drug benefit Part D. These are paid based on average sales price (ASP), plus a percentage (currently 6 percent) to compensate the physician for handling costs. This limited payment can have a negative impact on the willingness of physicians to use expensive products like regenerative medicine in their offices, particularly if the product handling requirements are complex and expensive to meet. The ASP system, introduced into Medicare in 2005, has been a particular issue for clinical oncology office-based practice, with reports that some physicians were starting to treat Medicare patients at the hospital rather than the office because of the reimbursement issues. ASP is a particularly important consideration for the developing regenerative medicine sector.

A manufacturer's ASP must be calculated by the manufacturer every calendar quarter and submitted to the Center for Medicare and Medicaid Services within 30 days of the close of the quarter. For each drug, CMS calculates a weighted average sales price using the data submitted by manufacturers, and then determines the Medicare payment of 106 percent of ASP, which is effective after a two-quarter lag.

Each report also must be certified by one of the following: the manufacturer's Chief Executive Officer (CEO); the manufacturer's Chief Financial Officer (CFO); or an individual who has delegated authority to sign for, and who reports directly to, the manufacturer's CEO or CFO.

Part B covered drugs and biologicals include drugs infused through DME, certain vaccines (influenza, pneumococcal, and hepatitis B), osteoporosis drugs, oral cancer drugs if the same drug is available in injectable form, anti-nausea drugs used as part of an anticancer chemotherapeutic regimen, erythropoiesis-stimulating agents, blood clotting factors for hemophilia patients, injectable drugs and immunosuppressive drugs for transplant patients. The Medicare program pays 80 percent of the expenditures for Part B drugs and the beneficiary is responsible for the

remaining 20 percent. Some or all of the copayment is usually covered by supplemental insurance in the same manner as other Medicare out of pocket expenses.

In cases where the ASP of a new drug during the first quarter of sales is unavailable, payment may be set at 106 percent of the wholesale acquisition cost (WAC), which is the manufacturer's list price to wholesalers. If the WAC is not yet available for the new drug, payment is based on the invoice price.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

Two critical issues arise for the developing regenerative medicine sector in physician payment. The first relates to the adequacy of payment for the physician services involved in the provision of a regenerative medicine treatment to a patient. It will be important for the manufacturer to make this determination before the product launches because physicians may be reluctant to use the product if the complexity of administration cannot be matched to an adequate payment rate. For new regenerative medicine products that can be used with standardized techniques, such as simple injections or infusions, the issue may never arise. However, as the product is being developed, it will be critical to market success to understand how, and how much, the physician will be paid for performing the service. Manufacturers can work with physician specialty societies to address payment limitations if they have been identified before product launch. Once a product comes to market, it is more difficult to address payment problems on a timely basis and market performance and patient access may suffer as a result.

Proper payment may also require new CPT codes to better describe and value the work the physician is performing when using the new therapy. Manufacturers need to identify this issue early in the development process so they can work with medical societies to obtain new codes on a timely basis.

The second issue relates to the payment for the regenerative medicine product itself. The use of ASP and a limited handling fee has reduced the payment available to physicians in their offices for Part B covered drugs. Many of these are expensive to purchase and require complex storage, preparation and management in the office setting. Increasingly these costs are being shifted to other providers, like hospitals, as physicians change the settings in which they will provide certain drug and biologics. To the extent that the manufacturer expects a strong market to develop in physician offices, the company will need to examine the costs of using the product in the office setting. A therapy that requires complex storage arrangements, is difficult and time consuming to administer, or requires physicians to hire specially trained and skilled clinical personnel may find reluctance on the part of the presumed buyers. Instead of developing an office market, the product may wind up being provided almost entirely in the hospital, with its own set of payment rules that differ greatly from those under which physicians operate. The 6 percent handling fee is a modest "profit" over the cost of the drug or biologic, so careful consideration will be needed on pricing points if the company is to succeed with the physicians and encourage them to use the treatment in the office setting.

8. MEDICARE ADVANTAGE MANAGED CARE PAYMENT POLICY (PART C)

BACKGROUND

The Medicare Advantage (MA) program allows Medicare beneficiaries to receive their Medicare benefits from private plans rather than from the traditional fee-for-service (FFS) program. Under some MA plans, beneficiaries may receive additional benefits beyond those offered under traditional Medicare and may pay additional premiums for them. Medicare pays plans a capitated rate for the 26 percent of beneficiaries enrolled in MA plans in 2012.

Available MA plans include health maintenance organizations (HMOs), preferred provider organizations (PPOs), private fee-for-service (PFFS) plans, and special needs plans (SNPs). For payment purposes, there are two different categories of MA plans: local plans and regional plans. Local plans may be any of the available plan types and may serve one or more counties. Regional plans, however, must be PPOs and must serve all of one of the 26 regions established by CMS. Each region comprises one or more entire states.

Under the MA program, Medicare buys insurance coverage for its beneficiaries from private plans with payments made monthly. The coverage must include all Medicare Part A and Part B benefits except hospice. All plans, except PFFS plans, must also offer an option that includes the Part D drug benefit. Plans may limit enrollees' choices of providers more narrowly than under the traditional fee-for-service (FFS) program. Plans may supplement Medicare benefits by reducing cost-sharing requirements, providing coverage of non-Medicare benefits, or providing a rebate of all or part of the Part B or Part D premium. To pay for these additional benefits, plans must use their cost savings in providing the

Medicare benefit and may charge a supplemental premium. These plans have become increasingly popular with beneficiaries, but may not be as hospitable to regenerative medicine products that are costly. This is because the managed care plan is able to exercise a greater degree of control over patient choice than is found in the fee-for-service environment.

A plan bidding process partially determines the Medicare payments they receive. Plans bid to offer Parts A and B coverage to Medicare beneficiaries (Part D coverage is handled separately). The bid is usually based on the cost to cover an average, or standard, beneficiary. The bid will include plan administrative cost and profit. CMS bases the Medicare payment for a private plan on the relationship between its bid and benchmark. The benchmark is a bidding target. The local MA benchmarks are determined under statutory formulas whereby county level rates vary depending on several factors.

When a plan offers Part D prescription drug benefits as part of its package, it submits a separate bid for the Part D portion. Payment for the Part D prescription drug portion of the plan benefits is calculated separately, the same way as if the plan were offering a stand-alone prescription drug package.

Aside from a few special payment incentives, payment for regional MA plans is determined like payment for local plans, except that the benchmarks are calculated differently.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

In many respects the issues in MA that can impact therapies like regenerative medicine are similar to the issues in managed care generally. The ability of the plan to limit physician and hospital choice could impact the availability of regenerative medicine to some beneficiaries. Market entry and penetration can be more complicated in a managed care environment.

Although a Medicare beneficiary enrolled in a MA program can access other providers, the beneficiary is responsible for the regular copayments and deductibles of traditional fee for service Medicare when doing so. Since many MA plans have little or no out of pocket expense for beneficiaries, the cost of going out of plan to take advantage of a potentially expensive therapy can be a strong disincentive.

Since MA plans are managed by private health insurance companies, there are always variations in the way each MA plan operates, even though they all have to provide the base Part A and Part B coverage. These differences may be a further deterrent to the use of regenerative medicine, particularly in the early years before the products have achieved wide acceptance.

MA plans now cover about 25 percent of all Medicare beneficiaries and further growth is forecast. Since their profitability depends on finding efficiencies and savings in providing medical services, they may be slow adaptors of the latest therapies, particularly costly ones. This is most likely for

those treatments whose perceived advantages are limited in comparison to current therapies. It is harder to deny the use of true breakthrough therapies, for example cures where none have existed before. However, much of medical development is incremental and plans can easily delay the use of new treatments until those increments have become substantial.

Overcoming these barriers depends in large part on the quality of the science supporting the regenerative medicine. Manufacturers will need to make sure that the data are strong and the products have the active endorsement of leading physicians. It is also important to make sure that manufacturers understand the patient population that has migrated to MA plans. The demographics might not favor the use of particular regenerative therapies, especially ones targeted to “orphan” conditions.

Further, it will be very important to work closely with medical directors in the MA world, making sure that their understanding of the power of regenerative medicine is robust. Companies should plan on a concerted effort that begins well before FDA signs off on a product to build expectation and support for the opportunities that regenerative medicine offers.

9. MEDICARE PAYMENT FOR PRESCRIPTION DRUGS (PART D)

BACKGROUND

In 2006, Medicare began a voluntary outpatient drug benefit known as Part D. A combination of stand-alone prescription drug plans (PDPs) and Medicare Advantage (MA)–Prescription Drug plans (MA–PDs) delivers the benefit. To receive the benefit Medicare beneficiaries must enroll directly in one portal or the other. Dual eligible patients (covered by Medicaid and Medicare) are automatically enrolled in a PDP. More than 30 million beneficiaries are enrolled in Part D through one of these pathways.

In each of 34 geographic regions, plans compete for enrollees on the basis of annual premiums, benefit structures, specific drug therapies covered, pharmacy networks, and quality of services. Plans bear some risk for their enrollees' drug spending. Overall, Medicare subsidizes premiums by about 75 percent and provides additional subsidies for beneficiaries who have low levels of income and assets.

Medicare's payments to plans are determined through a competitive bidding process, and enrollee premiums are tied to plan bids. Medicare does not negotiate directly with pharmaceutical firms over price, as does the VA for example, but leaves that to the individual PDPs.

The standard 2013 benefit includes:

- a \$325 deductible;
- coverage for 75 percent of allowable drug expenses up to a benefit limit of \$2,970;
- a \$4,750 catastrophic limit on true out-of-pocket spending; and
- about 5 percent coinsurance for drug spending above the out-of-pocket threshold.

The gap between the benefit limit and the catastrophic limit must be met by the patient either directly or through supplemental insurance. Costly medications drive beneficiaries into this uncovered space (called the "donut hole") very quickly, so there may be patient and provider resistance to some of the newer, more expensive products, particularly if physicians think the advantages are marginal. The Accountable Care Act includes provisions to eliminate the donut hole by 2020. Approximately 25 percent of beneficiaries reach the donut hole. A smaller percentage actually hit the catastrophic coverage level.

Plans can and often do offer alternative coverage structures. For example, a plan can offer a deductible lower than \$325, or use tiered copayments rather than coinsurance—provided that the alternative benefit meets certain tests of actuarial equivalence. Also, plans may offer additional drug coverage that supplements the standard benefit. Medicare payments to plans do not subsidize such supplemental coverage. The formulary used by plans may differ. Classes of drugs must be covered, but not every drug in a class, so there can be differences in what drugs are actually covered by a plan. Plans can change their formularies annually, so during an open enrollment period beneficiaries usually try to match the plan formulary to their pharmaceutical needs, particularly for long term medications for chronic conditions, and may change plans during the enrollment period as formularies change.

Plans use a variety of techniques to control costs including multiple tiers of drugs with differing costs to patients, step therapy requirements, prior authorization and quantity limits. Many plans have as many as five tiers, with the top tier usually reserved for specialty drugs and the bottom tier made up of preferred generic products.

Beneficiaries can request an exception to the limits in a plan, if a particular drug that is prescribed is not covered in the plan's formulary. There is an appeals process if the exception is denied by the plan.

Each plan submits bids annually to CMS by the first Monday in June. Those bids should reflect the plan's expected benefit payments plus administrative costs after they deduct expected federal reinsurance subsidies. Plans base their bids on expected costs for a Medicare beneficiary of average health. CMS then adjusts payments to plans based on the actual health status of the plans' enrollees. CMS pays plans a monthly prospective payment for each enrollee (the direct subsidy). This payment is adjusted by the enrollee's case mix and other subsidy factors.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

The answer to this question depends in large part on how the regenerative medicine product reaches the patient. If the product is used only in the hospital setting (inpatient or outpatient) Part A or Part B will pay the cost. Part B also covers drugs administered in physician offices. Part D becomes relevant only if the manufacturer has produced the regenerative medicine product to be made available directly to patients through the pharmacy prescription system. Whether the patient takes the therapy for a week or a year, if it is a regular outpatient prescription, then payment will fall into the Part D process. Of course, depending on a particular patient's needs at any given time, the product could be used in multiple settings, triggering payment and coverage by different segments of Medicare.

Many factors will influence a company's decision to be included under the prescription benefit and the decision usually has to be made early in the product's design. The nature of the disease or diseases treated, the expected condition of patients, the appropriate treatment location and potential side effects requiring active medical management are all factors that will influence the outcome. Ease of use by patients is another factor. Economics plays a role as well. If payment under the prescription benefit is not adequate, then companies are not likely to take that path, preferring to keep the payment within the medical benefit structure (this is true of public and private health plans). However, if economics and patient characteristics make the prescription benefit an attractive option, then the company can take the necessary steps in the product development and approval process to make that option available. Analysis of the various Part D options and plan payment rates and policies should be

conducted to aid in this determination. The anticipated elimination of the "donut hole" may ease concerns about the impact of expensive new products, so this policy change should be considered along with other issues in the program as a company decides whether Part D coverage is a useful option.

Assuming the prescription benefit route is a possibility, the anticipated cost of many regenerative medicines could be a barrier to incorporation into a formulary under Part D, except at the highest tiers. That translates into a higher out of pocket expense for many patients. Some patients may be eligible for subsidies, but that is hard to predict. Use of the exceptions process may work in some cases, but that is not a strong basis for a business plan. Very expensive therapies with high out of pocket cost must show more than limited clinical benefits if they are to be accepted by PDPs, patients and physicians. This puts a premium on good science, well communicated by the manufacturer.

Despite the indirect connections between CMS and manufacturers, the plans that run Part D have strong incentives to hold down costs and will be under increasing pressure to do so. This suggests that a Part D strategy should be very carefully analyzed early in product development so that a strong case can be built for proper payment and coverage by the participating plans.

As is almost always the case in healthcare coverage and payment, the strength of the science supporting the "breakthrough" qualities of the product will play a large role in how the product is ultimately received in the Part D system.

10. MEDICAID

BACKGROUND

Medicaid is the main public health insurance program for low-income people in this country. The program is also the dominant source of long-term care coverage in the United States. Medicaid is financed through a federal-state partnership, and each state designs and operates its own program within broad federal guidelines.

Enacted in 1965 by the same legislation that established Medicare, Medicaid is an entitlement program that provides assistance to all individuals who meet the criteria for eligibility. Medicaid now covers over 62 million Americans, more than Medicare or any single private insurer. Beneficiaries include a broad low-income population-- such as pregnant women, children and some parents in both working and jobless families; children and adults with diverse physical and mental health conditions and disabilities; and poor elderly and disabled Medicare beneficiaries (known as "dual eligibles"). Currently Medicaid covers more than 1 in 3 children and over 40% of births. In addition, more than 60 percent of people living in nursing homes are covered by Medicaid.

The Accountable Care Act (ACA) provided for a broad expansion of Medicaid to adults under age 65 with income at or below 138 percent of the federal poverty level (FPL), effective January 1, 2014, with full federal funding for the newly eligible group in the first three years and at least 90 percent funding thereafter. However, following the Supreme Court's decision on the ACA, each state will decide whether or not to implement the Medicaid expansion. There are other changes to Medicaid in the ACA that will affect every state's Medicaid program, regardless of whether the state decides to accept the expansion option. However, the basic format of the federal-state partnership remains.

Medicaid is the main source of coverage and financing for long-term services and supports (LTSS). Nearly 10 million Americans, about half of them elderly and about half of them

children and working-age adults with disabilities, need LTSS. LTSS are largely not covered by either Medicare or private insurance, but Medicaid covers nursing home and other institutional care as well as a broad range of home- and community-based LTSS that support independent living. Medicaid finances 40 percent of all long-term care spending. Over half of Medicaid long-term care spending is for institutional care, but a steadily growing share – 45 percent in 2011, up from 20 percent in 2000 – is going to home and community-based care.

The cost of Medicaid is shared by the federal government and the states. The federal government matches state Medicaid spending according to a formula in the federal Medicaid law. The federal match rate, known as the Federal Medical Assistance Percentage (FMAP), varies based on state per capita income – the lower a state's per capita income, the higher the state's FMAP. The federal floor is a 50 percent match. The current maximum match is 73.4 percent. The federal government funds about 57 percent of total Medicaid spending.

State participation in Medicaid is voluntary but all states now participate. Federal law specifies core requirements that all states must meet as a condition of receiving federal funding. However, beyond the core requirements, states have broad flexibility regarding eligibility, benefits, provider payment, delivery systems and other aspects of their programs. Medicaid really operates as more than 50 distinct programs – one in each state, the District of Columbia, and each of the U.S. Territories. Every state has a document called a Medicaid state plan that describes its program in detail. To make a change in its Medicaid program, a state must submit and receive CMS approval of a state plan amendment. However, states can seek federal waivers to test new approaches to operating their Medicaid programs outside of regular federal rules, with federal Medicaid matching funds.

Medicaid covers a diverse population, including children and parents, pregnant women, people with physical and mental disabilities and chronic diseases of all kinds, and seniors. To address the spectrum of their needs and their limited ability to pay for care out-of-pocket, Medicaid covers benefits typically covered by private insurance, but also many additional services, such as oral and vision care, transportation, and nursing home and community-based long-term care. Services provided by federally qualified health centers and certain other providers are also covered, reflecting the special role of these providers in serving the low-income population. States use numerous tools, such as prior authorization and case management, to manage utilization in Medicaid.

Nearly three-quarters of Medicaid beneficiaries receive some or all of their care through managed care arrangements. States are expanding managed care to more complex populations and are also pursuing managed LTSS. The vast majority of Medicaid enrollees in managed care arrangements are children and parents in low-income families, a relatively healthy population. Increasingly, though, many states are moving individuals with more complex needs, including people with disabilities and special needs and dual eligible beneficiaries, into risk-based managed care plans. In addition, there is growing interest among states in providing long-term services and supports through risk-based plans.

Most Medicaid beneficiaries are entitled to receive the mandatory services listed below, subject to a determination of medical necessity by the state Medicaid program or a managed care plan under contract to the state:

physicians' services; hospital services; (inpatient and outpatient); laboratory and x-ray services; early and periodic screening, diagnostic, and treatment (EPSDT) services for individuals under age 21; federally-qualified health center (FQHC) and rural health clinic (RHC) services; family planning services and supplies; pediatric and family nurse practitioner services; nurse midwife services; nursing facility services for individuals 21 and older; home health care for persons eligible for nursing facility services; and transportation services.

States have flexibility to cover many additional services that federal law designates as "optional" including:

prescription drugs; clinic services; care furnished by other licensed practitioners; dental services and dentures; prosthetic devices, eyeglasses, and durable medical equipment; rehabilitation and other therapies; case management; nursing facility services for individuals under age 21; intermediate care facility for individuals with intellectual disabilities (ICF/ID) services; home and community-based services (including under waivers); inpatient psychiatric services for individuals under age 21; respiratory care services for ventilator-dependent individuals; personal care services; hospice services; and habilitation services.

Medicaid benefits can vary widely from state to state. States cover different optional services. They also define amount, duration, and scope differently. Except for children, states can place limits on covered services – for example, by capping the number of physician visits or prescription drugs that are covered. Also, while federal law includes a "medically necessary" standard to ensure appropriate use of Medicaid services, states define and apply the medical necessity standard somewhat differently.

Although Medicaid is publicly financed, beneficiaries obtain their care primarily from private providers and health plans. States pay physicians, hospitals, and other providers for services furnished to Medicaid beneficiaries, purchasing services on a fee-for-service basis or through risk-based contracts with managed care plans, or by using a combination of these as well as other approaches.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

An insurance program the size of Medicaid is hard to ignore and there is no question that the health reform law will lead to significant program growth. Too many people and too many providers are involved for the regenerative medicine sector to ignore Medicaid altogether. However, the challenges for regenerative medicine companies are multiple and include the fact that each state program is different so multiple and sometimes conflicting layers of regulation are common; that reimbursements tend to be low for all services; that states may be slow to adopt new therapies for budgetary reasons; and that the influence of risk based managed care is pervasive in virtually every state.

Medicaid can present special issues for manufacturers of pediatric therapies or therapies targeted to pregnant women or other patient groups with high levels of Medicaid participation. These economics should be considered early in the product development process.

Given the complexities of Medicaid, it may be hard to address the entire program at one time. Manufacturers may want to consider working with states with Medicaid programs that broadly influence the actions of other states. Alternatively, companies may wish to develop product strategies that rely on Medicare or private health plans to be the early adopters, with Medicaid programs gradually following their lead.

Nonetheless, Medicaid will ultimately be a part of the market for most, if not all, regenerative medicine products. There are many requirements for discounting prices of drugs and biologics sold to the program's beneficiaries. Maintaining adequate pricing is challenging in this environment. These economic realities need to be carefully considered early in the product development cycle. Financial and marketing strategies need to incorporate the fiscal challenges presented by Medicaid.

11. HEALTHCARE REFORM -- IMPLICATIONS FOR REGENERATIVE MEDICINE

BACKGROUND

The Accountable Care Act (ACA) includes a handful of provisions specifically directed at the pharmaceutical industry—an industry user fee, a discount for Medicare Part D members in the “doughnut hole,” larger rebates for Medicaid, a regulatory pathway for biosimilars and new transparency requirements, but not much more. Most of these were part of an overall negotiation between the Administration and Congress with the pharmaceutical industry. By trading dollars to help defray the costs of healthcare reform, the industry was able to halt legislative efforts that would have had a much more negative impact.

While the fiscal impact is not small, particularly as Medicaid expands to cover a greater number of people, most experts have determined that it is not fatal to the industry, although it increases the pressures on the life sciences companies to change their business model in many ways. These revisions are additive to other fundamental changes in healthcare delivery that have been evolving in recent years, such as an increased emphasis on value for patients and payors and a variety of efforts to improve medical outcomes in virtually all delivery settings. While the result could be a better quality of care for more people, there is no question that a major aim of these emerging trends has been to control healthcare spending. In many ways, this is only the most recent element of a more expansive transformation of the industry driven by other state and federal changes and, perhaps more significantly, by broader trends in the marketplace.

The pharmaceutical industry is already responding to many of these changes and that response will continue for years to come as the full impact of the total collection of “health reforms” is realized. Companies that will be introducing new regenerative medicine products will operate in that new environment, but the kinds of reforms going into place may offer more opportunities to the regenerative medicine sector than challenges.

While the ACA brings direct impacts to life sciences companies, it may be the indirect impacts related to the changing nature of their relationships to other sectors and

the choice and consumption of their products that could be an even greater catalyst for transformation.

The primary goal of the ACA is to expand health insurance coverage for populations that have traditionally found it difficult, if not impossible, to secure affordable insurance. The downstream consequences of this decision and its implementation will be much more important to the life sciences industry than the dollars extracted during negotiations between industry and Congress as the law was written. There are three main elements in the law to achieve this ambitious coverage goal. First, health plans’ underwriting techniques, often key to profitability, are curtailed. For example, when the ACA is fully implemented, health plans will not be able to turn people away for pre-existing conditions, impose lifetime or annual caps on benefits and must spend a certain minimum of premiums collected on healthcare services. Their ability to charge based on health status will be limited.

Second, the law creates state health exchanges, essentially a new market for insurance for individuals, small business and others for whom the traditional insurance market has been unavailable.

Third, the law anticipated a significant expansion of Medicaid to provide insurance coverage to the largest segment of the uninsured. The decision of the Supreme Court to lift the mandate that states must expand their Medicaid programs will affect the size of the newly covered population, but many analysts expect that over time, states will fall into line. While expanded health insurance coverage usually means expanded use of health services, including regenerative medicine, the reimbursement rules for Medicaid are notoriously stingy. This may limit the opportunity for market success that could otherwise be anticipated from expanded health insurance coverage.

Since none of the provisions are fully implemented at this time, it is difficult to pinpoint their impact with certainty. However, there are several trends that most parties anticipate as the ACA moves forward.

Health plans will likely face constrained margins and greater competition. In order to maintain profitability they will be forced to become even more efficient in their spending on medical services. They will also seek ways to improve health outcomes among covered lives in order to reduce costs. They will be looking for business partners who can help them transition to a new way of doing business.

Consolidation in the health insurance industry is widely anticipated. Life sciences companies may see a reduction in the number and variety of formularies, and a move by health plans to coalesce around a limited number of standardized formulary models.

Comparative effectiveness will become a more important factor in health plan coverage decisions. New agents with marginal benefits may find market success elusive.

The customer base for pharmaceuticals, primarily physicians, is changing rapidly as doctors consolidate their practices or enter a variety of joint ventures with healthcare networks. The physician may no longer be the sole decider on life sciences products. In fact, non-physician purchasing agents, with an eye to saving money, may assume the role once held by doctors in determining which products will be available for their patients.

In order to remain profitable, health plans will need to find ways to manage the health of enrollees and beneficiaries more effectively. For example, they will need to keep patients with risk factors from progressing to chronic disease. Likewise, they will want to find ways to keep early stage patients from progressing to more serious chronic states.

Payors will also be looking for ways to reduce the rate of hospitalization and the use of expensive procedures. An important part of this effort will be to make sure that enrollees are properly and promptly diagnosed and then provided the most effective therapies. Part of this success will depend on finding ways to increase patient compliance with treatment regimens. Patient compliance is not a new issue, but it has been poorly addressed. Effective medical and cost management will require improvement in this area.

HOW DOES THIS IMPACT REGENERATIVE MEDICINE?

Companies already in the marketplace will need to adapt quickly to the changes coming from so many directions. For those regenerative medicine companies that have yet to enter the market, it is not too late to revise marketing strategies and financial expectations and align them with the emerging new reality.

However, regenerative medicine may find great opportunities in the brave new world of healthcare reform. Examining the challenges that face payors, regenerative medicine may be able to offer effective responses. For example, many products under development are intended to offer a cure where none has existed. To the extent that this future can be realized, the long term costs of caring for a seriously ill person may drop significantly, even if the initial therapy comes at a premium price. The expensive cycle of chronic disease could also change as new interventions reduce the impact of diseases like diabetes.

Many products will be used to increase the effectiveness of current therapies, thus reducing long term costs of care. Improved surgical outcomes, shorter lengths of stay, and reduced readmissions are all part of the payor strategy for profitability. Regenerative medicine can be a key component in all of these efforts. To the extent that regenerative medicine improves the quality of care, better patient compliance could follow.

To succeed, however, regenerative medicines will have to be “breakthroughs”, not merely additive or slight improvements, particularly if they are to command the premium prices that companies seek. Companies will have to provide health plans and providers data that support the effectiveness of the new products in comparison with existing therapies. While such studies are costly, they may be essential to making the case that the regenerative medicine product is clearly superior. Failure to make that case likely means that payors will apply the “least costly alternative” payment rule. This rule says that where different therapies produce similar outcomes, reimbursement will be at the level of the least expensive product or service.

To an increasing degree, the quality of the scientific data offered to payors will be the key to success in the future. Published results will be scrutinized even more carefully than is the case today. Failure to address the fundamental issues facing payors and providers in the new health systems will work against the success of the regenerative medicine industry. Innovation in product outcomes and market analysis will be the keys to the kingdom.