This article evaluates recent trends and challenges in health system management of exceedingly rare genetic diseases, from the perspective of the manufacturer, managed care organization, physician, and actuary.

Managing Drugs for Rare Genetic Diseases: Trends and Insights

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ABSTRACT

Managed care organizations generally pay for expensive drugs that treat rare genetic diseases because few patients have these conditions, the conditions are often life threatening, and the benefit design mandates coverage. In most cases, the cost-control measures and management restrictions applied to many other specialty pharmaceuticals do not make sense for the orphan drugs used to treat extremely rare genetic conditions because treatment alternatives usually are lacking for rare conditions (e.g., Gaucher's disease) and because the per member per month costs for truly rare conditions are low. The increasing number of biologic and injectable therapies for more common conditions, however, is prompting managed care decision makers to manage these new therapies more actively. There is a potential that treatments for rare disorders will be swept up in this broad-based response. This article provides definitions, background, and stakeholder perspectives on this topic and describes recent trends and challenges in health system management of exceedingly rare genetic diseases. The author suggests that current protocols are appropriate for managing rare and ultra-rare diseases, and that applying more active management practices to less rare diseases is neither efficient nor productive; in fact, it may be counterproductive.

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Learning objectives

Upon completion of this activity, participants will be able to:

- Offer several definitions of a "rare" disease.
- Explain perspectives on rare disease management held by many positions within the industry, including that of the manufacturer, an actuary, a physician, and the director of a managed care organization.
- Describe some existing and developing issues and difficult industry decisions related to management of patients with rare genetic diseases.
- Cite comparisons of management of therapies for rare genetic diseases and for more prevalent diseases.
- Formulate an opinion about whether reform of the current management protocols for rare diseases is required.

INTRODUCTION

Most managed care organizations routinely cover specialty pharmaceuticals for their approved indications, a policy that has been welcome (and, perhaps, life-saving) news to sufferers of the least common but most deadly of medical conditions. As stated by the National Organization of Rare Diseases (NORD): "Even though some orphan drugs may be priced higher than commonly used drugs, insurers … recognize that the small number of people using the product in any MCO will usually represent a small overall exposure to the health insurance company" (NORD 2004). With most health systems having internalized that rationale, today's patients who have rare genetic diseases maintain full access to these highly specialized therapies (Milne 2002, U.S. DHHS 2001).

Cost concerns with specialty pharmaceuticals

The heightened, generalized concern of MCOs regarding the high costs of biologic and injectable therapies is understandable. Currently, biological agents are the fastest grow-

ing category of drug expenditures. Moreover, the pipeline is brimming with these expensive and novel therapies (ExpressScripts 2002, Hoffman 2004, Johnson 2004, Rodgers 2003). Payers as well as insurers have valid concerns that certain biologic agents are likely to develop "mission creep," with their clinical use extending well beyond their original indications (Kocs 2003, Cuzzolin 2003, ASCO 2003).

The rising cost of specialty pharmaceuticals troubles insurers, employers, and health systems alike. Anecdotes abound about specialty drug costs for a single patient "breaking the bank" of small state Medicaid plans or private health plans. Many employers wonder if they can pay higher premiums to cover high-tech drugs. Not surprisingly, these cost concerns have translated into various internal management initiatives such as copayments or coinsurance. Yet, should all specialty therapies — including those for the most rare diseases — be aggressively managed to ensure proper use? When does such aggressive management make sense? What are the costs today, and what will they be tomorrow? In short, how can MCOs develop medical or pharmacy policies that continue coverage for ultra-rare genetic diseases while introducing appropriate and necessary controls on biologic and injectable agents used for more common conditions?

This article addresses these questions based on interactions with clinicians, pharmacists, researchers, and administrators in MCOs, insurance companies, employer groups, pharmacy benefit managers (PBMs), specialty pharmacy providers (SPPs), and research-based pharmaceutical and biotech companies. A special debt is due for ideas shared recently by members of the National Steering Committee on Rare Genetic Diseases, a meeting convened in March 2004 by the Zitter Group, under a grant from Genzyme Therapeutics.

HOW RARE IS RARE, AND WHY IT MATTERS

When is a disease rare? For a primary care physician, it might be the condition seen once in a lifetime (Phillips 2004). The World Health Organization states that a rare disorder is one that affects, at most, 0.65 out of every 1,000 individuals; the European Union sets the rate at 5 out of 10,000; the Australians, Japanese, and Americans set countrywide prevalences of 2,000, 50,000, and 200,000, respectively, for a given rare disease (Lavandeira 2002).

In the United States, the definition of rare as less than 200,000, or about 1 per 1,000, is derived from the Orphan Drug Act of 1983. Before passage of the act, many patients with rare diseases did not have access to effective medications (Rados 2003, Schulman 1997).

The 7-year marketing exclusivity and grants provided under the Act prompted development of about 250 orphan drugs in the last 2 decades (Rados 2003, FDA 2004). For MCOs, the 200,000 demarcation provides an arbitrary but useful distinction between truly widespread conditions amenable to biologic therapy — e.g., severe allergic asthma, hepatitis C infections, and rheumatoid arthritis (RA) — and less common disorders. Table 1 shows how these less common diseases also can be subdivided into meaningful categories, ranging from the "near rare" multiple sclerosis (MS) and Crohn's disease, to the "more-common rare" sickle cell ane-

TABLE 1 Diseases treated with biologic or injectable agents

From the common… to the rare… to the ultra-rare

Disease	(U.S.) Prevalence
Psoriasis	5.8–7.5 million
Hepatitis C infections	3.9 million
Rheumatoid arthritis	2.1 million
Severe allergic asthma	500,000
Crohn's disease	380,000–480,000
Multiple sclerosis	400,000
"Rare" is <200,000 as defined by Orphan Drug Act of 1983	
Alpha-1 antitrypsin deficiency	100,000
Sickle cell anemia	91,000
Multiple myeloma	63,000
Cystic fibrosis	30,000
Gastrointestinal stromal tumor	15,000
"Ultra-rare" is generally defined as <10,000	
Fabry's disease	5,000
Gaucher's disease	2,500
Tyrosinemia type 1	2,500
Mucopolysaccharidosis (MPS 1)	200

SOURCES: National Gaucher Foundation; National Heart, Lung, and Blood Institute; Calkins 1986; National Multiple Sclerosis Society; National Institute of Arthritis and Musculoskeletal and Skin Diseases; CDC 1998; Alpha One Foundation; Genzyme Corp.; and Rados 2003.

mia, to the "moderately rare" cystic fibrosis and hemophilia, and finally to the "ultra rare" genetic disorders such as mucopolysaccharidosis (MPS) 1 and tyrosinemia type 1.

Drawing these finer, prevalence-based distinctions among diseases is useful because the prevalence of each disease affects various cost considerations. From the manufacturer's perspective, for example, the development and commercialization costs are proportionally higher for the rarest of the rare diseases. This directly increases drug unit costs (see "The Manufacturer's Perspective" at right). Within each MCO's membership, the disease prevalence also determines the per member per month (PMPM) cost of treatment (see "The Actuary's Perspective" on page 58).

This PMPM perspective on costs for rare diseases is important relative to the use of high-cost biological agents. The majority of biological agents are orphan drugs (Figure 1), an association encouraged by specific incentives within the Orphan Drug Act's legislation (Haffner 2002a) and likely to be strengthened with further elucidation of the human genome (Haffner 2002b). These biological and injectable agents typically cost from $10,000 to $250,000 per year; national costs for these specialty drugs have increased 20 percent annually and are expected to reach $26 billion by 2006 (Tercero 2002, Hesselgrave 2003, *Manag Care* 2004). Injectables are used by only 0.2 percent of the population, while constituting about 8 percent of total medical costs ($140 million for each 1 million insured lives); injectable spending is projected to increase 20 percent to 40 percent annually (Johnson 2004).

Yet relatively little of the estimated $22 billion spent on biological and injectable agents goes to treating ultra-rare genetic diseases. In fact, over 75 percent of specialty drug spending goes to just five categories: oncology,

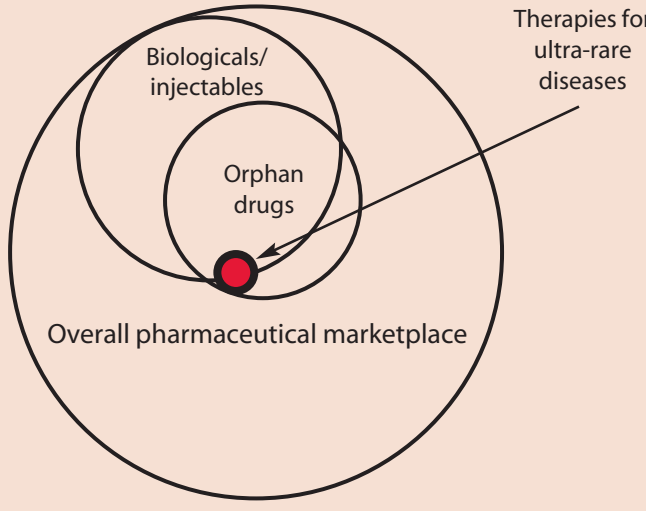
The manufacturer's perspective

Why do drugs for rare and ultra-rare diseases cost so much? The short answer is: because there are so few patients to pay for them. Beyond this obvious need to recoup drug costs and development costs (as much as $500 million per product) from a minuscule patient base, the commercialization costs of these drugs are high relative to other drugs. Extra services that add to incremental and marginal drug costs include patient advocacy and education, physician training and referral networks, inventory management, local/regional case management and regional/national guideline-policy development efforts, and long-term regulatory compliance. A related factor in chronically high costs is the lack of alternative treatments; the small patient-population size discourages development of "me-too" products that, in larger markets or even in "near-rare" markets, normally act to increase competition and reduce prices.

"The simplest thing we do after the research is completed is put the drug in the bottle. The most challenging thing we do is help develop a system that allows patients to be identified, accurately diagnosed, and optimally managed."

—David Meeker, MD, president,
Lysosomal Storage Disease Therapeutics, Genzyme Therapeutics

FIGURE 1 Therapies for ultra-rare diseases — a fraction of the swelling biological/injectable market



LEGEND: Biologicals and injectables will soon make up about a quarter of the overall drug market, which now exceeds $200 billion (*Manag Care* 2004, Hoffman 2004). Most orphan drugs, by definition, are for diseases of <200,000 prevalence, and therapies for ultra-rare genetic diseases are primarily biological or injectable agents. Despite their high unit costs, however, they constitute a relatively small share of the overall biological/injectable marketplace.

HIV/AIDS, renal disease, transplant medications, and hemophilia (CuraScript 2004). Considering just injectables, about 80 percent of spending goes to colony stimulating factors, products for hepatitis C, hemophilia factors, growth hormones, RA, interferons for MS, and intravenous immunoglobulin (Johnson 2004). Rituximab, with clinic and hospital sales of $941 million in 2003 (Hoffman 2004), is a prime example of a costly biologic indicated for a relatively common condition (B cell non-Hodgkin's lymphoma) and prescribed for added off-label uses (Kocs 2003).

Other costly new biological agents aimed at sizable patient populations include gefitinib for lung cancer, omalizumab for severe allergic asthma, etanercept for RA, bortezomib for multiple myeloma, and a range of disease-modifying agents for MS.

This brief review indicates that the biologics and injectables used to treat ultra-rare genetic diseases are not the main drivers of MCO specialty pharmacy costs.

On average, the number of patients with rare diseases in any one plan is simply too low — even with a drug unit cost of $50,000 to $200,000 per year — to increase the typical PMPM by more than a few pennies per month. Better targets for aggressive medical and pharmacy policies are biologic and injectable agents that are used by those patients who have the "more common rare" diseases (Table 1, page 54).

Thus, it may now be useful for MCOs to define "ultra-rare" with an actual numerical prevalence line, below which extra custom management is not productive. For diseases with prevalence above this line, however, some controls may still make clinical and economic sense.

The actuary's perspective

In typical health plans, only 0.1 percent (1 in 1,000) has claims that are over $250,000 to $300,000. The most expensive claims, such as for a patient with Gaucher's disease — where the prevalence is about 1 in 100,000 — are typically a sliver of overall managed care system costs. Per member per month cost for a comprehensive commercial (non-Medicare) managed care member today is about $250 to $350, of which about 15 percent or $40 to $50 goes for drugs. About $5 or $10 of PMPM costs are for biologicals/specialty drugs, which may flow through the prescription drug or medical benefit. Although that may seem like a small fraction of the total cost, even a difference of $5 PMPM is not negligible for some employers.

"Medical management techniques as employed by managed care — for example, routine concurrent review or case management — usually have a limited impact for those few, very expensive cases involving patients with very rare diseases. However, most managed care payers will continue to apply such techniques to ensure that all reimbursed services are medically necessary and are covered under the policy. Adverse selection or random fluctuations can cause a concentration of orphan drug patients that could be financially catastrophic to plans, especially smaller health plans or self-insured employers. As the number of orphan and ultra-orphan drugs increases, the need for a national reinsurance program to spread the risk will increase."

—Bruce Pyenson, FSA, MAAA, principal and consulting actuary, Milliman Inc., New York

MAINTAINING A LIGHT TOUCH IN MANAGEMENT OF THERAPY FOR RARE GENETIC DISEASES

A decade or more ago, the benefit design for injectables and orphan drugs was mostly "silent," a vestige of physician-controlled in-office administration of injectable agents, e.g., steroids and allergy shots. Today, several strategies are used to manage biologic and injectable agents more actively. In most cases, when a specialty product is approved by the U.S. Food and Drug Administration for its isolated condition, the MCO mirrors the approved labeling in benefit design and reimbursement decisions. This is the first step. The other now-familiar management methods that might then be applied to biological therapies include: prior authorization with blocking of off-label use; specialist referral; step therapy; tiered copayments; coinsurance; shifting benefit coverage from medical to pharmacy; management outsourcing to disease management vendors or university-based Centers of Excellence (COE); and the use of specialty pharmacy companies or case management vendors.

Management tactics usually are limited to a referral to a "super specialist" or COE, and aggressive cost-sharing techniques are not applied often to therapies for truly rare diseases. There are several reasons for this, the most immediate of which may be the potentially devastating financial effects of coinsurance on the individual with a rare disease.

If treatment for a rare disease costs $200,000 per year, a seemingly reasonable coinsurance of 20 percent could cost the patient a total of $40,000 per year — which is approximately the average annual income of a U.S. worker. Given that most of the ultra-rare genetic conditions are life threatening, the barriers of both coinsurance and out-of-pocket copayments seem inappropriate.

Beyond the compelling life-or-death aspect of the situation, however, the inappropriateness of these rationing devices also can be defined in economic terms. The economic rationale for copayments and coinsurance is to discourage patients from consuming medical care with a value that is less than the cost to the insurer. Nevertheless, the efficacy of these economic tools depends on an elastic demand curve with choices of many alternative treatments. With drugs for rare diseases, where the demand is inelastic and cost of therapy is extremely high, there are few reasons to support patient cost-sharing once the health insurer has authorized reimbursement for the drug.

Furthermore, while copayments can help avert questionable use (i.e., "Well let's treat just in case…") in many more common diseases, the decision to treat an ultra-rare genetic disorder is usually clearer. The therapies are targeted to physiologic pathways that tend to be highly disease-specific rather than multifactorial (Grabowski 2004). Physician specialists generally know these ultra-rare diseases when they see them and are able to choose the proper therapy with little hesitation (see "The Physician's Perspective" at right). Finally, since the rare condition is so narrowly defined in physiological and genetic terms, there is limited potential for use of the drug to expand beyond the original single indication.

Thus, while MCOs are highly motivated to ensure that biologic and injectable agents are used only for approved conditions, this well-founded desire to discourage inappropriate or questionable use of biologics needs to be instituted carefully — and applied selectively. The traditional techniques usually do not make economic sense in managing the products for the truly rare genetic diseases. This lack of fiscal rationale, combined with the likely lack of in-house clinical expertise on the disease, suggests that a quick referral to a COE (rather than any attempt to monitor with internal guidelines) may be the most efficient approach (see "The Managed Care Director's Perspective" on page 63).

The physician's perspective

As doorkeeper to expensive therapies for most rare diseases, the specialist physician often sets *de facto* policy for managed care organizations, either as part of the MCO's network or from within a university-based Center of Excellence. For example, one new therapy now being handled by such specialists is agalsidase beta for Fabry's disease, a serious metabolic genetic disorder that affects 1 in every 40,000 males. As part of the accelerated review and approval of its recombinant enzyme in April 2003, the manufacturer agreed to work with disease specialists to monitor long-term outcomes and maintain a patient registry. The decision to treat a patient with Fabry's disease depends on the genotype and the presence of progressive disease (Figure 2, page 60); not all patients require immediate treatment, and this difficult decision is a prime example of why the experienced specialist who has seen several of these extremely rare patients is best suited to manage therapy.

Fabry's disease, Gaucher's disease, and mucopolysaccharidosis (MPS 1) are just three types of lysosomal storage diseases (LSDs) that specialist pediatricians can now treat with specific replacement enzymes. Similar orphan drugs eventually may be available for at least 35 other rare lipid disorders (e.g., MPS II, IV, and VI; Niemann-Pick B and C; Pompe disease; and the neuropathic LSDs). Considering that the LSDs represent just one fertile area of ongoing research, the role of specialist physicians as "MCO guides" to the expanding universe of rare disorders becomes clear (Wilcox 2004). While primary care physicians need not learn how to manage patients with rare genetic diseases, they should know how to recognize referral triggers. In many cases, generalists also can work with these exceptional patients to educate each other about the rare disease. Selective education of family physicians and internists is key in MCOs.

"We have tried over the years to develop Centers of Excellence in lysosomal diseases. So, for example, we've set up a hub in Cincinnati, and we have a series of spokes reaching out to local physicians. This works well, because I can send the patients back to their own doctors and [I can then] collaborate with these local physicians. It forces the stream of education. The local doctors enjoy seeing the patients get better. And I don't need to see these patients every time they have a minor illness."

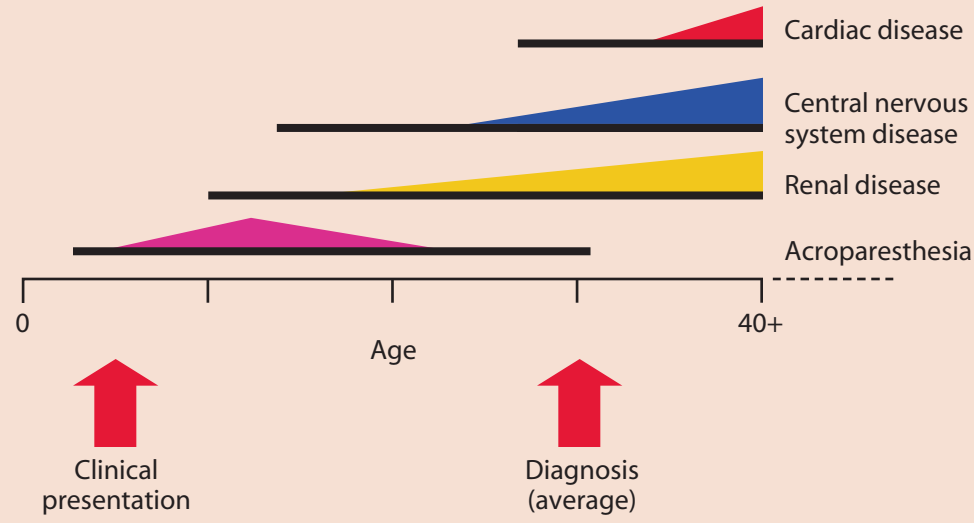
—Gregory A. Grabowski, MD, professor and director of human genetics, Cincinnati Children's Hospital Research Foundation

CHALLENGES AND STRATEGIES: MANAGING RARE GENETIC DISEASES

As more orphan products for rare diseases are introduced, the challenge of maintaining access to these products will remain a priority for MCOs, and decision makers will need to confront a range of related business challenges, including:

- *Lack of evidence on drug dosing, safety, and outcomes for ultra-rare disease.* Because the clinical trials for orphan drugs are necessarily small, providers and specialists will need to work alongside manufacturers to build and apply national registry data.
- *Clarity and consistency in billing*

FIGURE 2 Fabry's disease progression: When should therapy begin?



In Fabry's disease, the early damage caused by lipid deposition in small vessels usually remains unnoticed until major organs are affected later in life. A primary challenge for specialists in lysosomal disorders is to determine when to initiate therapy with the replacement enzyme in the course of this progression.

SOURCE: GRABOWSKi 2004

administration. With different specialists taking the lead in specific orphan diseases (e.g., pediatricians instead of oncologists), MCOs can no longer assume that providers know the fine points of coding for use of expensive orphan products. MCOs need to find a way for providers to capture costs accurately while giving them a safe "crosswalk" in coding to allow prompt payment. One increasingly popular approach is to have these drugs delivered to the provider by specialty pharmacies, simultaneously removing the cost and coding issues from the physician's office and allowing for cost-effective purchasing by the plan.

• *Near-term paucity of competition and market price control.* The small patient population makes development of multiple products for rare diseases less likely than is seen with drugs for other chronic conditions; the ultra-orphan markets are much smaller than others (e.g., MS and RA) for which more competing biologic products have been developed.

• *A tipping point ahead?* Currently, because ultra-rare genetic diseases occur so infrequently, the typical MCO's PMPM cost is still low, and decisions on patient access, physician barriers, and internal treatment guidelines need to be tempered with this actuarial perspective. At some future point, however — especially as pharmacogenomic research continues to subdivide diseases into microdiseases for which microtreatments will be developed — MCOs and society will face ethical decisions about access to effective treatments. These difficult questions about reimbursement and rationing of health care will need to be reassessed continually in the decades ahead.

To face the immediate challenges, every MCO can generate strategies based on its structure, history, clinical expertise, and policies. Several new MCO policies may be required. For example, as new tests and treatments for rare diseases become more common, managing all patients with rare diseases as special cases might soon become untenable. At some point, an MCO might need to acknowledge and evaluate this trend and inculcate an institutional culture of continuous learning and practical policy-making aimed at handling ultra-rare diseases. Partnerships with COEs or with manufacturers can contribute to this internal learning process.

Before approving reimbursement, medical and pharmacy directors can gather highly focused information about each new and impending orphan product, soliciting information from network specialists, clinical investigators, COEs, and drug-maker representatives and consultants. A product dossier from the manufacturer can provide up-to-date guid-

The managed care director's perspective

An intelligent managed care organization benefit design would start with obligatory coverage of the label indication. It then would make critical distinctions between specialty injectable products for more common conditions and for truly rare conditions in deciding when to employ pharmacy or medical benefit design features (e.g., tiers, prior authorization, case management). A plan might apply a copayment for an injectable asthma drug, for example, to allow the member to share costs and to have a role in the decision to use the product. Likewise, in a category of drugs for multiple sclerosis, where there are several products, there may be one or two preferred drugs with fixed copayments and one or two drugs with coinsurances of up to 25 percent. This type of arrangement can drive utilization to the preferred products. Similarly, a single-agent category can be created for rare genetic diseases such as Gaucher's, where the product is exempt from copayments and from prior authorization requirements.

"One quick solution to injectable costs is to throw [them] over the fence into pharmacy, and manage it as a pharmaceutical product. That's tempting but I didn't want to just play catch with myself, since I manage both medical and pharmacy subteams. So, last year, we redesigned our medical benefit to include a specialty pharmacy injectable benefit category. This medical benefit category looked, acted, and felt like a pharmaceutical benefit with copayments and two or three tiers — tier 1, for what we might call routine injectables for acute conditions; tier 2, for preferred specialty products; and tier 3 is being developed for products in areas like rheumatoid arthritis and psoriasis, where there are or will soon be choices of multiple specialty products.

"One way we deal with the growing cost burden to the employer is with a product design that shifts some costs to the employee. But care is needed, as there's a relationship between the amount of member out-of-pocket spending and the potential to create a barrier to care. You have to titrate it carefully." — Gary Owens, MD, medical director, Independence Blue Cross

ance for the P&T committee. In setting policy for use of new specialty pharmaceuticals, MCO staff can focus on size of patient population, nature of the disease, number of approved indications, ease of accurate diagnosis, number of (or potential for) off-label uses, unit cost, ability to save lives or prevent disability, size of evidence base, and availability of similar therapies.

In managing drugs for rare diseases, the patient's perspective must never be forgotten. Patients with rare genetic diseases are among the most vulnerable members of any health plan. They and their families need help complying with complex therapies and dealing with psychological issues, insurance matters, confidentiality and workplace concerns, and family counseling. The MCO, with its genetics counselors or through arrangements with other pharmacy benefits, COE, or specialty groups, can become the hub for this support. While the number of Web sites and support groups for individuals with rare diseases has grown, the role of the MCO as the lead adviser in helping members to locate quality sources of support and information is vital.

CONCLUSION

Orphan drug coverage is not in crisis. Today's patients with ultra-rare genetic diseases are receiving life-extending and life-saving drugs without significantly drawing away resources from patients with more prevalent diseases. The system works. Nevertheless, as MCOs gear up to manage the continuing waves of expensive biologics, they need to draw distinctions between therapies for ultra-rare genetic diseases and biologic therapies for more common disorders.

Making this distinction is important because each MCO's population with ultra-rare genetic diseases is usually too small to allow for efficient or expert management by the local MCO staff. In addition, these rare conditions typically do not merit special use policies, because off-label expansion is rare, alternative agents usually are not available, and, often, the conditions being treated are life-threatening. Moreover, in economic terms, the average PMPM costs are small for any given therapy for a rare genetic disease in an MCO.

Therefore, as MCOs redesign their specialty pharmacy benefits, care should be taken not to inadvertently limit access to therapies for rare genetic diseases. In coming years, MCOs undoubtedly will struggle to understand and incorporate new genetic tests and treatments into their benefit packages. This is an exciting and challenging time to be managing the specialty pharmaceutical benefit. The suggestions offered here should encourage readers to consider discriminating and rational strategies for managing the growing list of treatable rare diseases.

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CE/CME quiz and answer sheet can be found on pages 66–67.

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Instructions for obtaining CME credit

After reading *Managing Drugs for Rare Genetic Diseases: Trends and Insights,* select the one best answer to each of the following questions. Complete the accompanying form, evaluation, and answer key, and follow the instructions above for obtaining either CE or CME credit. There is no charge to participate in this program. After completing the quiz and adding your personal information, please tear out the answer sheet and return to:

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CE/CME QUESTIONS

1. **According to the author, which of the following is <u>NOT a reason to discourage</u> the use of aggressive cost techniques for truly rare diseases?**
   a. What seems like a reasonable coinsurance percentage can quickly become unaffordable due to the expensive nature of rare disease therapies.
   b. Spending company time on such an aggressive endeavor is not practical, given the small number of people these diseases normally affect.
   c. Allowing the affordability of copayments/coinsurance to become a barrier to care for a life-threatening disease is ethically inappropriate.
   d. The elastic demand curve that justifies the use of copayments/coinsurance does not exist when dealing with diseases that have very few treatment options.

2. **According to the author, what drives the cost of drugs for rare diseases so high?**
   a. The burden of generating revenue for the pharmaceutical company and sharing the expense of developing the drug is dispersed over a small patient population.
   b. The lack of treatment options means there is little competition to drive down cost.
   c. The accumulation of unusually high "hidden" expenses such as patient advocacy, physician training, inventory management, etc.
   d. All the above.

3. **The U.S. definition for rare diseases was defined by the _____ and set at a prevalence of _____ Americans.**
   a. Health Care Act of 1973; 1:3,000.
   b. 2003 Medicare Drug Bill; 1:2000.
   c. Orphan Drug Act of 1983; 1:1000.
   d. Biologics Control Act; 1:100.

4. Of the estimated $22 billion spent on biological and injectable agents, 75 percent is spent on just five categories: oncology, renal disease, transplant medications, HIV/AIDS, and _____.
a. Ultra-rare genetic diseases.
b. Central nervous system-related indications.
c. Hemophilia.
d. Autoimmune diseases.

5. According to the author, what should be done to overcome the lack of evidence on drug dosing, safety, and outcomes for ultra-rare diseases?
a. Providers and specialists should partner with manufacturers to build and apply a national registry system.
b. Clinical investigators should increase their trial recruitment efforts to fill more compelling study-sample sizes.
c. Investigators should broaden the recruitment criteria to allow genetically susceptible people to become eligible.
d. Researchers should use statistical methods to extrapolate as much information as possible from the data that is generated from current sample sizes.

6. According to the actuary's estimation, what percentage of the per member per month cost is allocated for drugs?
a. 10 percent.
b. 15 percent.
c. 20 percent.
d. 25 percent.

7. The physician used Fabry's disease in this article as an example of how specialists can:
a. Use their position as doorkeepers to expensive therapies to set *de facto* policy for MCOs.
b. Manage just about any disease with the proper training.
c. Have his/her hands tied by unreasonable decisions made by managed care executives.
d. All the above.

8. According to the managed care director's perspective, why is it important for MCOs to make critical distinctions between specialty injectable products when used off-label for more common and rare conditions?
a. To have a more complete understanding of the patient care being provided.
b. To drive utilization toward preferred products when multiple agents are being used for more common disease states.
c. So single-agent categories can be created for the truly rare diseases, and specialty products can be exempted from copayment and prior authorization requirements.
d. Both "b" and "c."

I have participated in the program *Managing Drugs for Rare Genetic Diseases: Trends and Insights*. I have reviewed all the materials and answered the CE/CME questions. I understand that a certificate for 0.1 CEU credits toward continuing pharmacy education or 1.0 credit of Category 1 PRA (Physician's Recognition Award) will be mailed to me upon receipt of this form, provided I receive a passing score of 70 percent or higher. I also understand that no fee is required for me to receive credit. Credit can be awarded for submissions received through Jan. 12, 2008.

Please print clearly.

Name: _____

Degree(s): _____

Title/Position: _____

Affiliation (university or hospital): _____

Home Address: _____

Business address: _____

Business telephone: _____

Business fax: _____

E-mail: _____

Signature: _____

Post-test answer sheet
Circle the letter of the correct answer.

1.	a	b	c	d
2.	a	b	c	d
3.	a	b	c	d
4.	a	b	c	d
5.	a	b	c	d
6.	a	b	c	d
7.	a	b	c	d
8.	a	b	c	d

Evaluation
Key:
1 = Strongly agree
2 = Agree
3 = Neutral
4 = Disagree
5 = Strongly disagree

Please circle the number of your response.

1. Overall, the materials were clear and to the point.
1 2 3 4 5

2. The difficulty level of the material was appropriate.
1 2 3 4 5

3. The program content was consistent with its description.
1 2 3 4 5

4. The content had substance.
1 2 3 4 5

5. The program content was relevant to my work.
1 2 3 4 5

6. The instructional material addressed important practice problems.
1 2 3 4 5

7. The printed material is likely to be used as a future reference.
1 2 3 4 5

8. My learning objectives for this program were addressed.
1 2 3 4 5

9. I gained new insight relevant to my work.
1 2 3 4 5

10. The program was well organized.
1 2 3 4 5