

SPECIAL SUPPLEMENT

M A N A G E D

Care

Outpatient Treatment of Deep Venous Thrombosis In Managed Care

HIGHLIGHTS

- Outpatient Therapy With Low-Molecular-Weight Heparin

- Proceedings of Regional Meetings
On Reimbursement

- Reimbursement Strategies in an Outpatient-
Based Disease Management Program

- Outpatient Treatment of DVT
In a 170,000-Member HMO

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Care

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Supplement Faculty

VICTOR F. TAPSON, M.D.
Pulmonary and Critical Care Medicine
Duke University Medical Center
Durham, N.C.

ALEX C. SPYROPOULOS, M.D.
Medical Director — Anticoagulation Services
Department of Internal Medicine — Hospitalist Division
Lovelace Health Systems
Albuquerque, N.M.

SAMEER ABU-SAMRAH, M.D.
Vice President and Regional Medical Director
Sierra Health Services
Las Vegas, Nev.

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Deep Venous Thrombosis: Outpatient Therapy With Low-Molecular-Weight Heparin

VICTOR F. TAPSON, M.D.

Pulmonary and Critical Care Medicine, Duke University Medical Center, Durham, N.C.

Introduction

Venous thromboembolism (VTE) constitutes a clinical spectrum encompassing deep venous thrombosis (DVT) and pulmonary embolism (PE). These entities are responsible for substantial morbidity and mortality. An exciting advance in this area of medicine involves the outpatient treatment of stable patients with DVT. This therapeutic approach, which has been greatly facilitated by the advent of low-molecular-weight heparin (LMWH) preparations, will be our primary focus. A very brief background of the scope of the problem of DVT and PE will be followed by a discussion of LMWHs and why these agents offer substantial advantages over standard, unfractionated heparin (UFH). The economic impact of outpatient therapy of DVT will then be addressed.

Deep venous thrombosis generally develops in certain predisposing settings including immobility, hypercoagulability, and injury to the lower extremities. Frequently, more than one risk factor is present. Awareness of these risk factors may provide the rationale for both prevention and clinical suspicion of DVT. Pulmonary embolism most commonly results from DVT occurring in the deep veins of the proximal lower extremities, that is, including the popliteal and more proximal veins. While calf vein thrombi do not generally embolize, they often propagate into the more proximal vessels substantially enhancing the risk of PE.

As many as 300,000 patients in the United States with VTE are diagnosed and treated each year. Since more than half of cases are

not diagnosed, as many as 600,000 cases may actually occur. It appears that PE is responsible for the deaths of 50,000 to 100,000 patients with an otherwise good prognosis. Many of these deaths would appear to be preventable. Thus, an aggressive approach to diagnosing and treating VTE is warranted. Traditionally, patients with DVT and PE have been treated in hospitals. The substantial trend toward more rapid hospital discharge or total outpatient treatment of medical and surgical patients now includes stable patients with DVT, primarily due to the development and clinical testing of LMWH preparations. Because DVT is so common, and because until recently it has required inpatient therapy, cost of treatment has been an important issue.

Low-molecular-weight heparins: background

Clinical interest in LMWHs developed after experimental studies suggested that these agents appeared to be as, or more, effective, and as safe as, or safer than, standard UFH. They also are clearly easier to use. These smaller heparin fractions differ from UFH in their pharmacokinetics, bioavailability, and anticoagulant profiles. Extensive clinical evaluation has resulted in the availability of a number of these agents in Europe, and now in the United States. Several of these agents have been FDA-approved for DVT prophylaxis in certain clinical settings, and one (enoxaparin), has also been approved for treatment of established DVT.

Specifically, enoxaparin is indicated for

patients presenting with DVT with or without PE. Enoxaparin is also FDA-approved for use as DVT prophylaxis for elective total hip replacement, total knee replacement, abdominal surgery, unstable angina, and non-Q wave myocardial infarction. The specific dose depends upon the indication.

A comparison of UFH with LMWH appears in Table 1, with some potential advantages of these preparations outlined. These advantages justify the recent intense interest in these drugs. The bioavailability of LMWH is significantly greater than for standard heparin, making dosing much more predictable. Once- or twice-daily dosing and subcutaneous delivery for prophylaxis and treatment of DVT greatly facilitate treatment. Not only is intravenous dosing unnecessary but laboratory monitoring is substantially reduced or eliminated. This minimizes phlebotomy and potentially reduces cost and discomfort. The safety profile of these agents appears at least equivalent to UFH, if not superior. Excellent, comprehensive reviews of the biophysical properties, anticoagulant effects, and pharmacokinetics of LMWH fractions have been published.

Although other LMWH preparations are available for certain indications, enoxaparin currently has the broadest range of indications for an LMWH in the United States. It is the only such agent that is FDA-approved for treatment of established DVT. It should be emphasized that there are at present no sufficient means by which to standardize LMWH preparations. Each of them should be considered a distinct anticoagulant. Unlike UFH, conclusions from clinical trials involv-

ing one LMWH preparation cannot be applied with confidence to other preparations. As data from clinical trials accumulate, clinicians will need to remain knowledgeable of developments pertaining to these agents. A number of excellent and informative clinical trials evaluating the use of LMWHs for preventing and treating established DVT have been published. These will not all be presented here. Instead, we will present a brief background followed by a review of the data for DVT treatment in the outpatient setting.

Anticoagulant effects, pharmacokinetics, and differences between LMWH preparations

Unfractionated heparin consists of lengthy glycosaminoglycan polymers that are heterogeneous in size with an average molecular weight of about 15,000 daltons. These molecules consist of about 50 monosaccharide units, including a unique pentasaccharide required for high-affinity binding to antithrombin III. Low-molecular-weight heparins, also glycosaminoglycans, are approximately one third of the size of UFH, and are diverse with a mean molecular weight of 4,000 to 5,000 daltons. The difference in size between UFH and LMWH results in an altered anticoagulant profile. The majority of the LMWH products are depolymerized porcine mucosal heparin preparations, prepared by chemical or enzymatic digestion methods. These methods include benzylation and alkaline hydrolysis (enoxaparin), optimized nitrous acid depolymerization (nadroparin), nitrous acid depolymerization

TABLE 1 Potential advantages of low-molecular-weight heparins over unfractionated heparin

- Comparable or superior efficacy
- Comparable or superior safety
- Superior bioavailability
- Once- or twice-daily dosing
- No laboratory monitoring
- Less phlebotomy
- Subcutaneous administration
- Earlier ambulation
- Outpatient therapy in certain patient subsets

(dalteparin), heparinase digestion (tinzaparin), peroxidative cleavage (ardeparin), optimized nitrous acid digestion (reviparin), and isoamylnitrate digestion (certoparin). While the different preparation methods result in products with similar molecular profiles, structural variations remain that impart significant differences in their biologic actions. Chemical modifications of various portions of the molecules, charge density, and degree of desulfation all affect the final product's characteristics. Because of these differences, antithrombin III activity, the effects on tissue factor pathway inhibitor, platelet factor 4, and heparin cofactor II would be expected to be different for the different preparations. Heparin and LMWH stimulate the release of tissue plasminogen activator and prostacyclin, and these processes would be expected to be different for different products. Each LMWH compound should be considered a distinct agent and should not, at the present time, be considered interchangeable with each other.

Antifactor Xa potency has been considered the primary measure of potency for these agents. This has been considered the primary explanation for the difference in anticoagulant activity between LMWH and UFH. The interaction between UFH and antithrombin III is known to accelerate the inactivation of thrombin as well as factors IXa and Xa. Maximal inhibition of thrombin requires the binding of heparin to both antithrombin III and the activated enzyme.

In contrast, the accelerated inactivation of factor Xa by the heparin/antithrombin III combination requires only the binding of UFH to antithrombin III and does not require the formation of the ternary complex. Heparin molecules smaller than 18 saccharide units are unable to bind thrombin and antithrombin III simultaneously, precluding maximal acceleration of the inactivation of thrombin by antithrombin III. These smaller LMWH molecules do, however, retain their ability to catalyze the inhibition of factor Xa by antithrombin III. For this reason, LMWH fractions appear to have relatively more anti-Xa than antithrombin activity and substan-

tially less effect upon the partial thromboplastin time. While UFH has an anti-Xa to antithrombin ratio of 1:1, the LMWH preparations have ratios ranging from 2:1 to 4:1. Unfractionated heparin contains a higher proportion of the pentasaccharide portion that has the high affinity for antithrombin III than LMWH fractions contain. In addition, these fragments catalyze thrombin (the more effective anticoagulant) inhibition to a lesser extent than factor Xa inhibition. However, the anticoagulant potency of UFH relative to LMWH may be decreased by several mechanisms. Platelet factor 4 is an effective inhibitor of UFH but does not affect LMWH. Reduced binding of LMWH to other proteins such as histidine-rich glycoprotein may enhance its anticoagulant effect relative to UFH. In addition, when factor Xa is bound to the platelet membrane in the prothrombinase complex, it can be inactivated by LMWH but not by UFH. Thus, a number of mechanisms may contribute to the anticoagulant differences between LMWH and UFH, and to the potential differences between different LMWH preparations.

As noted, bioavailability and pharmacokinetics differ between UFH and LMWH. The latter preparations have substantially lower affinity for plasma proteins and endothelial cells than UFH. When UFH binds to receptors on endothelial cells or macrophages, it is internalized and metabolized. The reduced binding of LMWH to endothelial cells as well as to plasma proteins contributes to superior bioavailability as well as to a plasma half-life that is up to four times as long as that of UFH. The enhanced bioavailability imparts a more predictable dose-response. Unlike UFH, the plasma half-lives of LMWH preparations are independent of dose. Renal failure may delay the clearance of LMWH.

Dosing enoxaparin in inpatients or outpatients

The dose of enoxaparin studied in outpatients, and the approved dose in this setting, is 1 mg/kg every 12 hours. Another regimen (1.5 mg/kg once-daily) has proven successful in inpatients presenting with DVT with or

without PE. In certain patient populations such as massively obese individuals, very small persons (<50 kg), or those with renal insufficiency, some experts recommend adjusting the dose of enoxaparin based upon measurement of anti-Xa levels. Other experts would consider using unfractionated heparin in these settings.

Adverse effects of LMWH preparations

As with UFH, bleeding remains the most significant adverse effect associated with LMWH. Based on clinical trials described later, LMWH preparations appear to be as safe or safer than UFH in this regard. The frequency of hemorrhagic complications occurring in patients receiving these agents in clinical trials is outlined subsequently.

Thrombocytopenia occurs with heparin, but can also develop in patients receiving LMWH. The incidence may be lower with LMWH. Osteoporosis may occur with use of heparin over an extended interval. Successful use of LMWH has been reported in a patient in whom osteoporosis had developed while on UFH, but inadequate data precludes a useful comparison between these substances.

As is the case with UFH, LMWH preparations do not cross the placenta, and these compounds appear to be safe for administration during pregnancy. However, randomized controlled trials in pregnant patients have not been conducted.

Outpatient therapy of deep venous thrombosis with LMWH

Low-molecular-weight heparin has been compared with continuous intravenous UFH for the treatment of established DVT. Clinical outcomes of patients with recurrent DVT and/or PE and bleeding events have been the primary endpoints in these trials. Our next focus will be on the pivotal North American trial leading to the approval of enoxaparin for established DVT in the outpatient arena.

Two large randomized trials published in the *New England Journal of*

Medicine in 1996 indicated that carefully selected patients with DVT could be safely treated at home. Levine and colleagues studied enoxaparin in Canada, while Koopman and colleagues studied nadroparin in Europe. In both trials, therapy with LMWH was safely initiated at home or continued at home after a brief hospitalization.

In Levine's study, 253 patients with established proximal DVT were treated as inpatients for at least five to seven days with intravenous UFH, while 247 received enoxaparin (1 mg/kg every 12 hours). The enoxaparin patients were hospitalized for an average of only 1.1 days, and 120 of these patients received the entire course of treatment in the outpatient setting. Warfarin (10 mg) was begun in all patients on the second day, and the International Normalized Ratio (INR) was checked daily. The heparin or enoxaparin was administered for at least five days and was discontinued when the INR was therapeutic (2.0 to 3.0) for two consecutive days. The recurrence rate for DVT and/or PE was 13 (5.3 percent) in the enoxaparin group and 17 (6.7 percent) in the UFH group at the three-month endpoint (Table 2). Neither these rates nor the rate of bleeding complications was significantly different between the groups.

Individuals experienced in outpatient therapy have emphasized that a well organized program is crucial for successful outpatient treatment. Specifically, patients need to be carefully screened for outpatient treatment. Individuals who can't self-administer the subcutaneous injection may still be consid-

TABLE 2 Recurrence of DVT and PE and incidence of bleeding

	Enoxaparin (n=247)	UFH (n=253)
DVT	11	15
PE	1	2*
Both	1	0
Bleeding	5	3
Total VTE	13(5.3%)	17 (6.7%)

* Two patients died during study

Source: Levine et al, N Engl J Med 1996

TABLE 3 Candidates with DVT appropriate for outpatient therapy with enoxaparin

- Do not require admission for another reason.
- Do not have extensive DVT and do not have PE.*
- Do not have excessive bleeding risk.
- Are compliant / understand instructions for follow-up.**
- Can self-inject or has family member or home health services to administer LMWH.

*Patients with extensive iliofemoral DVT, for example, should be admitted.

**Know symptoms consistent with recurrent or worsening DVT and those associated with PE.

TABLE 4 Outpatient therapy with enoxaparin for established DVT

- Screen candidate carefully (Table 3).
- Initiate enoxaparin at 1 mg/kg every 12 hours.*
- Initiate warfarin the same day (5 to 10 mg/day for initial dose).
- Administer enoxaparin for at least 5 days and until INR therapeutic for two consecutive days.**
- Consider checking CBC / platelet count at day 3 to 5.
- No monitoring of the enoxaparin is necessary.

* A dose of 1.5 mg/kg has proven effective in inpatients with DVT with or without PE.

** 2.0 to 3.0

ered for outpatient treatment if a member of the family can help, or if home-health nursing services are available. Patients receiving enoxaparin do not require monitoring of any blood parameters. Specifically no PTT measurement is necessary. Noncompliant or unreliable patients should be admitted for treatment. Options for outpatient management vary among institutions. All outpatient programs emphasize close follow-up and careful patient education about recognizing and responding to potential adverse events. Acceptable candidates for outpatient therapy are outlined in Table 3. The appropriate approach for initiating outpatient LMWH is outlined in Table 4.

Outpatient therapy with enoxaparin is becoming increasingly utilized. As long as appropriate precautions are taken, this approach is safe, effective and well accepted by the patient and involved health care professionals. Careful implementation of outpatient therapy has been endorsed by the American College of Chest Physicians.

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Reimbursement of Enoxaparin For Outpatient Therapy

PROCEEDINGS OF REGIONAL MEETINGS

Abstract: Standard treatment of deep venous thrombosis (DVT) previously required hospitalization so patients could receive continuous intravenous infusion of unfractionated heparin. However, on Dec. 31, 1998, enoxaparin (enoxaparin sodium) became the first low-molecular-weight heparin (LMWH) to receive an indication from the FDA for outpatient treatment of DVT without pulmonary embolism (PE). The manufacturer of enoxaparin, Rhône-Poulenc Rorer (RPR), states that outpatient use of enoxaparin can help managed care organizations (MCOs) and other health care systems to reduce health care costs by curtailing some of the expenses previously associated with hospitalization to treat uncomplicated DVT. To ascertain the extent to which reimbursement policies within managed care might impede patients' access to enoxaparin, RPR conducted 15 regional meetings during the summer of 1999. During these meetings, medical directors and other personnel associated with MCOs provided anecdotal information suggesting that a dominant method of reimbursing enoxaparin for outpatient therapy has yet to emerge in the United States; and that reimbursement methods appear to be divided equally among the pharmacy benefit, the medical benefit, and a "blended" system combining attributes of the pharmacy and medical benefits.

Introduction

Although some contemporary physicians might disagree, medical historians one day may claim that one of the virtues of MCOs as they evolved during the 1990s was to

bring clinical practice guidelines and disease management into the mainstream of clinical practice. These tools were intended to serve as rational means for eliminating regional variations in clinical practice. As John Wennberg and others discovered, regional practice variations stemmed primarily from differences in medical cultures (although they occasionally reflected differences in health insurance, with respect to procedures that were covered or not covered) — and they sometimes were cited as barriers to patients' access to the best treatment as determined by the available scientific evidence.

But in some instances the managed care industry itself is prone to seemingly irrational variations, such as in reimbursement policies for certain products. Could these policies inadvertently impede efforts by MCOs to provide patients with high-quality, cost-effective care? That has been a concern of Rhône-Poulenc Rorer during the past year after one of its products, enoxaparin (enoxaparin sodium), was approved for marketing by the FDA for outpatient treatment of uncomplicated deep venous thrombosis (DVT).

Specifically, the new indication provides for outpatient treatment of acute DVT without pulmonary embolism (PE) when enoxaparin is administered in conjunction with warfarin sodium. Other indications for enoxaparin include inpatient treatment of DVT in patients with or without PE, when administered in conjunction with warfarin sodium; prevention of ischemic complications of unstable angina and non-Q-wave

myocardial infarction, when concurrently administered with aspirin; and prevention of DVT in patients undergoing hip-replacement, knee-replacement, and abdominal surgery.

Without treatment, DVT frequently leads to PE, which is often fatal. The emboli invariably originate in the veins of the legs. DVT is difficult to diagnosis because its signs and symptoms are nonspecific. Shortness of breath could be due to COPD, heart failure, or pneumonia; and even leg pains, swelling, and cramps are not often diagnosed as DVT. To reduce the risk of PE, DVT requires prompt anticoagulation efforts.

Standard therapy for DVT used to be unfractionated heparin administered by continuous intravenous infusion during an inpatient stay of at least five days. More than 50 years ago, this drug was hailed as the solution to PE, but PE still remains one of the leading causes of death of hospitalized patients.

Unfractionated heparin is a mixture of large molecules — polysaccharide chains with a mean molecular weight of about 15,000 daltons. The low-molecular-weight heparins (LMWH) are prepared by breaking long chains of unfractionated heparin into mixtures of shorter chains; the mean molecular weight of enoxaparin is 4,500 daltons. The difference in chain length alters the way the drug behaves with respect to antithrombin, which regulates blood clotting. Unfractionated heparin and enoxaparin both can bind to antithrombin, greatly accelerating its interaction with factor Xa. Factor X is a precursor of the enzyme known as factor Xa (the “a” means activated), which regulates a critical step along the pathway for blood clotting. Because of its longer chain length, unfractionated heparin also forms a three-part complex with antithrombin and thrombin. The shorter length of enoxaparin and other LMWHs restricts their inhibition of thrombin in this fashion, so the LMWHs have far greater inhibitory activity against factor Xa.

Because it is such a large molecule, unfractionated heparin binds readily with endothelial cells, macrophages, and plasma proteins. In addition, the heterogeneity of the molecule mixture means heparin varies

from dose to dose in its biological activity. These characteristics cause unfractionated heparin to be unpredictable and relatively short-acting. Monitoring via laboratory tests therefore is required to reach and maintain a therapeutic level.

By contrast, enoxaparin, due to its reduced binding to these substances, produces a more predictable anticoagulant response. Reduced binding to endothelium means enoxaparin has better bioavailability at lower doses, and reduced binding to macrophages results in a longer half-life.

These characteristics — along with the finding that enoxaparin is as efficacious as standard heparin — helped secure FDA approval (received Dec. 31, 1998) for the marketing of enoxaparin for outpatient treatment of uncomplicated DVT. In the outpatient setting, enoxaparin is administered by subcutaneous injection twice a day. Please refer to “Deep Venous Thrombosis: Outpatient Therapy with Low-Molecular-Weight Heparin” by Victor Tapson, M.D., on Page 2, for details on the clinical use of enoxaparin.

As discussed by Alex C. Spyropoulos, M.D., and Sameer Abu-Samrah, M.D., in articles on Pages 14 and 21, although enoxaparin is more expensive than unfractionated heparin, the fact that enoxaparin may not require hospitalization for treatment of uncomplicated DVT can result in dramatic overall savings for a health care system. At a meeting in California, a participant reported savings of \$2,500 to \$2,800 per patient receiving outpatient treatment with enoxaparin.

Because it requires less monitoring, enoxaparin may result in modest savings when used instead of standard heparin for inpatient DVT therapy. In addition, heparin-induced thrombocytopenia, a common and serious side effect with unfractionated heparin, is rarely seen with enoxaparin. This in itself may present a strong argument for the cost-effectiveness of enoxaparin. On the face of it, it might appear that the potential savings from avoided hospitalizations and reduced side effects would make every MCO eager to provide enoxaparin for any patient

who could benefit from it.

As a result of an advisory board meeting in May 1999 about reimbursement issues that could affect the use of enoxaparin for outpatient therapy, RPR decided to obtain more information by conducting a series of 15 regional meetings from coast to coast with representatives of MCOs. An advantage of using so many local-market meetings was that it allowed the smaller MCOs to have a voice in a forum that wasn't dominated by representatives of the large, national MCOs.

The meetings revealed that, thus far, no standard method for reimbursement of enoxaparin has emerged among MCOs. An informal survey by RPR consultants disclosed that, nationwide, about a third of enoxaparin prescriptions for outpatient use are reimbursed through the pharmacy benefit, a third through the medical benefit, and a third through a system that blends both pharmacy and medical, by providing drug distribution to patients through pharmacies with the eventual charging back of the product to the medical benefit.

One participant in Boston argued that *any* pharmaceutical product cuts inpatient costs, and wondered whether "something special" should be done for enoxaparin. But the meetings revealed that the ways enoxaparin was reimbursed sometimes could affect patients' access to enoxaparin, and that MCOs were concerned about this issue.

Barriers to Reimbursement

Not top priority. One reason MCOs have different reimbursement scenarios for enoxaparin may be that outpatient treatment of DVT is not yet high on MCOs' lists of cost-containment strategies, due to physicians' general lack of experience with enoxaparin in an outpatient setting (the drug didn't receive FDA approval for outpatient use until Dec. 31, 1998).

Asthma, diabetes, and congestive heart failure are among the diseases commanding the most attention from MCOs in terms of cost containment, often through disease management programs. Some participants thought a disease-management approach

could be applied to uncomplicated DVT, too.

In Denver, where participants said outpatient use of enoxaparin was not among their top 10 cost-containment issues, one person offered a simple explanation for why DVT had not been identified as a potential source of savings: Nobody was looking for it. He thought it might be worthwhile for his organization to check the records for patients hospitalized with DVT to determine if the savings from using enoxaparin for outpatient therapy would be significant enough; he thought a savings of as little as 5 percent to 10 percent would justify the effort.

Injectable drugs. As a new, low-priority item, enoxaparin in many cases has been inserted into existing reimbursement structures that may not be appropriate for this novel indication — a self-injectable medication that can replace another drug whose administration requires lengthy hospitalization. Concerns about cost and patients' misuse or abuse of injectable products historically have colored the ways they have been reimbursed. For many years, the only injectable drug covered under a pharmacy benefit was insulin. Today, many other self-injectable drugs, such as sumatriptan (for treatment of migraine), are routinely reimbursed through the pharmacy benefit to make the drug readily available without subjecting the patient to an office visit, let alone hospitalization.

Across the nation, MCOs varied widely in their treatment of injectable products. The medical director of an MCO in Colorado said his plan covered enoxaparin under either the pharmacy benefit or the medical benefit, depending on how it is administered and obtained. A San Diego participant reported that injectable drugs administered in an office setting, by definition, were covered under his plan's medical benefit.

As a self-injectable drug, enoxaparin is neither fish nor fowl. It's not subject to abuse, and it's not believed to be dangerous, so restrictions on its availability due to concerns for patients' safety would not seem to

"We've shown that for every patient we treat as an outpatient, our cost savings is around \$2,500 to \$2,800 per patient."

—*Newport Beach, Calif.*

apply (although one participant expressed strong opposition, for safety reasons, to allowing patients to self-inject enoxaparin). Enoxaparin is relatively expensive, but its use in an outpatient setting, which usually is covered under the pharmacy benefit, is reported to result in significant savings in hospitalizations — which always are covered under the medical benefit. Hence MCOs' difficulty in dealing with enoxaparin for outpatient therapy. Should it be processed as a pharmacy benefit or a medical benefit?

Pharmacy reimbursement as barrier.

As the meetings unfolded, reimbursement of enoxaparin through a patient's pharmacy benefit was identified as a potential barrier to therapy — and an invitation to unnecessary costs. Even though the cost of enoxaparin for outpatient treatment of DVT constitutes a relatively low percentage of the total cost of therapy, if the enoxaparin is reimbursed through the pharmacy benefit, its cost nevertheless may be high enough to preclude its use by some patients, particularly by patients whose pharmacy benefit has a yearly cap — or who lack a pharmacy benefit.

A case manager in Boston said there was no way patients in her organization could obtain enoxaparin at a pharmacy and not have the cost charged to their annual cap. In Minneapolis, a participant reported that the cost of one treatment course with enoxaparin had been sufficient to cause many patients in the system's plan for the elderly to reach the maximum provided by their yearly pharmacy benefits. It took the organization several months to devise a way to redistribute those costs, which now are reimbursed through the medical benefit.

Likewise, a pharmacy benefits director in Philadelphia said his organization had to grapple with the problem of discharging a enoxaparin-eligible patient from the hospital, knowing that the patient had no money left under the pharmacy cap, which had a limit of \$100 per year. The organization agreed that it made no sense to require such a patient to spend five extra days in the hospital, because the patient was not allowed, by a strict interpretation of the rules, to

receive enoxaparin on an outpatient basis. To avoid this kind of expensive problem, this organization ruled that henceforth enoxaparin would be covered not as a pharmacy benefit but as a medical benefit.

In Boston, a pharmacy operations manager said an advantage of reimbursing enoxaparin as a pharmacy benefit was that this mode of access makes it easy for a patient to obtain the drug. In his organization, the drug first is passed through the pharmacy benefit, but it eventually is billed to the medical coverage through a charge-back mechanism. This blended approach concentrates on first getting the drug to the patient who needs it, and worrying later about which ledger to put it in. Table 1 lists the advantages and disadvantages of the pharmacy, medical, and blended-benefit schemes.

Formularies. When the pharmacy benefit is employed, formularies come into play. Formularies once came in two varieties, open and closed. But patients preferred the wide choice offered by an open formulary. MCO marketers liked an open formulary, too, because it made it easier for them to enroll new members. The disadvantage for the MCO was that the open formulary was expensive.

In an attempt to stake out a middle ground, many MCOs began to institute three-tier co-pays, which require a member to make a copayment of, say, \$35 to receive a drug that is not on the formulary's list of approved products. By comparison, the co-pay for a first-tier drug (usually generic) might be just \$5 or \$10, and the co-pay for a second-tier drug (branded) might be \$15 or \$20. Instead of fixed prices for each tier, some MCOs now require patients to pay a percentage of the drug's cost, which directly ties the amount of the co-pay to the cost of the drug.

Consultants to RPR have reported that their market research has shown, however, that it's less difficult to get a physician to do the paperwork for prior authorization than it is to induce a patient to hand over \$35 or more for a third-tier co-pay. In effect, a third-

Table I Advantages and disadvantages of reimbursement systems for enoxaparin

Pharmacy benefit	Medical benefit	Blended system
<p>Advantages</p> <ul style="list-style-type: none"> • Easy acquisition of drug by patients, in general • Less cost to plan, compared to reimbursing home health care agencies or physicians' offices • Easy generation of utilization data 	<p>Advantages</p> <ul style="list-style-type: none"> • No copayment for patient • Patients can receive drug without regard to annual pharmacy cap • If provided through home health care, patient does not have to worry about where to acquire drug • Cost of drug that reduces hospital costs is accounted for on medical side 	<p>Advantages</p> <ul style="list-style-type: none"> • Focus is on providing appropriate patients with ready access to enoxaparin before worrying about how enoxaparin will be tracked • May be able to eliminate copayment
<p>Disadvantages</p> <ul style="list-style-type: none"> • Copayment may deter some patients from acquiring drug • Annual cap on benefit may pose financial hardship, preventing some patients for obtaining enoxaparin • Some pharmacies do not stock enoxaparin, because of its cost • If plan has "siloeed" pharmacy benefit, financial savings from reduced hospitalization are of no concern to managers of pharmacy budget • Some patients lack pharmacy benefit 	<p>Disadvantages</p> <ul style="list-style-type: none"> • Cost of providing drug through home health care is greater • More difficult to track utilization 	<p>Disadvantages</p> <ul style="list-style-type: none"> • May be cumbersome to implement

tier co-payment is tantamount to a closed formulary.

Availability of product. Lack of widespread availability of enoxaparin through pharmacies was cited as another hindrance to its use. Pharmacies that stock enoxaparin tend to be near hospitals, but outlying pharmacies may not have it on hand because it is expensive to keep in stock. A director of care management systems in Georgia said that sometimes patients whose injectable drugs were covered under the pharmacy benefit would go to the pharmacy only to learn that enoxaparin was unavailable and had to be ordered. She thought the best way for a patient to get the drug quickly was through a home health

care provider under the medical benefit.

In Chicago, the access problem was solved by having one company serve as a warehouse for enoxaparin and distribute it throughout the metropolitan region.

Peculiar perceptions. Is the most expensive therapy equated with the most effective therapy in the minds of patients? A few participants feared that may be the case, which would confound attempts to craft rational reimbursement schemes.

In New York, where fee-for-service care remains dominant, a health plan medical director said he was afraid that New Yorkers who did not need enoxaparin for long-term treatment (for which it is not yet indicated) nevertheless would demand it because of

their perception that a more-expensive drug is better than a less-expensive drug.

In Boston, a participant wondered whether patients' perceptions of the standard of care for DVT would affect their willingness to accept home therapy with enoxaparin. That is, if patients diagnosed with DVT were under the impression that the standard of care for their condition should be inpatient treatment with unfractionated heparin, would they believe they were receiving substandard care if they were told they could be treated at home with self-injectable enoxaparin? Would they think, "I'm very ill, and I should be in the hospital for this condition. Are they sending me home just to save money?"

But in most other regions, participants thought patients would welcome therapy that would enable them to reduce or eliminate their days of hospitalization. Hospitals were not viewed as places where patients wanted to be, if they had a choice in the matter.

A New York medical director wondered how physicians affiliated with a hospital might react if outpatient use of enoxaparin were to deny their institution what otherwise could be a seven-day admission. Aside from the ethical obligation of physicians to provide patients with therapy that represents the standard of care, it was pointed out that physicians who are capitated wouldn't make

more money because a patient was in a hospital for seven days instead of just one or two. In fact, under capitation, physicians presumably would benefit financially by moving a patient from inpatient to outpatient status, provided the patient benefited from this strategy. Moreover, hospitalists who work for MCOs strive to

help patients be discharged from the hospital as quickly as possible, although it was acknowledged that house staff and hospitalists employed by a hospital might not push for as quick a discharge.

A California participant offered the interesting observation that instead of being

underutilized, enoxaparin was being overutilized (though not by strict definition) in a residency program. Because the residents were comfortable with the dosing scheme for enoxaparin, which resulted in fewer calls for them during the middle of the night, they were routinely giving hospitalized patients enoxaparin instead of unfractionated heparin. Her comment prompted another participant to wonder whether, as the result of getting more sleep, the residents were able to provide their patients with better care the following day.

Resources for Reimbursement

Pathways to therapy. Regardless of their geographic region, if MCOs had satisfactorily addressed the question of appropriate use of enoxaparin and reimbursement mechanisms for it, patients were found to flow through a health care system in similar fashion. The patient's point of entry into the system did not matter — the initial diagnosis of DVT could be made at an emergency department, hospital, urgent care facility, or primary care office. After confirmation of DVT, health plan approval was secured for treatment with enoxaparin. Some health plans maintained toll-free numbers with 24-hour access to facilitate reimbursement or prior approval. Next, a case manager was assigned to the patient, who then would receive the drug through various mechanisms — pharmacy, home health care, even an outside vendor who would deliver the product to the patient's home. All these plans ascertained that the patients had been well instructed in the rationale for their therapy, the importance of adhering to therapy, and the techniques of self-injection; patients invariably were required to administer the first injection as part of their education.

Resource requirements. Health plans that could identify patients who would benefit from outpatient therapy with enoxaparin and then make the drug readily and easily available for them had certain features in common. The first was an algorithm or protocol for managing patients with DVT. The second was a diagnostic imaging center to

“The cost of the drug is actually very minimal if you know that the patient will not come back to the hospital. What you're looking for is readmission and length of stay — that's all there is to it.”

—Chicago

confirm the diagnosis of DVT. Next came coordination of the patient's care, through case managers, hospitalists, home health care, anticoagulation clinics, or a combination of these.

Virtual anticoagulation clinic. Anticoagulation clinics were regarded as a powerful tool for making sure a patient with DVT received appropriate care. The clinics need not be physical entities — a person with a computer program could suffice to keep track of patients and the therapy they were receiving. In the Lovelace Health Systems, in New Mexico — one of the nation's oldest MCOs that is now a wholly owned subsidiary of Cigna Health care — after the physician had diagnosed DVT and was confident the patient was an appropriate candidate for outpatient therapy with enoxaparin, the physician would call in a referral to home health care and also refer the patient to the Lovelace anticoagulation clinic.

In California, however, a participant remarked that a certain group of physicians refused to refer patients to his organization's anticoagulation clinic because they believed they could provide better management of these patients themselves. The participant suspected that the outcomes of the patients who were denied the services of the clinic were worse than the outcomes for other patients whose care was coordinated by it.

Prior approval. In general, prior approval of a drug is seen by physicians and their patients as a red flag — a means for an MCO to avoid reimbursing a product altogether. But with respect to enoxaparin, several health plans use prior approval — sometimes through a toll-free number with 24-hour access — as a signal flag, a way to alert the system to the entry of a patient with DVT. Their goal was to provide the patient with seamless reimbursement for enoxaparin in order to keep the patient out of the hospital, and prior approval provided the means for giving this patient high visibility within the health plan.

At the Minneapolis forum, fears were expressed that even if prior authorization was used in this fashion simply to identify

patients using enoxaparin, the phrase carries such negative connotations with physicians that the specter of red tape could lead them to continue using unfractionated heparin.

Physician education. Across the nation, physician education was viewed by many participants as the key to appropriate use of enoxaparin.

But it was not seen as a universal solution: In New York, for example, the medical director of a large MCO said many doctors are remiss about following guidelines and thinking about TQI (Total Quality Improvement) or anything involving standardization or improvement in the care they give. He claimed that this is a national problem that is worse in New York, particularly Manhattan.

It was suggested that physician education about the benefits of enoxaparin for outpatient therapy could be streamlined by educating first the hospitalists who are employed by MCOs, inasmuch as hospitalists are supposed to suggest strategies for speeding the discharge of patients, when appropriate.

Conclusion

Feedback from participants affiliated with MCOs in 15 regional meetings conducted by RPR during the summer of 1999 suggests that, because of its relatively recent indication for outpatient treatment of uncomplicated DVT, enoxaparin is not yet widely regarded by MCOs as a means to reduce health care costs by reducing or eliminating hospitalizations. No single mode of reimbursement has yet to emerge for outpatient use of enoxaparin. Reimbursement through the pharmacy benefit usually provides patients with ready access to the drug, and it also allows MCOs to track usage and cost easily, but it may impede some patients' use of enoxaparin, due to annual caps on their benefit, high copayments, limited availability of the drug at pharmacies, or lack of a pharmacy benefit. Reimbursement through the medical benefit eliminates financial considerations that might restrict use of the agent.

But whatever the means of reimbursement, many clinicians now see outpatient treatment of DVT as the coming standard.

Reimbursement Strategies in an Outpatient-Based Disease Management Program for the Treatment of Deep Venous Thrombosis in an Integrated Health Care System

ALEX C. SPYROPOULOS, M.D.

Medical Director — Anticoagulation Services, Department of Internal Medicine-Hospitalist Division
Lovelace Health Systems, Albuquerque, N.M.

Introduction

Outpatient-based treatment strategies using low-molecular-weight heparin (LMWH) for the management of venous thromboembolic disease (VTE) are gaining acceptance in U.S. health systems. Recent large, multicenter, randomized, controlled trials have shown that home treatment for DVT using LMWH is at least as safe and effective as conventional in-hospital treatment using intravenous, unfractionated heparin (UH) for selected patients.¹⁻³ Meta-analysis of these clinical trials also seems to bear this out.⁴

In addition, recent cost-effectiveness analyses from a third-party payer perspective suggest that VTE treatment with LMWH has the potential to generate large cost-savings to a particular health system through two mechanisms: 1) avoidance of hospitalization in a subset of patients and 2) reduction in the hospital length-of-stay in another subset of patients.⁵⁻⁸

These cost-savings analyses remained robust in the face of conservative eligibility criteria for outpatient treatment, shifted resource utilization in the outpatient setting, and initial inpatient treatment using LMWH, which is associated with higher initial pharmacoeconomic costs than UH.

Lastly, a subset of these same pharmacoeconomic studies indicate that further net savings to a health care system may be expected from improved long-term clinical outcomes and quality-of-life measures,

including greater quality-adjusted life expectancy.

Although cost-effectiveness analyses for outpatient-based DVT treatment programs in a clinical trial setting favor the use of LMWH therapy, there is at present no actual pharmacoeconomic data regarding its use in routine clinical practice in the U.S. health care sector, especially in a managed care setting. This becomes especially important in an insurance-financed system where the explicit goal of health care reimbursement is to reduce costs while maintaining or improving quality of care. Toward this end in developing a clinical practice guideline for the treatment of deep venous thrombosis (DVT) that included a safe, efficacious, and potentially cost-effective home treatment strategy, our institution, an integrated health maintenance organization, instituted a disease management program (called Episodes of Care) for a pharmacy-managed outpatient DVT program.

This article will discuss the impact of the outpatient DVT treatment program within Lovelace Health Systems, especially in terms of third-party payer reimbursement strategies in a managed care setting. The key concepts of maximization of hospital economic efficiency by maximizing reimbursements relative to expenditures via patient selection and risk stratification strategies in outpatient-based DVT treatment protocols will also be discussed.

The “Episodes of Care” Hospital-in-the-Home Program for DVT Treatment — the Lovelace Health Systems Experience

Lovelace Health Systems is a fully integrated health care delivery system within a 235-licensed bed hospital that encompasses both staff-model and network service providers and serves approximately 240,000 members (including commercial, Medicaid, and Medicare members) within the state of New Mexico. Under the Lovelace Episodes of Care Disease Management Program, a multidisciplinary team of physicians, nurses, pharmacists, social workers, and data management personnel developed a hospital-in-the-home program for outpatient-based treatment of uncomplicated, proximal lower extremity DVT using the LMWH enoxaparin. The choice of enoxaparin as the LMWH for DVT treatment was based on both literature reviews and a large clinical trial supporting its use in home-based DVT treatment in addition to the fact that it was on the formulary.

Preliminary projected cost comparison analysis of 37 theoretical patients with DVT (DRG 453.8) treated with inpatient therapy using IVUH and outpatient-based therapy using LMWH revealed an annual projected cost savings to the health system of \$97,885 per 37 patients treated or \$2,646 per patient treated with LMWH (Table 1). These projected cost savings were mostly due to decreased hospital length of stay at a fixed cost of \$495 per hospital bed/day and factored in expansion of outpatient services such as education, phone calls, and follow-up visits to the anticoagulation clinic with home treatment. Assumptions of the cost comparison analysis included a six-day hospital stay for DVT based on 1996 data for average length of stay (LOS) and a conservative strategy of home treatment of DVT advocating a minimum 24-hour hospital LOS for patients treated with LMWH for observation purposes.

The home treatment program affected pharmacy operations in three ways. First, pharmacy would incur the expense of enoxaparin for outpatient treatment which was at the time available only in a 30mg pre-

filled syringe at \$11.92 per syringe and necessitating a treatment dose of 1mg/kg SQ every 12 hours. The projected cost to a 75kg person for six days of therapy with enoxaparin would be \$358. Because medication costs would have been an issue for certain patient groups (especially the Medicare and Medicaid population of which some members had medication caps at \$500 per year) pharmacy and senior administration would need to grant approval for outpatient use of enoxaparin free of charge or make use of an indigent program for qualified individuals, made available by the drug's manufacturer, Rhône-Poulenc Rorer. In these cases, pharmacy's drug costs would increase yet the health system would accrue overall cost savings from avoidance of hospitalization. Second, pharmacy staff would be diverted to refill enoxaparin syringes in order to provide a single injection per dose, an activity that was time-consuming. Lastly, the home treatment program was initiated in conjunction with the expansion of the clinical pharmacist-managed anticoagulation clinic, necessitating the addition of staff in the form of one full-time clinical pharmacist-tract provider and support staff.

Three treatment alternatives were developed based on the time of day, patient reliability, physician comfort level, and a set of absolute and relative exclusionary criteria that precluded home treatment. Patients with a low-risk profile that did not meet exclusionary criteria would be treated in a completely outpatient-based fashion using LMWH. Patients with a high-risk profile that met one or more absolute exclusionary criteria were treated in-hospital with IV UH. Patients who were felt to have a moderate risk profile based on comorbidity or insurance, compliance or other factors would be treated with an abbreviated hospitalization using LMWH followed by ultimate hospital discharge (usually within 24 hours) and home health support if they ultimately were felt to be acceptable outpatient candidates by the treating physician. A summary of the outpatient treatment protocol is shown in Figure 1.

The protocols went into effect in March,

1997 and by August, 1998 a total of 102 eligible patients who did not meet exclusionary criteria had been treated on an outpatient-basis using LMWH, which represented 61 percent of all patients with DVT (DRG 453.8). Of the 102 outpatients, 69 percent or 70/102 were treated on a completely outpatient basis and the remaining 31 percent or

32/102 were treated with reduced hospitalization. In terms of short-term clinical outcomes for quality control (within 90 days of diagnosis), data published elsewhere revealed a DVT recurrence rate of 1.9 percent and a major bleed rate of 0 percent for the patients treated in an outpatient basis.⁹ These results represented one of the lowest

TABLE 1 Projected Cost Estimates for IP therapy with UH and OP therapy for LMWH for Lovelace Health Systems

Cost administering IP standard unfractionated heparin (IP)

Annual number of patients	37
Annual patient days*	222
Number of dosages/patient day	4
Annual total dosages	888

*LOS is assumed to be 6.0 days on average

	Expense type	Per dosage amount (\$)	Per pt. day amount (\$)	Per year amount (\$)
Personnel				
Physician	Var. by day	38.03	38.03	8,442
Pharmacy nurse monitor	Var. by day	6.25	25.00	5,550
Educator (1 hour per patient)	Var. by pt.	20.00	20.00	740
Lab personnel	Var. by day	17.00	68.00	15,096
Subtotal personnel expenses		81.28	151.03	29,828
Drugs and supplies				
Drug (Unfr. heparin)				
– pre-mix bag (1/day)	Var. by day	4.17	4.17	926
– vial for bolus (1–2)	Var. by day	1.00	2.00	444
– IV and IV tubing	Var. by day	5.00	5.00	1,110
– PTT test kit (q 6 hours)	Var. by day	5.00	20.00	4,440
Subtotal supply expenses		15.17	31.17	6920
Room maintenance				
LOS in room				
– Room charge	Var. by day	460.00	460.00	102,120
– Housekeeping	Var. by day	10.00	10.00	2,220
– Laundry	Var. by day	5.00	5.00	1,110
– Room, equip., depreciation	Fixed by day	20.00	20.00	4,440
Subtotal room expenses		495.00	495.00	109,890
TOTAL EXPENSES		591.45	677.20	146,638

TABLE 1, continued

Cost administering low-molecular-weight heparin (OP) with 24-hour hospital stay

Annual number of outpatients	37
Number of dosages/outpatient day	2
Number of days for dosage	6
Annual patient days (IP)	37
Annual patient days (OP)	185
Annual total dosages	444

	Expense type	Per dosage amount (\$)	Per IP + OP day amount (\$)	Per year amount (\$)
Drugs				
– Medication	Var. per day	11.92	59.60	13,231
– Filling of syringes (OP Rx)	Var. per pt.	12.00	12.00	444
– Syringes	Var. per pt.	1.00	1.00	74
– Sharps container	Var. per pt.	5.00	5.00	185
Subtotal drug expenses		29.92	77.60	13,934
Physician				
– PCP (Two consult)	Var. per pt.	38.03	38.03	2,814
Room maintenance				
LOS in room				
– Room charge	Var. per pt.	460.00	460.00	17,020
– Housekeeping	Var. per pt.	10.00	10.00	370
– Laundry	Var. per pt.	5.00	5.00	185
– Room, equip., depreciation	Var. per pt.	20.00	20.00	740
Subtotal room expenses		495.00	495.00	18,315
Education				
– RPN/Nurse educator (1 hour/patient)	Var. by pt.	25.00	25.00	925
Follow-up phone calls				
– Anticoagulation clinic (15 minutes each)	Var. by day	5.00	5.00	925
Follow-up visits				
– Home health RN (1 hour/patient/day)	Var. per day	54.00	54.00	9,990
– PT value by home health (stick)	Var. per day	10.00	10.00	1,850
Subtotal follow-up expenses		64.00	64.00	11,840
TOTAL EXPENSES		656.95	704.63	48,753
TOTAL ANNUAL SAVINGS FROM LMWH				97,885

FIGURE 1 Lovelace Health Systems' Protocol For Outpatient Low-Molecular-Weight Heparin Therapy

1. The treating physician is ultimately responsible for the patient's care.
2. At the time the diagnosis of DVT is made, the treating physician will decide whether the patient can be treated as an outpatient or will need to be admitted to the hospital.
3. If the decision is made for outpatient care, then the following steps should be taken:
 - The patient will be referred immediately to the anticoagulation clinic where care will be coordinated and teaching will be started.
 - Members of the anticoagulation clinic will have the initial lab work drawn consisting of CBC, SMA-12, PT, APTT, and urinalysis.
 - LMWH will be given in the form of enoxaparin SQ, at a dosage of 1mg/kg q 12 hours for a minimum of five days.
 - The administration of the first dose of enoxaparin will be coordinated by the anticoagulation clinic personnel.
 - Orders to home health care and case management will be sent by anticoagulation clinic personnel.
 - While in the anticoagulation clinic, the patient will be taught what LMWH is and how to self-administer it. If the patient is capable of learning the procedure and instituting it, then he/she will be allowed to return home to give self next dose in 12 hours. If not, arrangements will be made for HHC to visit the home to give the next dose.
 - All dosages of enoxaparin for home use will be drawn up in the anticoagulation clinic at the time of the patient's first visit there.
 - If the patient is incapable of self-administration but is still homebound, HHC will visit the home twice daily for the duration of heparin therapy to give the enoxaparin (i.e., at least five days). If the patient is able to self-administer, then HHC will visit once daily. During that time, the patient will also be taught about the use of warfarin.
 - Platelet counts will be drawn by HHC on days 3 and 5.
 - He/she will be started on warfarin 5-10mg on day 1 while in anticoagulation clinic, and daily protimes will be drawn by the HHC nurse. Anticoagulation clinic personnel will be called with protime results, and will determine daily dosages.
 - Activity at home: Bed rest except to bathroom only for the first day, then up ad lib after that.
 - The treating physician should see the patient for a follow-up appointment in one week.
 - Noninvasive venous examination should be done at the end of warfarin treatment to establish a new baseline.

reported for an outpatient DVT treatment program and compared favorably to our institution's previous inpatient experience with a comorbid matched group. In addition, the protocol received high patient and provider satisfaction indices from a standardized questionnaire.

As part of the Anticoagulation Episodes of Care pharmacoeconomic data analysis, an actual cost comparison was done comparing initially the first 124 patients treated with the DVT treatment protocol using LMWH versus a standardized group treated in 1996 with conventional in-hospital therapy using IV UH. The results are summarized in Table 2 and based upon true costs when applicable.

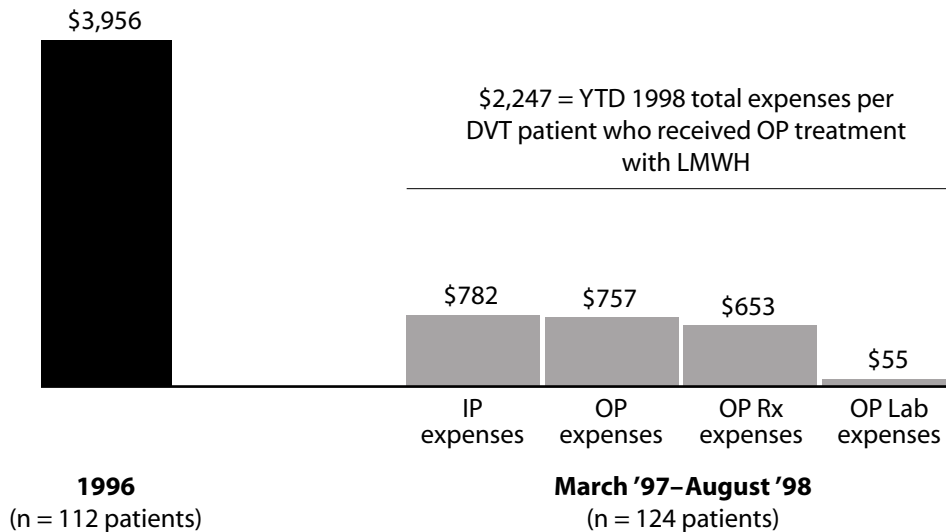
In-patient expenses included personnel (physician, nursing, etc.), fixed hospital costs of \$495 per day for room and maintenance, drugs, supplies and lab tests. Outpatient expenses included personnel costs and anticoagulation clinic services (education by teaching nurses, home health, follow-up calls, and visits by the anticoagulation clinic). Outpatient treatment expenses included the cost of enoxaparin, the cost of filling of syringes by pharmacy staff, and supplies such as syringes and sharps containers. Outpatient lab expenses included monitoring of warfarin by PT testing.

Average total cost for inpatient DVT treatment was \$3,956 per patient in 1996 versus \$2,247 for outpatient DVT treatment using LMWH in 1997-1998, a true cost savings of \$1,709 per patient treated. Outpatient expenses that reflected maintenance and support costs of the anticoagulation clinic were substantial and represented over 33 percent of total outpatient costs (\$757 per patient). The cost of enoxaparin (including supplies and the filling of syringes by pharmacy staff) was substantial and reflected over 29 percent of total outpatient costs. However, the sum of these costs was less than total fixed hospital costs.

Total real cost savings to the delivery system was estimated at \$211,792 during the observational period. Although the figure of \$1,709 cost savings per patient treated was less than the projected \$2,647 estimate, fur-

TABLE 2 Actual Cost Comparison Between IP DVT Treatment With IVUH (1996) and OP DVT Treatment With LMWH (1997-1998)

\$3,956 = 1996 total expenses per DVT patient prior to development of OP treatment with LMWH



ther subanalysis revealed that cost savings improved to \$2,076 per patient if 15 oncology patients treated off-protocol were excluded. In addition, after the advent of pre-filled enoxaparin syringes that reduced the variable cost of pharmacist time to fill individual syringes, an additional cost savings of \$397 per patient treated was established, making a true cost savings figure of \$2,473 per patient treated for the outpatient DVT program.

Discussion

Pharmacoeconomic analysis of a pharmacy-managed, outpatient-based DVT treatment program in an integrated health care delivery system such as Lovelace Health Systems reveals substantial cost savings to the health care system with excellent short-term clinical outcomes and improved patient satisfaction indicators. By careful patient selection and risk stratification criteria, hospital economic and technical efficiency is maximized, since fixed hospital costs would only

be applied to those subset of patients with DVT (i.e., high risk) that require the high cost of services necessitated by hospitalization. By treating the moderate-to-low risk groups on an outpatient basis, one is able to maximize reimbursements and efficient use of resources relative to expenditures since the costs of providing these services (anticoagulation clinic, home health service, LMWH preparation and supplies) is still less expensive than the costs of hospitalization. As reflected in the adverse outcome data, quality of care would still be maintained in these two groups of patients. In addition, if some of the outpatient services are already in place (such as an existing Warfarin clinic, telemedicine service, or home health service), then the expansion of these services in the form of staff, benefits, lab supplies, building maintenance and utilities to include outpatient DVT patients may represent only marginal cost accrual to the health care system, making an outpatient DVT program more cost-effective. Lastly, if pharmacy cost

of the LMWH is made less expensive (such as the advent of pre-filled syringes or multi-dose vials) then overall outpatient treatment costs may also be substantially reduced.

From a third-party payer perspective, reimbursement decision-making involves ways of reducing costs while maintaining quality of care. As such, outpatient-based treatment strategies for DVT using LMWH in select patients represents a “win-win” situation with reduction of overall costs of treatment and maintenance (or possibly improvement) of clinical outcomes and improvement of patient quality-of-life. The economic goal of DVT treatment is to safely and efficaciously treat appropriate patients at home where savings would appear to be substantial. Indeed, it would not be surprising if future DRGs for DVT treatment reflected a reduced hospital length of stay to reflect outpatient treatment strategies.

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Outpatient Treatment Of DVT in a 170,000-Member HMO

SAMEER ABU-SAMRAH, M.D.

Vice President and Regional Medical Director, Sierra Health Services

Since the efficacy of enoxaparin in the setting of unstable angina, post-orthopedic, and abdominal surgery prophylaxis and in the treatment of DVT is well documented, I became very excited to hear in 1998 that the FDA had approved enoxaparin for the outpatient treatment of DVT.

As the medical director of utilization for a network and staff-model managed care organization with 170,000 enrollees in Las Vegas, I had always felt the need to decrease the inpatient days both for financial and quality reasons: Hospitals are not the safest place for patients with DVT. Since the initial comparison study of fractionated and unfractionated heparin for the treatment of DVT over 10 years ago, I have urged physicians to use low-molecular-weight heparin in less acute settings, i.e. subacute facilities or the home, for the appropriate patients with DVT.

Since then, many physicians have tried it with success and now it is not only the trend, but also the expectation of most of the third-party payers.

Progressive MCOs immediately recognized the quality, safety, cost savings, and patient convenience and thus made enoxaparin for the treatment of outpatient DVT a medical, rather than pharmacy, benefit.

Such organizations immediately created the appropriate infrastructure and protocols that support the success of the treatment and reduce the hassles to the treating physician. At worst, the cost of outpatient treatment with enoxaparin is 25 percent that of an acute hospital bed day.

At this HMO, outpatient enoxaparin ther-

apy has been handled as a medical benefit since it was instituted in late 1998. There was never an issue of covering it under the medical benefit because the medical savings greatly outweighed the cost of the drug.

The first move was to get buy-in from the treating physicians. We made the drug available in all of our urgent care facilities and made agreements with all the ERs in the network to administer the first dose of enoxaparin immediately when the diagnosis of DVT is confirmed. Then we created the outpatient protocol with home health agencies to administer the remaining treatments twice daily.

In the HMO's ambulatory facilities, about 95 percent of all patients with proven DVT were appropriate for outpatient management and were treated with enoxaparin and experienced no complications.

Nationally, the average cost for an inpatient day is more than \$1,000, according to the American Hospital Association. The average cost per day for home health plus enoxaparin is about \$250, about one fourth the cost of inpatient care.

In this era of cost-consciousness and demand for cost containment, I would be surprised to learn that a third-party payer was not making the outpatient treatment of DVT with enoxaparin a medical benefit with no copay to its members. The treatment is safe, efficacious, of high quality, and economical. After all, with outpatient treatment, you don't have to be concerned about the inpatient complications such as nosocomial infections, falls, and medication errors, just to name a few.

