



THE HEMOPHILIA ALLIANCE, INC.

Integrating Pharmacy with Comprehensive Care

April 28, 2006

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2005N-0428

To Whom It May Concern:

This letter serves as a response from the Hemophilia Alliance, Inc. to the February 1, 2006 Federal Register Notice (71 Fed. Reg. 21, 5200, 5203). The Hemophilia Alliance, Inc. (the "Alliance") is a 501(c)(6) trade association representing fifty Hemophilia Treatment Centers ("HTCs") who either have, or are considering having, a factor distribution program under Section 340B of the Public Health Service (PHS) Act. You have asked for responses to the questions:

- (a) Whether the proposed exclusion should be expanded to allow registered blood establishments that also provide health care services to distribute drugs other than blood derivatives that might be used to treat blood disorders;
- (b) The number of entities affected and how often drugs used to treat blood disorders are distributed by registered blood establishments and whether the nature of this practice is critical and if there is any negative impact on public health if the exclusion allows only for the distribution of blood derivatives; and
- (c) Whether HTCs should be included within the scope of the exception.

Background

Hemophilia

Hemophilia is a hereditary bleeding disorder that predominantly affects males. Persons with hemophilia lack one or other protein, known as factors, that prevents their blood from forming clots which can lead to prolonged bleeding. This prolonged bleeding, left untreated or under treated, leads to joint damage or even death. Treatment of hemophilia is primarily through the administration of clotting factor to replace the factor which the affected individual is lacking.

The most significant cost faced by the patient with hemophilia is the cost of clotting factor concentrate. At current market prices, an adult person with moderate to severe hemophilia will spend approximately \$100,000 per year on clotting factor and a pediatric patient about half that. This amount would be to cover routine outpatient usage. On an inpatient basis a person with hemophilia could easily exceed \$100,000 on minimal stay in the hospital.

Hemophilia Treatment Centers (HTCs)

Hemophilia care is managed through a nationwide network of hemophilia diagnostic and treatment centers (HTCs) that provide a range of comprehensive services. A comprehensive care center, if established in a central location, provides for efficient use of resources and offers all services in one location. HTCs incorporate the concept of treating the whole person and his or her family by case management of the medical and psychosocial issues related to hemophilia, other clotting disorders and HIV infection. Since the patient is monitored regularly, there is a heavier focus on prevention, not just treatment, and long-term treatment costs are reduced. The benefits of comprehensive care are evident in terms of quality of life, decreased morbidity and extension of longevity. In fact, a recent CDC study showed that treatment of hemophilia at HTCs reduced mortality by 40% when compared to individuals treated outside of the HTC system of care.¹ In addition to helping persons with hemophilia become more independent and productive, comprehensive care has also been used as a model of delivering health care for other chronic illnesses.

The national hemophilia program pioneered the concept of regionalization for chronic care in the United States. The establishment of a core center within a multi-state region of HTCs was created to enhance coordination of specialized medical services over the widest possible geographic area. It has allowed treaters of this rare chronic illness to communicate closely about clinical and research issues, to facilitate referrals and to gain administrative efficiencies through collaboration.

The federal government, through the Maternal and Child Health Bureau (MCHB) of the Department of Health and Human Services and The Centers for Disease Control and Prevention (CDC) fostered this network of regional centers of excellence anchored by a core regional program. It is their belief that this model is effective for delivering the highest standard of care to geographically dispersed patients.

The regional core center has responsibility for coordinating regional strategies for improving hemophilia care and preventing the complications of hemophilia and to work with all hemophilia treatment centers to provide professional education and clinical consultation. In turn,

¹ J. Michael Soucie et al in "Mortality among males with hemophilia: relations with source of medical care" – *Blood* 15 July 2000; Vol. 96, No. 2: 437-442.

the HTC's within the region provide expertise and consultation to primary care providers, hospitals and other non-specialists when these providers see hemophilia patients.

One key component of this collaboration between the HTC and providers such as hospitals that are not affiliated with an HTC is the provision of clotting factor on an "as needed" basis. In conjunction with the delivery of the clotting factor is the consultation on the management of the patient. In the case of blood banks expertise in hemophilia was developed when the only treatment available was cryoprecipitate (cryo) and fresh, frozen plasma (FFP). The blood banks coordinated the delivery of these products to hospitals when they had to treat hemophilia patients. At that time most hemophilia treatment had to be done at a hospital and coordinating the product delivery and the care management was critical.

Even though today much of hemophilia treatment takes place at the home, there are still many times when a patient must turn to a hospital for care. When this happens at a hospital that does not have an HTC the coordination of product delivery and care management is as critical (if not more so given the complex dosing of drugs now being used) as it was in the 1960's and 1970's with cryo and FFP. However, this longstanding system of care delivery is threatened with the prospect of the implementation of this proposed rule. If implemented as proposed, the rule would take away the critical role HTC's play in clotting factor delivery to hospitals as well as the patient care management that also takes place. The following comments address our concern with the proposed rule.

Comments

- (a) **Whether the proposed exclusion should be expanded to allow registered blood establishments that also provide health care services to distribute drugs other than blood derivatives that might be used to treat blood disorders;**

This question raises two issues. First the provision of health care services by registered blood establishments and second, what is meant by a "blood derivative."

- (i) Health Care Services Provided by Registered Blood Establishments

The Proposed Rule states, ". . . the sales restrictions in § 203.22 would not apply to the sale, purchase or trade of . . . any blood derivatives by a registered blood establishment that qualifies as a health care entity as long as all the health care services that it provides **are related to its activities as a registered blood establishment.**"² (Emphasis added.)

² 71 Fed. Reg. 21 at 5202.

We believe that “related activities” should include the diagnosis and on-going treatment of persons with hemophilia and related bleeding disorders. The Alliance has two members that qualify as federally funded HTC’s and are also registered blood establishments. The care that they provide is of utmost importance to ensuring adequate access to care for persons with bleeding and related disorders in their catchment area. The staff at these centers are experts in the care of hemophilia and their expertise is relied upon by caregivers who do not specialize in hemophilia.

These registered blood establishments that are HTC’s also provide blood derivatives (and other drugs) to institutions who do not have their own supply of these products. For this reason, it is important that it be clarified that the health care services that registered blood establishments provide to persons with hemophilia and related bleeding disorders be considered to be “related to (their) activities as a registered blood establishment.”

By clarifying this relationship, there would not be a risk of other health care entities registering as blood establishments as mentioned in the Proposed Rule.³ These entities are primarily blood establishments and are precisely the types of entities that the Proposed Rule contemplates would be subject to the proposed exception. “Health Care Services” that a registered blood establishment can provide should be defined to include, “such services as may be delivered pursuant to the registered blood establishment’s designation as a federally funded comprehensive Hemophilia Diagnostic Treatment Center receiving a grant under Section 501(a)(2) of the Social Security Act.”⁴

(ii) Definition of Blood Derivatives

Blood derivatives are described in the Proposed Rule as prescription drugs that include: Albumin, antihemophilic factor, Factor IX Complex, alpha-2 anti-trypsin and immune globulin.⁵

The term “blood derivative” is inaccurate and can lead to confusion. Many of the products used to treat hemophilia are not “blood derivatives” but instead are synthetic recombinant products. Therefore there should be clarification that “antihemophilic factor” includes all clotting factor therapies used to treat hemophilia and related bleeding disorders. This appears to be the intent as it is unlikely a rule would allow a registered blood establishment to distribute a particular type of antihemophilic factor that is blood derived but not another because it is a recombinant therapy.

The proposed exclusion should therefore be expanded to allow registered blood establishments that provide health services, to distribute drugs that are not blood derivatives that

³ *Id.*

⁴ This is enabling legislation establishing HTC’s and the National Hemophilia Program within the Department of Health and Human Services’ Health Resources Services Administration. See Attachment 1.

⁵ 71 Fed. Reg. at 5201.

might be used to treat blood disorders. In addition, it should be clarified that “health services” includes services provided by registered blood establishments that are also HTCs.

- (b) The number of entities affected and how often drugs used to treat blood disorders are distributed by registered blood establishments and whether the nature of this practice is critical and if there is any negative impact on public health if the exclusion allows only for the distribution of blood derivatives; and**

The Alliance does not represent registered blood establishments in general, only those who are also HTCs. Our HTC members who are also registered blood centers routinely distribute clotting factor concentrate. These registered blood establishments distributed over 50 million units of clotting factor in 2005. Of this amount, 17 million or 34% went to persons other than a consumer or patient and would therefore be prohibited if it were found that the services they provide to persons with hemophilia are not “related to (their) activities as a registered blood establishment.” Were this to happen, several hospitals would be without clotting factor leaving patients vulnerable to lack of access to the appropriate medical treatment. This practice is therefore critical to the provision of care in the areas where these registered blood establishments serve. For this reason, it is imperative that the health care services given by these registered blood establishments to persons with hemophilia, and related disorders, be considered sufficiently related to the activity of the registered blood establishment.

- (c) Whether HTCs should be included within the scope of the exception.**

HTCs, like registered blood establishments, currently play a critical role in the distribution of clotting factor to ensure the appropriate care of persons with hemophilia and related bleeding disorders. In 2005, fourteen or 28% of the membership of the Alliance distributed approximately 40 million units of clotting factor to institutions in need of these products.

In many instances, hospitals, both large and small, that are not affiliated with an HTC do not keep an inventory of clotting factor. The main reason for this is the cost of the factor concentrate. According to the Centers for Medicare and Medicaid Services (CMS) website, the Average Sales Price (ASP) for Recombinant, the most widely used Factor VIII product, is approximately \$0.86⁶. To purchase 200,000 units, which is an amount that could easily be used by one patient who has presented at the hospital with trauma and is then admitted, a hospital would have to spend \$172,000. This expenditure would have to be made without knowing if the product will be used or not. The hospital has to take on the risk of the outlay on this expensive,

⁶ www.cms.hhs.gov/providers/drugs/asp.asp. The website gives prices at the CMS reimbursement rate of ASP + 6% + \$0.15. The Recombinant Factor VIII price for second quarter 2006 is \$1.058. By subtracting the \$0.14 and removing the 6% you get \$0.86/unit.

rare drug. Instead, the hospital can opt to purchase the drug from the HTC to avoid this risk. It is usually not an option for the hospital to order the product directly from the manufacturer because the manufacturers will generally only sell to established customers. In addition, these products are generally not available through traditional wholesalers with whom these hospitals have relationships.

Even if these hospitals are able to obtain clotting factor from a source other than the HTC, it would likely be at a higher cost than what they are currently paying. HTCs do not have a profit motive to consider when setting their price and often sell to these hospitals at below market prices.

Coordination between the HTC and the hospital utilizing the factor is also important because it enhances the actual delivery of care to the patient. The hospitals purchasing from HTCs recognize the expertise that exist at the HTCs. Not only do the hospitals receive the factor from the HTC, they receive consultations and patient management. Without this expert consultation from the HTC there could be inappropriate management of the patient which could lead to more factor utilization and therefore more expense. Having the HTC do the distribution and the consultation leads to an efficient system that works best for the patient and the hospital.

Consequently, prohibiting HTCs from distributing clotting factor would have a tremendous adverse affect on access to care for the bleeding disorder patients these hospitals serve. If the hospitals decide not to have a source for clotting factor, it would lead to patients having to travel miles for care. With a rare disorder that requires prompt treatment traveling extra distances will lead to higher morbidity and even mortality. If there is no coordination between the hospital and HTC, the patient will not get the benefit of expertise which is so critical to a successful outcome.

By allowing HTCs to be included as part of the proposed exclusion, you will allow a system of care delivery that has existed, in some instances, since the 1960's to continue. This is in the best interest of the hospitals which receive the clotting factor and their patients.

Summary

In our comments we have outlined the following:

- **HTCs should be included within the scope of the proposed exclusion.**
- HTCs currently play a critical role in the distribution of clotting factor.
- If HTCs are not allowed to distribute clotting to hospitals that do not routinely have an inventory of these products, this will have an adverse impact on access to care for persons with bleeding disorders.

- **The proposed exclusion should be expanded to allow registered blood establishments to distribute drugs other than blood derivatives that are used to treat bleeding disorders.**
- The definition of “blood derivatives” should be clarified to cover all antihemophilic factor both recombinant and plasma-derived.
- It should be clarified that health care services provided by registered blood establishments which are comprehensive diagnostic treatment center receiving a grant under Section 501(a)(2) of the Social Security Act are considered to be “related activities to (their) activities as a registered blood establishment.”
- The practice of registered blood establishments that are also HTC providing clotting factor to hospitals is critical to the provision of care in the areas receiving the factor.

The Hemophilia Alliance appreciates the opportunity to comment on this important proposed rule. We hope our comments are helpful and strongly urge the FDA to give full consideration of our requests. The Alliance is available to discuss our comments with you in more detail. Please direct questions or inquiries you may have to me at 202/872-6764 or by email at derek.robertson@ppsv.com.

Sincerely,

Derek Robertson
General Counsel

SOCIAL SECURITY ACT

SEC. 501. [42 U.S.C. 701] (a) To improve the health of all mothers and children consistent with the applicable health status goals and national health objectives established by the Secretary under the Public Health Service Act for the year 2000, there are authorized to be appropriated \$850,000,000 for fiscal year 2001 and each fiscal year thereafter—

(2) for the purpose of enabling the Secretary (through grants, contracts, or otherwise) to provide for special projects of regional and national significance, research, and training with respect to maternal and child health and children with special health care needs (including early intervention training and services development), for genetic disease testing, counseling, and information development and dissemination programs, for grants (including funding for comprehensive hemophilia diagnostic treatment centers) relating to hemophilia without regard to age, and for the screening of newborns for sickle cell anemia, and other genetic disorders and follow-up services;

SEC. 502. [42 U.S.C. 702] (a)(1) Of the amounts appropriated under section [501\(a\)](#) for a fiscal year that are not in excess of \$600,000,000, the Secretary shall retain an amount equal to 15 percent for the purpose of carrying out activities described in section [501\(a\)\(2\)](#). The authority of the Secretary to enter into any contracts under this title is effective for any fiscal year only to such extent or in such amounts as are provided in appropriations Acts.