The Inhibitor Committee of the AHCDC considers recombinant porcine FVIII (Obizur) to be a valuable agent for the treatment of bleeding in patients with acquired hemophilia (AH), and supports the inclusion of this product in the inventory of the CBS. The AHCDC Executive and Board endorses the following recommendations of the Inhibitor Committee regarding the use of Obizur in patients with AH:

1. We recommend that Obizur be distributed only to hospitals associated with Hemophilia Treatment Centres

Rationale for the recommendation: For many rare diseases, the clinical and diagnostic expertise required for the optimal care of affected patients is available only in specialized centres of excellence. This is the case for AH, for which these centres of excellence in Canada are part of a national network of Hemophilia Treatment Centres (HTC). HTC have practitioners with clinical experience and specialized expertise in managing AH. HTC have rapid access to coagulation laboratories with the ability to perform the assays necessary to establish the diagnosis of AH and to monitor its progress and treatment, and to do so with acceptable turn-around times. In the specific case of Obizur, anti-porcine factor VIII (FVIII) assays are required to identify those AH patients in whom anti-porcine FVIII inhibitor titres are low enough to anticipate that Obizur might be effective, and for monitoring for the development of anti-porcine FVIII inhibitors during therapy; these assays will only be available and validated at a local HTC or at a laboratory designated as a reference site for HTCs. The Transfusion Medicine laboratories at HTC sites are also able to handle and reconstitute Obizur, which can be time-consuming and labour-intensive, given that single doses may require pooling the contents of over 20 vials. For all these reasons, patients with AH who are deterimined to need Obizur should receive care at HTC. Nevertheless, it is recognized that on occasion it may be desirable to initiate treatment with Obizur at another site prior to patient transfer to an HTC; this should be done only with the guidance of the HTC physician who will be assuming ongoing care for that patient.

2. We recommend that the prescribing of Obizur be limited to practitioners who are Medical Directors of HTC or their designates.

Rationale for the recommendation: This is a corollary of the first recommendation. All the physicians in Canada who regularly treat patients enrolled in HTC are active members of the AHCDC. These practitioners are skilled in the recognition and investigation of bleeding in congenital hemophilia and related bleeding disorders, and in the use of clotting factor concentrates and ancillary agents. This skill set translates to the use of Obizur for management of AH. HTC-affiliated clinicians closely follow the scientific literature in this rapidly evolving field and make it a focus of their continuing educational activities. They have a degree of expertise in AH that cannot be matched by other practitioners, including other academic and community hematologists. Furthermore, given the rarity of AH it is important that HTC physicians see all new cases so as to expand and maintain their expertise in its management and in the use of Obizur. Furthermore, in anticipation that Obizur might be approved in the foreseeable future for use in congenital hemophilia A patients with inhibitors, it is important that HTC physicians gain more experience in its use. The AHCDC network provides its members with easy access for advice on managing challenging cases, and it functions as a research collaborative through which they can pool their experience to contribute to the medical literature. The AHCDC also maintains a safety surveillance database (CHESS) to which any adverse events associated with Obizur will be reported. Therefore AHCDC members practicing in HTC are uniquely able to prescribe Obizur with the benefit of clinical expertise and laboratory guidance. This will protect patients from the risks of over and under-treatment, and will also promote responsible resource utilization by avoiding potential wastage due to inappropriate use of this product.

3. We recommend that treatment with Obizur should be individualized, but broadly based on the available medical literature and on the product monograph.

Rationale for the recommendation: In a bleeding patient with proven AH therapy can be initiated with desmopressin, human FVIII concentrate, APCC, recombinant FVIIa, or Obizur. Any of these agents can be an appropriate choice as first-line or second-line therapy. A decision algorithm is beyond the scope of this document, but the expert physician will consider factors such as the site and severity of the bleed event, the patient's previous response to any of these agents (if known), factor VIII plasma activity (more relevant to diagnosis than to choice of hemostatic agent), anti-porcine and anti-human FVIII inhibitor titers, and co-morbidities. When Obizur is selected as the agent of choice, the regimen should be broadly based on both the product monograph and the available literature (relevant publications are listed in the bibliography): patients with AH who are actively bleeding or who need hemostatic coverage for procedures, and whose anti-porcine FVIII Bethesda titre is less than 20 BU. These general principles will not identify every circumstance in which an experienced HTC physician might determine that Obizur would be of use, however, and Obizur should be available for use outside these parameters when deemed necessary. Many HTC physicians will have personal experience with the use of the plasma-derived porcine FVIII concentrate Hyate:C, which was withdrawn from the market in 2004. This experience can be a valid guide to assist in designing individual Obizur treatment regimens, just as the experience with plasma-derived human FVIII concentrates guided the use of their recombinant analogs in the 1990s. The use of Obizur in patients with congenital hemophilia A and FVIII inhibitors is not a labeled indication; however experienced HTC physicians may consider using Obizur when these patients are undergoing major surgery or experiencing serious bleeding events, in those rare circumstances when it is considered preferred to inhibitor bypassing agents.

Bibliography

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