



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Anti-Inhibitor Coagulant  
Complex Vapor Heated (Feiba®  
VH)**

**Effective Date ..... 5/15/2009  
Next Review Date..... 5/15/2010  
Coverage Policy Number ..... 4047**

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## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2009 CIGNA

## Coverage Policy

**CIGNA covers anti-inhibitor coagulant complex vapor heated (Feiba® VH) as medically necessary for the treatment of spontaneous bleeding episodes or to cover surgical interventions in EITHER:**

- individuals with hemophilia A and B with inhibitors
- non-hemophiliac individuals with acquired inhibitors to Factors VIII, XI, and XII

## General Background

### FDA Approved Indications

Feiba VH (AICC) is indicated for the control of spontaneous bleeding episodes or to cover surgical interventions in hemophilia A and hemophilia B patients with inhibitors. In addition, the use of Feiba Immuno (AICC) has been described in a few non-hemophiliacs with acquired inhibitors to Factors VIII, XI, and XII. One case has been reported where Feiba Immuno (AICC) was effective in a patient with von Willebrand's disease with an inhibitor. Clinical experience suggests that patients with a Factor VIII inhibitor titer of less than 5 B.U. may be successfully treated with Antihemophilic Factor. Patients with titers ranging between 5 and 10 B.U. may either be treated with Antihemophilic Factor or Feiba VH (AICC). Cases with Factor VIII inhibitor titers greater than 10 B.U. have generally been refractory to treatment with Antihemophilic Factor.

## FDA Recommended Dosing

Clinical trials have demonstrated that the response to treatment with Feiba Immuno (AICC) may differ from patient to patient with no correlation to the patient's inhibitor titer. Response may also vary between different types of hemorrhage (e.g. joint hemorrhage vs. CNS hemorrhage). As a general guideline, a dosage range of 50 to 100 Units of Feiba VH (AICC) per kg of body weight is recommended. However, care should be taken to distinguish between the following four indications, all of which have undergone careful clinical evaluation:

- **Joint Hemorrhage**

In joint hemorrhage, a dose of 50 units per kg of body weight is recommended at 12-hour intervals, which may be increased to doses of 100 units per kg of body weight at 12-hour intervals. Treatment should be continued until clear signs of clinical improvement appear, such as relief of pain, reduction of swelling or mobilization of the joint.

- **Mucous Membrane Bleeding**

A dose of 50 units per kg of body weight is recommended to be given at 6-hour intervals under careful monitoring (visible bleeding site, repeated measurements of the patient's hematocrit). If hemorrhage does not stop, the dose may be increased to 100 units per kg of body weight at 6-hour intervals. Two such administrations or 200 units per kg of body weight a day should not be exceeded.

- **Soft Tissue Hemorrhage**

For serious soft tissue bleeding such as retroperitoneal bleeding, doses of 100 units per kg of body weight at 12-hour intervals are recommended. A daily dosage of 200 units per kg of body weight should not be exceeded.

- **Other Severe Hemorrhages**

Severe hemorrhages, such as CNS bleedings have been effectively treated with doses of 100 units per kg of body weight at 12-hour intervals. Sometimes, Feiba VH (AICC), Vapor Heated may be indicated at 6-hour intervals until clear clinical improvement is achieved.

Hemophilia A is a deficiency in factor VIII (FVIII) caused by a genetic mutation on the X chromosome. Hemophilia B is a deficiency in factor IX and is clinically indistinguishable from hemophilia A. Factor assays are used to confirm a diagnosis. Most patients with severe hemophilia are managed at home and are rarely admitted to the hospital for severe bleeding. Early and adequate treatment stops extremely painful bleeding into the joints and muscles. Inadequately treated patients become debilitated due to these bleeds and may be confined to a wheelchair as a young adult.

Feiba VH, Anti-Inhibitor Coagulant Complex, Vapor Heated, is a freeze-dried sterile human plasma fraction with Factor VIII inhibitor bypassing activity. Feiba VH contains Factors II, IX, and X, mainly non-activated, and Factor VII mainly in the activated form. The product contains approximately equal unitages of Factor VIII inhibitor bypassing activity and Prothrombin Complex Factors.

In a pre-clinical study to determine the virus inactivating efficacy of vapor heating, samples of bulk Feiba Immuno (AICC) were spiked with  $2 \times 10^6$ /mL infectious units of HIV and subjected to vapor heat treatment. The residual virus titer was found to be less than 1 infectious unit/0.5 mL. A clinical study 4 testing Antihemophilic Factor treated by a similar vapor heating procedure has shown none of 4 lots used in the study to produce non-A, non-B hepatitis in intensively followed patients naive to blood product administration.

The safety and efficacy of Anti-Inhibitor Coagulant Complex has been demonstrated by two prospective clinical trials. The first, conducted by Sixma and collaborators during 1979 and early 1980, was a randomized double-blind study comparing the effect of Anti-Inhibitor Coagulant Complex and Prothromplex (a nonactivated prothrombin complex concentrate) in 15 patients with hemophilia A and inhibitors to Factor VIII. A total of 150 bleeding episodes (primarily joint and musculoskeletal plus a few mucocutaneous) were treated. A single dose of 88 units per kg of body weight was used uniformly for treatments with Anti-Inhibitor Coagulant Complex. The study showed that, based on subjective patient evaluation, Anti-Inhibitor Coagulant Complex was fully effective in 41.0% and partly effective in 24.6% of episodes (i.e., combined effectiveness of 65.6%), while Prothromplex was rated fully effective in 25.0% and partly effective in 21.4% of episodes (i.e., combined effectiveness of 46.4%).

The second study with Anti-Inhibitor Coagulant Complex was a multiclinic study conducted by Hilgartner et al. It was designed to evaluate the efficacy of Anti-Inhibitor Coagulant Complex in the treatment of joint, mucous membrane, musculocutaneous and emergency bleeding episodes such as central nervous system hemorrhages and surgical bleedings. In 49 patients with inhibitor titers of greater than five Bethesda Units (from nine cooperating hemophilia centers), 489 single doses were given for the treatment of 165 bleeding episodes. The usual dosage was 50 units per kg of body weight, repeated at 12-hour intervals (six-hour intervals in mucous membrane bleedings), if necessary. Bleeding was controlled in 153 episodes (93%). In 130 (78%) of the episodes, hemostasis was achieved with one or more infusions within 36 hours. Of these, 36% were controlled with one infusion within 12 hours. An additional 14% of episodes responded after more than 36 hours. Of the 489 single doses, only 18 (3.7%) caused minor transient reactions in recipients. Ten out of 49 patients (20%) showed a rise in their inhibitor titers. In five of these patients (10%), the rise was tenfold or more. However, of these ten patients, three had received Factor VIII or Factor IX concentrates within two weeks prior to treatment with Anti-Inhibitor Coagulant Complex. These anamnestic rises have not been observed to interfere with the efficacy of Anti-Inhibitor Coagulant Complex.

Another study sought to increase comprehension of the full therapeutic profile of Feiba by evaluating its safety and efficacy in the settings of acute bleeding, surgery, and prophylaxis. Information was collected through a post-marketing surveillance study; questionnaire booklets were distributed to 72 treatment centers in the United States and Europe. The booklets contained questions related to patient demographics, inhibitor titre determinations, and Feiba treatment. Information comprising 200 Feiba treatment periods and representing >4500 infusions was available for 63 patients with inhibitors. Twelve patients were in more than one treatment group. Efficacy was determined by a subjective global evaluation and was good or excellent in 82% of all acute, and 91% of all surgical treatments. Additionally, prophylactic treatment resulted in improved or stabilized clinical orthopedic status in 11 of 13 patients (85%). Based on available data, Feiba was judged safe in all treatment situations by the small number of adverse events (<0.04%). No thrombotic complications occurred during any treatment episode. Results indicated that Feiba was safe and effective in acute, surgical, and prophylactic treatment settings, supporting the utility of Feiba as a treatment option for patients with inhibitors. However, prospective studies are advised.

The use of Feiba VH (AICC) is contraindicated in patients who are known to have a normal coagulation mechanism. In the course of treatment with preparations containing the prothrombin complex, thromboembolic events may occur particularly after high doses and/or in patients with thrombotic risk factors. After application of high doses (single infusion of 100 units per kg of body weight and daily doses of 200 units per kg of body weight) of Feiba VH (AICC), laboratory and/or clinical signs of DIC have occasionally been observed. In individual instances myocardial infarction was found to occur after high doses and/or prolonged administration and/or in the presence of risk factors predisposing to myocardial infarction. As with all human plasma products, any kind of allergic reaction may be seen ranging from mild, short-term urticarial rashes to severe anaphylactoid reactions. Administration of Feiba VH (AICC) should be discontinued immediately, if such signs appear. Allergic reactions should be treated with antihistamines and glucocorticoids. Shock should be treated in the usual way.

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## Coding/Billing Information

**Note:** This section is not in use.

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## References

1. Baxter Healthcare Corporation. Feiba<sup>®</sup> VH (Anti-Inhibitor Coagulant Complex Vapor Heated) package insert. Westlake Village, CA: Baxter Healthcare Corporation. April 2005.
2. Bolton-Maggs PH, Pasi KJ. Hemophilias A and B. *Lancet* 2003; 361:1801-1809.
3. Dimichele D, Négrier C. A retrospective postlicensure survey of FEIBA efficacy and safety. *Haemophilia*. 2006 Jul;12(4):352-62.

4. McEvoy GK, ed. AHFS 2009 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2009.

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## Policy History

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<b>Pre-Merger Organizations</b>	<b>Last Review Date</b>	<b>Policy Number</b>	<b>Title</b>
CIGNA HealthCare	3/15/2008	4047	Anti-Inhibitor Coagulant Complex Vapor Heated (Feiba <sup>®</sup> VH)
Great-West Healthcare	1/2007	P05.102.1	Hemophilia

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