

**הודעה על החמרה (מידע בטיחות) בעלון לרופא**  
**(מעודכן 3102.50)**

תאריך \_\_\_\_ October 22, 2013 \_\_\_\_

שם תכשיר באנגלית ומספר הרישום

**Antihemophilic Factor (Human) Hemofil M Method Monoclonal**

**112 94 25372 00**

שם בעל הרישום Teva Medical (Marketing) Ltd., Haorgim St 8, Ashdod 77100

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	טקסט נוכחי	טקסט חדש
Indication		
Contra-indications	Known hypersensitivity to mouse protein is a contraindication to the use of HEMOFIL M AHF.	<p><b>HEMOFIL M is contraindicated in patients with a known hypersensitivity to the active substance, to excipients, or to mouse proteins.</b></p> <p><b>Known hypersensitivity to mouse protein is a contraindication to the use of HEMOFIL M AHF.</b></p>
Posology, dosage & administration	<p>The careful control of the substitution therapy is especially important in cases of major surgery or life threatening hemorrhages.</p> <p>Although dosage can be estimated by the calculations above, it is strongly recommended that whenever possible, appropriate laboratory tests including serial AHF assays be performed on the patient's plasma at suitable intervals to assure that adequate AHF levels have been reached and are maintained.</p> <p>Other dosage regimens have been proposed such as that of Schimpf, et al, which describes continuous maintenance therapy.<sup>6</sup></p> <p><b><u>Intravenous Syringe Injection</u></b></p> <p>Parenteral drug products should be inspected for particulate matter and discoloration prior to administration. whenever solution and container permit</p> <p><b><u>Rate of Administration</u></b></p> <p>Preparations of <b>HEMOFIL M AHF</b> can be</p>	<p><b>HEMOFIL M is to be administered only intravenously.</b></p> <p><b>If bleeding is not controlled with the prescribed dose, the plasma level of Factor VIII should be determined and a sufficient dose of HEMOFIL M administered to achieve a satisfactory clinical response.</b></p> <p><b>Under certain circumstances (e.g., presence of a low titer inhibitor) doses larger than those recommended may be necessary as per standard care. In patients with high titer Factor VIII inhibitors, HEMOFIL M therapy may not be effective and other therapeutic options should be considered.</b></p> <p><b>The dosage and duration of treatment depend on the severity of Factor VIII deficiency, the location and extent of the bleeding, and the patient's clinical condition. Careful control of replacement therapy is especially important in cases of major surgery or life threatening hemorrhages.</b></p> <p><b>Although dosage can be estimated by the calculations above, it is strongly</b></p>

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#### **Intravenous Syringe Injection**

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration. Do not administer if particulate matter or discoloration is found whenever solution and container permit.

#### **Rate of Administration**

Preparations of HEMOFIL M AHF can be administered at a rate of up to 10 mL per minute with no significant reactions (See Precautions: Increase in Pulse rate).

~~The pulse rate should be determined before and during administration of HEMOFIL M AHF. Should a significant increase occur, reducing the rate of administration or temporarily halting the injection usually allows the symptoms to disappear promptly.~~

#### **Hypersensitivity**

Allergic-type hypersensitivity reactions, including anaphylaxis, have been reported with HEMOFIL M and have been manifested by, for example, bronchospasm, dyspnea, hypotension, chest pain, facial edema, urticaria, rash, flushing, pruritus, nausea.

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HEMOFIL M, Antihemophilic Factor (Human) (AHF), Method M, Monoclonal Purified, is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses,

**Special Warnings and Special Precautions for Use**

### **Neutralizing Antibodies**

The development of neutralizing antibodies (inhibitors) to Factor VIII is a known complication of the treatment of patients with Hemophilia A. Inhibitors have predominantly been reported in previously untreated patients. The risk of developing inhibitors is correlated to the extent of exposure to Factor VIII, the risk being highest within the first 20 exposure days, and to other genetic and environmental factors. The risk for inhibitor development depends on a number of factors relating to the characteristics of the patient (e.g., type of the Factor VIII gene mutation, family history, ethnicity), which are believed to represent the most significant risk factors for inhibitor formation.

### **Transmission of Infectious Agents**

HEMOFIL M, Antihemophilic Factor (Human) (AHF), Method M, Monoclonal Purified, is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. **Appropriate vaccination (against hepatitis A and B) should be considered for patients in regular/repeated receipt of plasma-derived products including HEMOFIL M.** Despite these measures, such products can still potentially transmit disease. Because this product is made from human **plasma blood**, it may carry a risk of transmitting infectious agents, e.g., viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. **This also applies to unknown or emerging viruses and other pathogens.** ALL infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Baxter Healthcare Corporation. The physician should discuss the risks and benefits of this product with the patient.

### **Factor VIII Inhibitors**

Patients should be evaluated for the development of Factor VIII inhibitors if the expected plasma Factor

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### **Formation of Antibodies to Mouse Protein**

Although no hypersensitivity reactions have been observed, because **HEMOFIL M** AHF contains trace amounts of mouse protein (less than 0.1 ng/AHF activity units), the possibility exists that patients treated with this product may develop hypersensitivity to the mouse proteins.

The pulse rate should be determined before and during administration of **HEMOFIL M** AHF. Should a significant increase occur, reducing the rate of administration or temporarily halting the injection usually allows the symptoms to disappear promptly.

Certain components used in the packaging of this product contain natural rubber latex which may cause allergic reactions. Use precaution when treating patients with sensitivity to natural rubber latex.

VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose.

No benefit may be expected from this product in treating other deficiencies.

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#### **Increase in Pulse Rate**

The pulse rate should be determined before and during administration of **HEMOFIL M AHF**. Should a significant increase occur, reducing the rate of administration or temporarily halting the injection usually allows the symptoms to disappear promptly.

#### **Latex Sensitivity**

Certain components used in the packaging of this product contain natural rubber latex which may cause allergic reactions. Use precaution when treating patients with sensitivity to natural rubber latex.

**Precautions**

**Interaction with Other Medicaments and Other Forms of Interaction**

#### **Nursing Mothers**

The safety of **HEMOFIL M** for use in nursing mothers has not been established. It is not known whether this drug is excreted into human milk. Physicians should carefully consider the potential risks and benefits for each specific patient before prescribing **HEMOFIL M**. **HEMOFIL M** should be given to nursing mothers only if clinically indicated.

**Fertility, Pregnancy and Lactation**

### Adverse Reactions from Clinical Trials

The adverse reactions presented in this section have been identified based on clinical trial experience with **HEMOFIL M** in patients previously treated with other Factor VIII concentrates or blood products (N = 74), and previously untreated patients (PUPs; N = 50).

Allergic reactions may be encountered from the use of Antihemophilic Factor (Human) preparations. See **Information for Patients**. The protein in greatest concentration in **HEMOFIL M AHF** is Albumin (Human). Reactions associated with albumin are extremely rare, although nausea, fever, chills or urticaria have been reported.

Clinical Trial Adverse Reactions		
System Organ Class (SOC)	Preferred MedDRA Term	Number of Cases (Frequency Percentage)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	Factor VIII inhibition	3 (5.7%) <sup>a</sup>
NERVOUS SYSTEM DISORDERS	Dizziness	1 (0.8%)
	Headache	1 (0.8%)
	Dysgeusia	1 (0.8%)
	Pyrexia	1 (0.8%)
GENERAL DISORDERS AND		
ADMINISTRATION SITE CONDITIONS	Infusion site inflammation	2 (1.6%)

<sup>a</sup> In a study that included 43 evaluable PUPs and 10 minimally treated patients (MTPs), i.e., patients with a single exposure to other Factor VIII concentrates or blood products, 3 of the total of 53 patients (5.7%) developed an inhibitor while on study.

**HEMOFIL M** was administered to 11 patients previously untreated with Antihemophilic Factor (Human). They have shown no signs of hepatitis or HIV infection following three to nine months of evaluation.

A study of 25 patients treated with **HEMOFIL M**, and monitored for three to six months has demonstrated no evidence of

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### Adverse events

antibody response to mouse protein. More than 1,000 infusions of **HEMOFIL M** have been administered during the clinical trials. Reported events included a single episode each of chest tightness, fuzziness and dizziness, and one patient reported an unusual taste after each infusion.

#### **Post-marketing Adverse Reactions**

In addition to clinical trials, the following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then by Preferred Term.

#### **IMMUNE SYSTEM DISORDERS:**

Anaphylaxis, Hypersensitivity reactions

#### **EYE DISORDERS:** Visual impairment,

Ocular hyperemia

#### **CARDIAC DISORDERS:** Cyanosis,

Bradycardia, Tachycardia

#### **VASCULAR DISORDERS:** Hypotension,

Flushing

#### **RESPIRATORY, THORACIC, AND**

#### **MEDIASTINAL DISORDERS:**

Bronchospasm, Dyspnea, Cough,

Hyperventilation

#### **GASTROINTESTINAL DISORDERS:**

Diarrhea, Vomiting, Nausea, Abdominal pain

#### **SKIN AND SUBCUTANEOUS TISSUE**

#### **DISORDERS:** Urticaria, Rash, Pruritus,

Hyperhidrosis

#### **GENERAL DISORDERS AND**

#### **ADMINISTRATION SITE**

#### **CONDITIONS:** Facial edema, Edema,

Chills, Fatigue, Chest pain, Musculoskeletal pain, Irritability

- Advise patients to report any adverse reactions or problems following **HEMOFIL M** administration to their physician or healthcare provider.
- Advise pregnant women or immune compromised individuals of the

Some viruses, such as parvovirus B19 or hepatitis A, are particularly difficult to remove or inactivate at this time. Parvovirus B19 most seriously affects pregnant women, or immune-compromised

**Information  
for Patients**

affects of Parvovirus B19. Symptoms of parvovirus B19 infection include fever, drowsiness, chills, and runny nose followed about two weeks later by a rash, and joint pain.

- Inform patients of the signs and symptoms of hepatitis A which include several days to weeks of poor appetite, tiredness, and low-grade fever followed by nausea, vomiting, and pain in the belly. Dark urine and a yellowed complexion are also common symptoms. Patients should be encouraged to consult their physician if such symptoms appear.
- Inform patients of the early signs of hypersensitivity reactions including hives, generalized urticaria, facial edema, flushing, nausea, tightness of the chest, wheezing, dyspnea, hypotension, and anaphylaxis. Advise patients to discontinue use of the product and contact their physician if these symptoms occur.

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Overdosage

Incompatibilities

		Special precautions for disposal and other handling advice
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