1 INDICATIONS AND USAGE

Primary Humoral Immunodeficiency Diseases (PI)

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia.

2 DOSAGE AND ADMINISTRATION

For intravenous use only. When used for the treatment of primary humoral immunodeficiency diseases, Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response. If the patient is at risk of developing renal insufficiency (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered. If the patient is at risk of developing renal dysfunction (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered.

3 ADVERSE REACTIONS

Adverse drug reactions are relatively rare and blood transfusion reactions are uncommon. The most common reactions are fever and rash. They are usually mild and self-limiting.

4 CONTRAINDICATIONS

Oetagam 5% liquid is contraindicated in patients known to have an allergy to IgA, IgG, IgM or IgE. Patients who have received Oetagam 5% liquid and who subsequently develop a severe anaphylactic reaction should not be re-administered.

5 DOSAGE FORMS AND STRENGTHS

Oetagam 5% liquid is supplied in 1.0 g, 2.5 g, 5.0 g, 10.0 g or 25.0 g single-use bottles.

6 ADVERSE REACTIONS

The most common adverse drug reactions associated with Oetagam 5% liquid are injection site reactions and chills. Other common reactions include fever and rash. They are usually mild and self-limiting.

7 PATIENT COUNSELING INFORMATION

For information on the use of Oetagam 5% liquid in the patient's own words, see Boxed Warning and Patient Counseling Information (17).

8 DOSAGE AND ADMINISTRATION

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia. Oetagam is a hyperimmune human immunoglobulin product designed to replace the patient's own immunoglobulin. It is indicated for the prophylaxis and/or treatment of primary humoral immunodeficiency diseases. Oetagam is a polyspecific immunoglobulin and contains all the immunoglobulin classes and subclasses represented in normal human serum. Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response.

9 ADVERSE REACTIONS

The most common adverse drug reactions associated with Oetagam 5% liquid are injection site reactions and chills. Other common reactions include fever and rash. They are usually mild and self-limiting.

10 DOSAGE AND ADMINISTRATION

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia. Oetagam is a hyperimmune human immunoglobulin product designed to replace the patient's own immunoglobulin. It is indicated for the prophylaxis and/or treatment of primary humoral immunodeficiency diseases. Oetagam is a polyspecific immunoglobulin and contains all the immunoglobulin classes and subclasses represented in normal human serum. Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response.

11 ADVERSE REACTIONS

The most common adverse drug reactions associated with Oetagam 5% liquid are injection site reactions and chills. Other common reactions include fever and rash. They are usually mild and self-limiting.

12 PATIENT COUNSELING INFORMATION

For information on the use of Oetagam 5% liquid in the patient’s own words, see Boxed Warning and Patient Counseling Information (17).

13 comprehensive list of the full prescribing information is not available.

14 WARNING: THROMBOSIS, RENAL FAILURE AND ACUTE RENAL FAILURE

Oetagam 5% liquid must be administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response. If the patient is at risk of developing renal insufficiency (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered. If the patient is at risk of developing renal dysfunction (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered.

15 DOSAGE FORMS AND STRENGTHS

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia. Oetagam is a hyperimmune human immunoglobulin product designed to replace the patient's own immunoglobulin. It is indicated for the prophylaxis and/or treatment of primary humoral immunodeficiency diseases. Oetagam is a polyspecific immunoglobulin and contains all the immunoglobulin classes and subclasses represented in normal human serum. Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response.

16 ADVERSE REACTIONS

The most common adverse drug reactions associated with Oetagam 5% liquid are injection site reactions and chills. Other common reactions include fever and rash. They are usually mild and self-limiting.

17 PATIENT COUNSELING INFORMATION

For information on the use of Oetagam 5% liquid in the patient’s own words, see Boxed Warning and Patient Counseling Information (17).

18 WARNING: THROMBOSIS, RENAL FAILURE AND ACUTE RENAL FAILURE

Oetagam 5% liquid must be administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response. If the patient is at risk of developing renal insufficiency (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered. If the patient is at risk of developing renal dysfunction (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered.

19 DOSAGE FORMS AND STRENGTHS

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia. Oetagam is a hyperimmune human immunoglobulin product designed to replace the patient's own immunoglobulin. It is indicated for the prophylaxis and/or treatment of primary humoral immunodeficiency diseases. Oetagam is a polyspecific immunoglobulin and contains all the immunoglobulin classes and subclasses represented in normal human serum. Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response.

20 ADVERSE REACTIONS

The most common adverse drug reactions associated with Oetagam 5% liquid are injection site reactions and chills. Other common reactions include fever and rash. They are usually mild and self-limiting.

21 PATIENT COUNSELING INFORMATION

For information on the use of Oetagam 5% liquid in the patient’s own words, see Boxed Warning and Patient Counseling Information (17).

22 WARNING: THROMBOSIS, RENAL FAILURE AND ACUTE RENAL FAILURE

Oetagam 5% liquid must be administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response. If the patient is at risk of developing renal insufficiency (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered. If the patient is at risk of developing renal dysfunction (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered.

23 DOSAGE FORMS AND STRENGTHS

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia. Oetagam is a hyperimmune human immunoglobulin product designed to replace the patient's own immunoglobulin. It is indicated for the prophylaxis and/or treatment of primary humoral immunodeficiency diseases. Oetagam is a polyspecific immunoglobulin and contains all the immunoglobulin classes and subclasses represented in normal human serum. Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response.

24 ADVERSE REACTIONS

The most common adverse drug reactions associated with Oetagam 5% liquid are injection site reactions and chills. Other common reactions include fever and rash. They are usually mild and self-limiting.

25 PATIENT COUNSELING INFORMATION

For information on the use of Oetagam 5% liquid in the patient’s own words, see Boxed Warning and Patient Counseling Information (17).

26 WARNING: THROMBOSIS, RENAL FAILURE AND ACUTE RENAL FAILURE

Oetagam 5% liquid must be administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response. If the patient is at risk of developing renal insufficiency (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered. If the patient is at risk of developing renal dysfunction (e.g., on the basis of age, pre-existing renal disease, or concomitant medications), a lower dose may be administered.

27 DOSAGE FORMS AND STRENGTHS

Oetagam is an immunoglobulin intravenous (human) 5% liquid, indicated for treatment of primary humoral immunodeficiency diseases (PI) such as congenital agammaglobulinemia, common variable immunodeficiency, Kielland agammaglobulinemia, Wiskott-Aldrich syndrome and X-linked hypogammaglobulinemia. Oetagam is a hyperimmune human immunoglobulin product designed to replace the patient's own immunoglobulin. It is indicated for the prophylaxis and/or treatment of primary humoral immunodeficiency diseases. Oetagam is a polyspecific immunoglobulin and contains all the immunoglobulin classes and subclasses represented in normal human serum. Oetagam 5% liquid is administered by infusion. The dose of Oetagam 5% liquid can be determined by monitoring clinical response.
6 ADVERSE REACTIONS

The most common adverse reactions observed with Octagam 5% liquid treatment have been immediately following administration (see Warning and Precautions [5.1]). Subjects may experience a transient feeling of warmth, tightness of the chest, headache, flushing, and/or palpitations. If severe or prolonged, they should contact their physicians immediately if such symptoms occur. (See Warnings and Precautions [5.3], [5.5], and [5.8]).

The adverse reactions listed below were observed during post-approval use of Octagam 5% liquid.

Table 2: Adverse Reactions Occurring in 5% of Subjects Receiving Octagam 5% liquid

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>35</td>
</tr>
<tr>
<td>Fatigue</td>
<td>27</td>
</tr>
<tr>
<td>Vomiting</td>
<td>27</td>
</tr>
</tbody>
</table>

Laboratory Abnormalities

Standard clinical laboratory evaluations were performed in the study. Three subjects (7%) had measles, mumps, and rubella. Inform the immunizing physician of recent therapy with Octagam 5% liquid, as antibodies in Octagam 5% liquid may interfere with the response to live viral vaccines, such as vaccinations which the patient may be receiving.

The adverse reactions (i.e. adverse events that were assessed as treatment related) reported by at least 1% of subjects during post-approval use are below.

10 OVERDOSAGE

Table 3: In vitro reduction factor during Octagam 5% liquid manufacturing

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH4 treatment</td>
<td>≥ 4.33</td>
</tr>
<tr>
<td>TNBP not more than 1 mcg</td>
<td>≥ 18.22</td>
</tr>
<tr>
<td>Octoxynol not more than 1 mcg</td>
<td>≥ 6.71</td>
</tr>
<tr>
<td>Protein, of which not less than 96% is human normal aggregates, not less than 90% monomers and dimers and not more than 3% fragments.</td>
<td></td>
</tr>
</tbody>
</table>

11.1 Composition

Octagam 5% liquid contains a broad spectrum of IgG antibodies against bacterial and viral pathogens, as well as antibodies against certain tumor-associated antigens.

11.2 Mechanism of Action

Octagam 5% liquid supplies a broad spectrum of opsonic and neutralizing IgG antibodies against bacteria or their toxins. The mechanism of action in Flh has not been fully elucidated.

12 Pharmacodynamics

Due to the high concentration of mainly immunoglobulin G (IgG) by a broad spectrum of antibodies against various infectious agents, the efficacy of this product in the donor population, Octagam 5% liquid which is prepared from pooled material from not less than 1,500 donors, has an IgG titer distribution similar to that of native human plasma. Adequate doses of Immune Globulin 5% liquid are known to be low titer in 5% of patients.

12.2 Pharmacokinetics

In vivo data in healthy volunteers indicates that Octagam 5% liquid is rapidly distributed and has a half-life of approximately 20 days. In healthy patients, the elimination half-life is longer and ranges from 20 to 40 days. The elimination half-life of specific antibodies varies with the titer and is known to be inversely related to the titer of the antibody.

Table 4: In vitro reduction factor during Octagam 5% liquid manufacturing

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trough IgG Level</td>
<td>≥ 10</td>
</tr>
<tr>
<td>MCV</td>
<td>≥ 10</td>
</tr>
<tr>
<td>MCH</td>
<td>≥ 10</td>
</tr>
<tr>
<td>MCHC</td>
<td>≥ 10</td>
</tr>
</tbody>
</table>

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Incarceration studies and the genotoxicity studies showed no evidence of carcinogenic properties of TNBP and Octoxynol [11].

13.2.2 Animal Toxicology and/or Pharmacology

The studies were considered positive for genotoxicology, toxicology, local tolerance or pharmacokinetics with Octagam 5% liquid.

13.3.19.2 Animal Toxicology and/or Pharmacology

The studies were considered positive for genotoxicology, toxicology, local tolerance or pharmacokinetics with Octagam 5% liquid.

The animal toxicology studies were carried out in rats (5 males and 5 females) and in hamsters (5 males and 5 females) for the following times:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global reduction factor</td>
<td>≥ 14.07</td>
</tr>
</tbody>
</table>

14 CLINICAL STUDIES

14.1 Clinical investigation study

In this study, 10 patients including 5 children with the ages of 1 to 10 years old were treated with a high dose of Immune Globulin 5% liquid in conjunction with other active agents for children with moderate to severe IRM. The patients received Octagam 5% liquid at a dose of 100 mg/kg per day for 14 days and/or 28 days. No deaths or serious adverse events were reported during the study period. Table 6 summarizes the other efficacy data such as work/school days missed, days in the emergency department for acute problems.

Table 5: PK Parameters of Octagam 5% liquid in the clinical study

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNBP not more than 1 mcg</td>
<td>≥ 18.22</td>
</tr>
<tr>
<td>Octoxynol not more than 1 mcg</td>
<td>≥ 6.71</td>
</tr>
</tbody>
</table>

14.2.2 Animal Toxicology and/or Pharmacology

The studies were considered positive for genotoxicology, toxicology, local tolerance or pharmacokinetics with Octagam 5% liquid.

14.3.19.2 Animal Toxicology and/or Pharmacology

The studies were considered positive for genotoxicology, toxicology, local tolerance or pharmacokinetics with Octagam 5% liquid.

14.4.1 Animal Toxicology and/or Pharmacology

The studies were considered positive for genotoxicology, toxicology, local tolerance or pharmacokinetics with Octagam 5% liquid.

15.1 Composition

Octagam 5% liquid contains a broad spectrum of IgG antibodies against bacterial and viral pathogens, as well as antibodies against certain tumor-associated antigens.

15.2 Mechanism of Action

Octagam 5% liquid supplies a broad spectrum of opsonic and neutralizing IgG antibodies against bacteria or their toxins. The mechanism of action in Flh has not been fully elucidated.

16.2 Pharmacodynamics

Due to the high concentration of mainly immunoglobulin G (IgG) by a broad spectrum of antibodies against various infectious agents, the efficacy of this product in the donor population, Octagam 5% liquid which is prepared from pooled material from not less than 1,500 donors, has an IgG titer distribution similar to that of native human plasma. Adequate doses of Immune Globulin 5% liquid are known to be low titer in 5% of patients.

16.2.2 Pharmacokinetics

In vivo data in healthy volunteers indicates that Octagam 5% liquid is rapidly distributed and has a half-life of approximately 20 days. In healthy patients, the elimination half-life is longer and ranges from 20 to 40 days. The elimination half-life of specific antibodies varies with the titer and is known to be inversely related to the titer of the antibody.

Table 6: Summary of Secondary Efficacy Variables.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reduction Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNBP not more than 1 mcg</td>
<td>≥ 18.22</td>
</tr>
<tr>
<td>Octoxynol not more than 1 mcg</td>
<td>≥ 6.71</td>
</tr>
<tr>
<td>Protein, of which not less than 96% is human normal aggregates, not less than 90% monomers and dimers and not more than 3% fragments.</td>
<td></td>
</tr>
</tbody>
</table>

17 PATIENT COUNSELING INFORMATION

Information for Patients

17.1.1 Information on patients who are infected with human immunodeficiency virus (HIV)

Inform patients of the early signs of hyperimmunoglobulinemia including headaches, malaise, fever, nausea, and myalgia. They should contact their physicians immediately if such symptoms occur. (See Warnings and Precautions [5.3], [5.5], and [5.8]).

Instruct patients to immediately report the following signs and symptoms to their health care provider:

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.

- Symptoms of angioedema, face oedema, or cutaneous vasculitis, gastrointestinal ulcerations, or cutaneous lesions which may involve the face, extremities, or trunk.

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.

- Symptoms of angioedema, face oedema, or cutaneous vasculitis, gastrointestinal ulcerations, or cutaneous lesions which may involve the face, extremities, or trunk.

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.

- Symptoms of angioedema, face oedema, or cutaneous vasculitis, gastrointestinal ulcerations, or cutaneous lesions which may involve the face, extremities, or trunk.

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.

- Symptoms of angioedema, face oedema, or cutaneous vasculitis, gastrointestinal ulcerations, or cutaneous lesions which may involve the face, extremities, or trunk.

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.

- Symptoms of angioedema, face oedema, or cutaneous vasculitis, gastrointestinal ulcerations, or cutaneous lesions which may involve the face, extremities, or trunk.

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.

- Symptoms of angioedema, face oedema, or cutaneous vasculitis, gastrointestinal ulcerations, or cutaneous lesions which may involve the face, extremities, or trunk.

- Symptoms of thrombosis which may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, palpitations, or chest pain.