Immune globulin intravenous, human – ifas (Panzyga™)
Abbreviated New Drug Update (ANDU)

September 2018

OVERVIEW

• Indications
  □ Treatment of primary humoral immunodeficiency (PI) in patients ≥ 2 years old, including, but not limited to, congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies
  □ Treatment of adults with chronic immune thrombocytopenia (ITP) to raise platelet counts to control or prevent bleeding

• It is a solvent/detergent (S/D)-treated, sterile preparation of highly purified immunoglobulin G (IgG) attained from pooled human plasma. It is an infusion solution administered intravenously (IV).

• Contraindications/Warnings
  □ Contraindications: patients with a history of severe systemic hypersensitivity reactions, such as anaphylaxis, to human immunoglobulin and in patients with an IgA-deficiency with antibodies against IgA and history of hypersensitivity
     The potential for severe hypersensitivity exists. Should a reaction occur, discontinue the infusion immediately and begin appropriate treatment.
  □ Boxed warnings inform of the potential development of thrombosis, renal dysfunction, and acute renal failure.
  □ Warnings
     Aseptic meningitis syndrome (AMS)
     Risk of viral transmission including the possibility Creutzfeldt-Jakob disease variant and Creutzfeldt-Jakob disease (CJD) agent
     Delayed hemolytic anemia can develop after treatment
     Transfusion-related acute lung injury, (TRALI), also known as noncardiogenic pulmonary edema, may occur within 1 to 6 hours following IVIG administration.

• Drug Interactions
  □ Panzyga should be administered separately from other drugs or IV solutions.
  □ Do not mix with other immune globulins.
- Antibodies in Panzyga may interfere with live viral vaccine response (measles, mumps, and rubella). Administration of live viral vaccines, if required, should be delayed for ≥ 3 months from the time of administration.

- Common Adverse Effects
  - PI: the most common adverse reactions occurring > 5% of subjects in clinical trials were headache (22%), abdominal pain (14%), fever (14%), nausea (10%), sinusitis (8%), bronchitis (6%) and fatigue (6%).
  - Chronic ITP: the most common adverse reactions seen in > 5% of subjects in clinical trials were headache (50%), fever (23%), nausea (18%), vomiting (10%), dizziness (10%), and anemia (10%).

- Pregnancy
  - No human data are available to indicate the presence or absence of drug-associated risk in pregnancy. Animal reproduction studies have not been conducted.

- Pediatric Use
  - In the treatment of PI, Panzyga was evaluated in 25 pediatric patients ranging in age from 2 to 15 years. Twenty-five percent of PI patients exposed to Panzyga were children (2 to 12 years old). Pharmacokinetics, efficacy, and safety were similar to those founds in adults. There are no specific dosing requirements in pediatric patients.
  - In treating ITP, safety and effectiveness of Panzyga have not been established in pediatric patients.

- Geriatric Use
  - Studies did not include sufficient numbers of subjects ≥ 65 years of age to determine whether geriatric subjects respond differently from younger subjects. Patients ≥ 65 years of age may be at increased risk for developing adverse thromboembolic events and acute renal failure. Recommended doses should not be exceeded and minimum practicable infusion rates should be employed.

- Availability and Dosage
  - The solution contains 10% IgG (100 mg/mL) for IV administration. It is supplied as 1 g (10 mL), 2.5 g (25 mL), 5 g (50 mL), 10 g (100 mL), 20 g (200 mL), and 30 g (300 mL) single-use bottles.

- Recommended Dosing:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosage</th>
<th>Initial Infusion Rate</th>
<th>Max Infusion Rate in New Patients</th>
<th>Max Infusion Rate in Experienced Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>300 to 600 mg/kg (3 to 6 mL/kg) every 3 to 4 weeks</td>
<td>1 mg/kg/min (0.01 mL/kg/min)</td>
<td>8 mg/kg/min (0.08 mL/kg/min)</td>
<td>12 to 14 mg/kg/min (0.12 to 0.14 mL/kg/min)</td>
</tr>
<tr>
<td>ITP</td>
<td>1 g/mL (10 mL/kg) daily for 2 consecutive days</td>
<td>1 mg/kg/min (0.01 mL/kg/min)</td>
<td>8 mg/kg/min (0.08 mL/kg/min)</td>
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</table>
• Clinical Trials
  □ The efficacy and safety of Panzyga were evaluated in 2 separate clinical trials, 1 for each indication. Study 1 considered use of Panzyga in the treatment of PI and was a prospective, open-label, single-arm, multicenter study consisting of 51 children and adults with PI. Patients in the study received Panzyga infusions dosed between 200 to 800 mg/kg of body weight every 3 or 4 weeks. Study enrollees participated in the study for a mean time period of 360 days. The mean age of patients was 26.8 years (range: 2 to 65 years). The observed rate for the primary efficacy endpoint of the annual number of serious bacterial infections per patient (pneumonia, bacteremia or sepsis, osteomyelitis/septic arthritis, visceral abscesses, or bacterial meningitis) was 0.08 (4 infections over 50.2 patient-years).

  □ The second study, evaluated Panzyga in the treatment of chronic ITP in adults (n=40). It was a prospective, open-label, single-arm, multicenter study and assessed efficacy, safety, and tolerability in patients with a platelet count of ≤ 20 x 10⁹/L. The median patient age was 32 years (range: 18 to 72 years). The patients consisted of 43% female and 57% male participants with the large majority, 90%, being Caucasian and the remaining 10% being Asian. Patients on Panzyga received a 2 g/kg dose given as 2 daily 1 g/kg IV on 2 consecutive days. Platelet counts were measured on days 1 to 8, 15, and 22. The study assessed patient response rates; response was defined as an increase in platelet count ≥ 50 x 10⁹/L within 7 days following the first infusion. There were 36 patients in the full analysis set; of these 29, (81%; 95% CI: 64%-92%), were considered responders.

CLINICAL CONSIDERATIONS

• Octapharma’s Panzyga provides another option in the treatment of PI and chronic ITP with immune globulin products.

• Other IVIG products indicated for treatment of these diseases include Bivigam™, Carimune™, Flebogamma™ (10% strength only), Gammagard Liquid™, Gammagard SD™, Gammaked™, Gammaplex™, Gamunex-C™, Octagam™, and Privigen™.

• The final product selected for treatment should include considerations of specific diagnosis, previous product use and tolerance, timeframe since last dosage, preferred route of administration, specific patient condition and existing comorbidities as well as specific product parameters.
**SUGGESTED UTILIZATION MANAGEMENT**

<table>
<thead>
<tr>
<th>Anticipated Therapeutic Class Review (TCR) Placement</th>
<th>Immune Globulins</th>
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<tbody>
<tr>
<td>Clinical Edit</td>
<td></td>
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<tr>
<td></td>
<td>Prior authorization will be required if product is determined to be non-preferred.</td>
</tr>
</tbody>
</table>

**Initial Criteria**

Patient must:
- Have a diagnosis of Primary Humoral Immunodeficiency (PI) or Chronic Immune Thrombocytopenia (ITP); **AND**
- Have baseline values for blood urea nitrogen (BUN) and serum creatinine obtained within 30 days of initial request; **AND**
- If using for PI –
  - Patient must be 2 years of age or older; **AND**
  - Patient’s IgG level is < 200 mg/dL **OR both** of the following:
    - Patient has a history of multiple hard to treat infections as indicated by at least **one** of the following:
      - Four or more ear infections within 1 year; **OR**
      - Two or more serious sinus infections within 1 year; **OR**
      - Two or more months of antibiotics with little effect; **OR**
      - Two or more pneumonias within 1 year; **OR**
      - Recurrent or deep skin abscesses; **OR**
      - Need for intravenous antibiotics to clear infections; **OR**
      - Two or more deep-seated infections including; **OR**
      - Septicemia; **AND**
    - The patient has a deficiency in producing antibodies in response to vaccination; **AND**
      - Titers were drawn before challenging with vaccination; **AND**
      - Titers were drawn between 4 and 8 weeks of vaccination
  - If using for ITP –
    - Patient must be ≥ 18 years of age; **AND**
    - Patient is at increased risk for bleeding as indicated by a platelet count > 30 X 10⁹/L; **AND**
    - The patient has a history of failure, contraindication, or intolerance to corticosteroids; **AND**
    - Duration of illness > 6 months; **AND**
    - Patient is not currently receiving other IVIG therapy; **AND**
    - Patient is does not have a history of severe hypersensitivity reactions, including anaphylaxis, to human IVIG preparations; **AND**
    - Patient is not IgA-deficient with documented antibodies to IgA or have a history of hypersensitivity
Renewal Criteria
Patient must:
- Demonstrate documented efficacy in both PI and chronic ITP; **AND**
- Not have any treatment-limiting adverse effects or history of hypersensitivity; **AND**
- Continue to meet criteria identified above; **AND**
- Be absent of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: acute kidney injury, thrombosis, hemolysis, hypersensitivity, pulmonary adverse reactions, volume overload, etc.; **AND**
- Have a BUN and serum creatinine obtained within the last 6 months and the concentration and rate of infusion adjusted accordingly; **AND**
- Meet the disease-specific criteria below:
  - Primary Immunodeficiency (PI)
    - Disease response as evidenced by decrease in the frequency and/or severity of infection
  - Chronic Immune Thrombocytopenia/ITP
    - Disease response as indicated by the achievement and maintenance of a platelet count of ≥ 50 X 10^9/L as necessary to reduce the risk for bleeding

<table>
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<tr>
<th>Quantity Limit</th>
<th>PI: 600 mg/kg every 3 weeks (maximum dosing)</th>
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<tr>
<td></td>
<td>Chronic ITP: 1 g/kg/day for 2 consecutive days (maximum dosing)</td>
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<tr>
<td>Duration of Approval</td>
<td>1 year</td>
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<tr>
<td>Drug to Disease Hard Edit</td>
<td>None</td>
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</tbody>
</table>

**REFERENCES**

1 Panzyga [package insert]. Hoboken, NJ; Octapharma USA; August 2018.
2 Panzyga [package insert]. Hoboken, NJ; Octapharma USA; August 2018.