HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VPRIV safely and effectively. See full prescribing information for VPRIV.

VPRIV® (velaglucerase alfa) for injection, for intravenous use
Initial U.S. Approval: 2010

----------RECENT MAJOR CHANGE----------
Dosage and Administration (2.4)..... 12/2020

----------INDICATIONS AND USAGE----------
VPRIV is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease. (1)

----------DOSAGE AND ADMINISTRATION----------
- Recommended Starting Dose in Adults and Pediatric Patients 4 Years of Age or Older:
  - Patients Naïve to Enzyme Replacement Therapy: 60 Units/kg (2.1)
  - Patients being treated with stable imiglucerase dosages for Gaucher disease: Can switch to VPRIV at previous imiglucerase dose two weeks after last imiglucerase dose (2.2)
- Determine number of vials to be reconstituted based on patient's actual weight and prescribed dose (2.3)
- Supplied VPRIV lyophilized powder must be reconstituted with Sterile Water for Injection (2.3)
- Reconstituted VPRIV solution must be diluted in 100 mL of 0.9% Sodium Chloride Injection prior to intravenous infusion (2.3)
- Administer the diluted VPRIV solution through an in-line low protein-binding 0.2 or 0.22 µm filter (2.4)

----------DOSAGE FORMS AND STRENGTHS----------
For injection: 400 units lyophilized powder single-dose vials (3)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
Hypersensitivity Reactions Including Anaphylaxis:
- Hypersensitivity reactions including anaphylaxis have occurred (5.1)
- Ensure that personnel administering product are adequately trained in cardiopulmonary resuscitative measures, and have ready access to emergency medical services (5.1)
- Consider slowing infusion rate, treatment with antihistamines, antipyretics and/or corticosteroids, and/or stopping treatment if a hypersensitivity reaction occurs during an infusion. Consider pre-treatment with antihistamines and/or corticosteroids in patients with prior reactions (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥ 10%) are: hypersensitivity reactions, headache, dizziness, abdominal pain, nausea, back pain, joint pain, prolonged activated PTT, fatigue/asthenia, and pyrexia (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Shire Human Genetic Therapies, Inc. at 1-800-828-2088 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VPRIV is indicated for long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Starting Dosage in Patients Naïve to Enzyme Replacement Therapy

VPRIV should be administered under the supervision of a healthcare professional. The recommended starting VPRIV dosage in naïve adults and naïve pediatric patients 4 years of age and older is 60 Units/kg administered every other week as a 60-minute intravenous infusion. The dosage can be adjusted based on achievement and maintenance of each patient's therapeutic goals.

2.2 Switching from Imiglucerase to VPRIV

Adults and pediatric patients 4 years of age and older currently being treated on a stable dosage of imiglucerase for type 1 Gaucher disease may be switched to VPRIV by starting treatment with VPRIV at the previous imiglucerase dosage two weeks after the last imiglucerase dose. VPRIV should be administered under the supervision of a healthcare professional as a 60-minute intravenous infusion. The dosage can be adjusted based on achievement and maintenance of each patient's therapeutic goals.

2.3 Reconstitution of the VPRIV Lyophilized Powder

VPRIV is a lyophilized powder, which requires reconstitution and dilution, using sterile technique, prior to intravenous infusion. VPRIV should be prepared as follows:

(a) Determine the number of vials to be reconstituted based on the individual patient's weight and the prescribed dose.
(b) Inject 4.3 mL of Sterile Water for Injection, USP into a vial containing VPRIV lyophilized powder.
(c) Mix gently. DO NOT SHAKE. The reconstituted VPRIV solution will have a 100 Units/mL concentration (400 Units VPRIV in 4 mL of solution).
(d) If additional vials are needed, repeat steps (b) and (c).
(e) Visually inspect the reconstituted VPRIV solution in the vials. The solution should be clear to slightly opalescent and colorless. Do not use if the solution is discolored or if foreign particulate matter is present.
(f) With a single syringe, withdraw the calculated dose of drug from the appropriate number of vials. Using a separate syringe, withdraw air from a bag of 100 mL of 0.9% Sodium Chloride Injection suitable for intravenous administration. Then dilute the calculated dose of VPRIV directly into the 0.9% Sodium Chloride Injection. Mix gently. DO NOT SHAKE. Slight flocculation (described as white irregular shaped particles) may occasionally occur. Diluted solution with slight flocculation is acceptable for administration.
(g) Because VPRIV contains no preservatives, use the reconstituted VPRIV solution and the diluted VPRIV solution immediately. If immediate use is not possible, the reconstituted VPRIV solution or the diluted VPRIV solution may be stored for up to 24 hours at 2ºC to

8ºC (36ºF to 46ºF). Do not freeze and protect from light. Complete the infusion within 24 hours of reconstitution of vials.

(h) Vials are for one-time use and only for one patient. Discard any unused solution.

2.4 Important Administration Instructions

Administer the diluted VPRIV solution through an in-line low protein-binding 0.2 or 0.22 µm filter over 60 minutes. Do not infuse VPRIV with other products in the same infusion tubing because the compatibility of a VPRIV solution with other products has not been evaluated.

2.5 Premedication to Reduce Risk of Subsequent Hypersensitivity Reactions

Consider pre-treatment with antihistamines and/or corticosteroids in patients who exhibited symptoms of hypersensitivity associated with prior velaglucerase alfa product infusions. Appropriate medical support should be readily available when VPRIV is administered *[see Warnings and Precautions (5.1)]*.

3 DOSAGE FORMS AND STRENGTHS

For injection: 400 units of a sterile, white to off-white, lyophilized powder in single-dose vials for reconstitution and dilution.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions Including Anaphylaxis

Hypersensitivity reactions, including anaphylaxis, occurred in clinical studies and postmarketing experience *[see Adverse Reactions (6.1)]*. Hypersensitivity reactions were the most commonly observed adverse reactions in patients treated with VPRIV in clinical studies. Patients were not routinely pre-medicated prior to infusion of VPRIV during clinical studies. The most commonly observed symptoms of hypersensitivity reactions were: headache, dizziness, hypotension, hypertension, nausea, fatigue/asthenia, and pyrexia/body temperature increased. Generally the reactions were mild and, in treatment-naïve patients, onset occurred mostly during the first 6 months of treatment and tended to occur less frequently with time. Additional hypersensitivity reactions of chest discomfort, dyspnea, pruritus and vomiting have been reported in post-marketing experience.

As with any intravenous protein product, hypersensitivity reactions are possible, therefore appropriate medical support including personnel adequately trained in cardiopulmonary resuscitative measures and access to emergency measures should be readily available when VPRIV is administered. If anaphylactic or other acute reactions occur, immediately discontinue the infusion of VPRIV and initiate appropriate medical treatment.

The management of hypersensitivity reactions should be based on the severity of the reaction, e.g., slowing the infusion rate, treatment with medications such as antihistamines, antipyretics and/or corticosteroids, and/or stopping and resuming treatment with increased infusion time. In cases where patients have exhibited symptoms of hypersensitivity to velaglucerase alfa or excipients in the drug product or to other enzyme replacement therapy, pre-treatment with antihistamines and/or corticosteroids may prevent subsequent reactions.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure of 94 patients with type 1 Gaucher disease who received VPRIV at doses ranging from 15 Units/kg to 60 Units/kg every other week in 5 clinical studies. Fifty-four (54) patients were naïve to enzyme replacement therapy (ERT) and received VPRIV for 9 months and 40 patients switched from imiglucerase to VPRIV treatment and received VPRIV for 12 months *[see Clinical Studies (14)]*. Patients were between 4 and 71 years old at time of first treatment with VPRIV, and included 46 male and 48 female patients.

The most serious adverse reactions in patients treated with VPRIV were hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

The most commonly reported adverse reactions (occurring in ≥10% of patients) that were considered related to VPRIV are shown in Table 1. The most common adverse reactions were hypersensitivity reactions.

Table 1: Adverse Reactions Observed in ≥ 10% of Adult and Pediatric Patients with Type 1 Gaucher Disease Treated with VPRIV in the Pooled 5 Clinical Studies

Adverse Reaction	Naïve to ERT N = 54 Number of patients (%)	Switched from imiglucerase to VPRIV N = 40 Number of patients (%)
Hypersensitivity reaction*	28 (52)	9 (23)
Headache	19 (35)	12 (30)
Dizziness	12 (22)	3 (8)
Pyrexia	12 (22)	5 (13)
Abdominal pain	10 (19)	6 (15)
Back pain	9 (17)	7 (18)
Joint pain (knee)	8 (15)	3 (8)
Asthenia/Fatigue	8 (15)	5 (13)
Activated partial thromboplastin time prolonged	6 (11)	2 (5)
Nausea	3 (6)	4 (10)

*Denotes any event considered related to and occurring within up to 24 hours of VPRIV infusion, including one case of anaphylaxis.

Less common adverse reactions affecting more than one patient (>2% in the treatment-naïve group and > 3% in patients switched from imiglucerase to VPRIV treatment) were bone pain, tachycardia, rash, urticaria, flushing, hypertension, and hypotension.

Adverse Reactions in Pediatric Patients
The safety profile of VPRIV was similar between pediatric patients (ages 4 to 17 years) and adult patients. Adverse reactions more commonly seen in pediatric patients compared to adult patients include (>10% difference): rash, aPTT prolonged, and pyrexia.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to VPRIV in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In clinical studies, 1 of 54 (2%) enzyme treatment-naïve patients treated with VPRIV developed IgG antibodies to VPRIV. One additional patient developed IgG antibodies to VPRIV during an extension study. In both patients, the IgG antibodies to VPRIV were determined to be neutralizing in an *in vitro* assay. The presence of IgG antibodies to VPRIV was not associated with hypersensitivity reactions. It is unknown if the presence of IgG antibodies to VPRIV is associated with a higher risk of infusion reactions. Patients with an immune response to other enzyme replacement therapies who are switching to VPRIV should continue to be monitored for antibodies to VPRIV.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of VPRIV. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal disorders: vomiting (in some cases vomiting can be serious, requiring hospitalization and/or drug discontinuation)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data on use of velaglucerase alfa in pregnant women includes more than 300 pregnancies reported from the pharmacovigilance database and published observational cohort studies, including the international Gaucher Disease registry. While available data cannot definitively establish or exclude the absence of a velaglucerase alfa associated risk during pregnancy, these data have not identified an association with use of velaglucerase alfa during pregnancy and major birth defects, miscarriage, or adverse maternal or fetal outcomes. In animal reproduction studies no fetal harm was observed in rats or rabbits when velaglucerase alfa was administered

intravenously during organogenesis at doses with exposures up to 1.8 times and 4.3 times, respectively, the recommended human daily dose *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of major birth defects, loss, and other adverse outcomes. In the U.S. general population, the estimated major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and Embryo/Fetal Risk

Women with Type 1 Gaucher disease have an increased risk of spontaneous abortion, especially if disease symptoms are not treated and controlled pre-conception and during a pregnancy. Pregnancy may exacerbate existing Type 1 Gaucher disease symptoms or result in new disease manifestations. Type 1 Gaucher disease manifestations may lead to adverse pregnancy outcomes including hepatosplenomegaly which can interfere with the normal growth of a pregnancy, and thrombocytopenia which can lead to excessive bleeding .

Data

Animal Data

Embryo-fetal development studies with velaglucerase alfa have been performed during the period of organogenesis in pregnant rats (gestation days 7 through 17) and rabbits (gestation days 6 through 18). In pregnant rats intravenous doses up to 17 mg/kg (102 mg/m^2, about 1.8 times the recommended human dose of 60 Units/kg or 1.5 mg/kg or 55.5 mg/m^2 based on the body surface area) were administered two to three times weekly. In pregnant rabbits intravenous doses up to 20 mg/kg (240 mg/m^2, about 4.3 times the recommended human dose of 60 Units/kg based on the body surface area) were administered two to three times weekly. These studies did not reveal any evidence of impaired fertility or harm to the fetus due to velaglucerase alfa.

In a pre- and postnatal development study, velaglucerase alfa was administered intravenously to pregnant rats twice weekly from gestation day 6 to lactation day 19. There was no evidence of any adverse effect on pre-and postnatal development at doses up to 17 mg/kg/day (102 mg/m^2, about 1.8 times the recommended human dose of 60 Units/kg based on the body surface area).

8.2 Lactation

Risk Summary

There are no data available on the presence of velaglucerase alfa in human milk. The reported cases from the pharmacovigilance database are insufficient to determine any effects on the breastfed infant or on milk production. Endogenous beta-glucocerebrosidase is present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VPRIV and any potential adverse effects on the breastfed child from VPRIV or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of VPRIV have been established for enzyme replacement therapy (ERT) in patients between 4 and 17 years of age with type 1 Gaucher disease. Use of VPRIV in this age group is supported by evidence from adequate and well-controlled studies of VPRIV in 74 adult patients and 20 pediatric patients. The safety and efficacy profiles were similar between pediatric and adult patients *[see Adverse Reactions (6.1), Clinical Studies (14)]*. The efficacy and safety of VPRIV has not been established in pediatric patients younger than 4 years of age.

8.5 Geriatric Use

In clinical studies of VPRIV in Gaucher's disease, a total of 56 VPRIV-treated patients were 65 years of age or older including 10 patients who were 75 years of age or older. Among 205 patients who switched from imiglucerase to VPRIV, 52 patients were 65 years of age or older of which 10 were 75 years and older. The adverse reaction profile in elderly patients was consistent with that previously observed across pediatric and adult patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be approached cautiously, considering potential comorbid conditions.

11 DESCRIPTION

Velaglucerase alfa is a hydrolytic lysosomal glucocerebroside-specific enzyme produced by gene activation technology in a human fibroblast cell line. Velaglucerase alfa is a glycoprotein of 497 amino acids and a molecular weight of approximately 63 kDa. Velaglucerase alfa has the same amino acid sequence as the naturally occurring human enzyme, glucocerebrosidase. Velaglucerase alfa contains five potential N-linked glycosylation sites; four of these sites are occupied by glycan chains. Velaglucerase alfa contains predominantly high mannose-type N-linked glycan chains. The high mannose type N-linked glycan chains are specifically recognized and internalized via the mannose receptor present on the surface on macrophages, the cells that accumulate glucocerebroside in Gaucher disease.

VPRIV is dosed by units/kg, where one unit of enzyme activity is defined as the quantity of enzyme required to convert one micromole of p-nitrophenyl ß-D-glucopyranoside to p-nitrophenol per minute at 37ºC.

VPRIV (velaglucerase alfa) for injection is supplied as a sterile, preservative free, white to off-white lyophilized powder in single-dose vials for intravenous infusion after reconstitution and dilution. Each single-dose vial contains 400 units of velaglucerase alfa, and citric acid, monohydrate (5.04 mg), polysorbate 20 (0.44 mg), sodium citrate, dihydrate (51.76 mg), and sucrose (200 mg). After reconstitution with 4.3 mL Sterile Water for Injection, USP, the final concentration is 100 units/mL with a pH of approximately 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Gaucher disease is an autosomal recessive disorder caused by mutations in the GBA gene, which results in a deficiency of the lysosomal enzyme beta-glucocerebrosidase. Glucocerebrosidase catalyzes the conversion of the sphingolipid glucocerebroside into glucose and ceramide. The enzymatic deficiency causes an accumulation of glucocerebroside primarily in the lysosomal compartment of macrophages, giving rise to foam cells or "Gaucher cells". Velaglucerase alfa catalyzes the hydrolysis of glucocerebroside, reducing the amount of accumulated glucocerebroside. In clinical trials VPRIV reduced spleen and liver size, and improved anemia and thrombocytopenia.

In this lysosomal storage disorder (LSD), clinical features are reflective of the accumulation of Gaucher cells in the liver, spleen, bone marrow, and other organs. The accumulation of Gaucher cells in the liver and spleen leads to organomegaly. Presence of Gaucher cells in the bone marrow and spleen lead to clinically significant anemia and thrombocytopenia.

12.3 Pharmacokinetics

In a multicenter study conducted in pediatric (N=7, 4 to 17 years old) and adult (N=15, 19 to 62 years old) patients with type 1 Gaucher disease, pharmacokinetic evaluations were performed at Weeks 1 and 37 following 60-minute intravenous infusions of VPRIV 60 Units/kg every other week. Serum velaglucerase alfa concentrations declined rapidly with a mean half life of 11 to 12 minutes. The mean velaglucerase alfa clearance ranged from 6.72 to 7.56 mL/min/kg. The mean volume of distribution at steady state ranged from 82 to 108 mL/kg (8.2% to 10.8% of body weight).

No accumulation or change in velaglucerase alfa pharmacokinetics over time from Weeks 1 to 37 was observed upon multiple-dosing 60 Units/kg every other week.

Based on the limited data, there were no notable pharmacokinetic differences between male and female patients in this study. The effect of age on pharmacokinetics of velaglucerase alfa was inconclusive.

The effect of anti-drug antibody formation on the pharmacokinetic parameters of velaglucerase alfa is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with velaglucerase alfa.

In a fertility study in male and female rats, velaglucerase alfa did not cause any significant adverse effect on male or female fertility parameters up to a maximum intravenous dose of 17 mg/kg (102 mg/m^2, about 1.8 times the recommended human dose of 60 Units/kg based on the body surface area).

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies of VPRIV for Gaucher Disease

The efficacy of VPRIV was assessed in three clinical trials in a total of 99 patients with type 1 Gaucher disease: 82 patients age 4 years and older received VPRIV and 17 patients age 3 years and older received imiglucerase. Studies I and II were conducted in patients who were not currently receiving Gaucher disease-specific therapy. Study III was conducted in patients who were receiving imiglucerase treatment immediately before starting VPRIV. The long-term safety of VPRIV was assessed in Study IV, an open-label extension trial in a total of 93 patients with type 1 Gaucher disease ages 3 years and older. Patients who had completed Studies I to III were eligible to participate in Study IV. In Studies I through IV, VPRIV was administered intravenously over 60 minutes at a maximum dose of 60 Units/kg every other week. Doses above 60 Units/kg were not studied in these trials.

14.2 Clinical Trials of VPRIV as Initial Therapy

Study I was a 12-month, randomized, double-blind, parallel-dose-group, multinational trial in 25 patients age 4 years and older with Gaucher disease-related anemia and either thrombocytopenia or organomegaly. Patients were not allowed to have had disease-specific therapy for at least the previous 30 months; all but one had no prior therapy. The mean age was 26

years and 60% were male. Patients were randomized to receive VPRIV at a dose of either 45 Units/kg (N=13) or 60 Units/kg (N=12) every other week. The recommended starting dose in naïve patients is 60 Units/kg. The 45 Units/kg dosage is not recommended as a starting dose in naïve patients *[see Dosage and Administration (2.1)]*.

At baseline, mean hemoglobin concentration was 10.6 g/dL, mean platelet count was 97 x 10^9/L, mean liver volume was 3.6 % of body weight (% BW), and mean spleen volume was 2.9 % BW.

For all studies, liver and spleen volumes were measured by MRI. The changes in clinical parameters after 12 months of treatment are shown in Table 3. The observed change from baseline in the primary endpoint, hemoglobin concentration, was considered to be clinically meaningful in the 60 Units/kg dose, in light of the natural history of untreated Gaucher disease.

Table 3: Mean Change from Baseline to Month 12 for Clinical Parameters in Patients with Type 1 Gaucher Disease Initiating Therapy with VPRIV Given Every Other Week in Study I

Clinical Parameter	VPRIV 45 Units/kg# N = 13 Mean ± SE	VPRIV 60 Units/kg N = 12 Mean ± SE
Hemoglobin concentration change (g/dL)	2.4 ± 0.4†	2.4 ± 0.3*
Platelet count change (x 10^9/L)	41 ± 14†	51 ± 12†
Liver volume change (% BW)	-0.30 ± 0.29	-0.84 ± 0.33
Spleen volume change (% BW)	-1.9 ± 0.6†	-1.9 ± 0.5†

SE = standard error of the mean
# The recommended starting dose in naïve patients is 60 Units/kg. The 45 Units/kg dosage is not recommended as a starting dose in naïve patients *[see Dosage and Administration (2.1)]*.
† Statistically significant changes from baseline after adjusting for performing multiple tests
* Primary study endpoint was hemoglobin concentration change in the 60 Units/kg group, $p < 0.001$

Study II was a 9-month, randomized, double-blind, active-controlled (imiglucerase), parallel-group, multinational study in 34 patients age 4 years and older. Patients were required to have Gaucher disease-related anemia and either thrombocytopenia or organomegaly. Patients were not allowed to have had disease-specific therapy for at least the previous 12 months. The mean age was 30 years and 53% were female; the youngest patient who received VPRIV was age 4 years. Patients were randomized to receive either 60 Units/kg of VPRIV (N=17) or 60 Units/kg of imiglucerase (N=17) every other week.

At baseline, the mean hemoglobin concentration was 11.0 g/dL, mean platelet count was 171 x 10^9/L, and mean liver volume was 4.3 % BW. For the patients who had not had splenectomy (7 in each group) the mean spleen volume was 3.4 % BW. After 9 months of treatment, the mean absolute increase from baseline in hemoglobin concentration was 1.6 g/dL ± 0.2 (SE) for patients treated with VPRIV. The mean treatment difference in change from baseline to 9 months [VPRIV – imiglucerase] was 0.1 g/dL ± 0.4 (SE).

In both studies, examination of age and gender subgroups did not identify differences in response to VPRIV among these subgroups. The number of non-Caucasian patients in these studies was too small to adequately assess any difference in effects by race.

In Study IV, treatment naïve patients were administered VPRIV. Treatment-naïve patients continued to show improvements in clinical parameters (hemoglobin concentration, platelet count, liver volume, and spleen volume) compared with baseline for up to 60 months of treatment with ERT.

14.3 Clinical Trial in Patients Switching from Imiglucerase Treatment to VPRIV

Study III was a 12-month, open-label, single-arm, multinational study in 40 patients age 9 years and older who had been receiving treatment with imiglucerase at doses ranging between 15 Units/kg to 60 Units/kg for a minimum of 30 consecutive months. Patients also were required to have a stable biweekly dose of imiglucerase for at least 6 months prior to enrollment. The mean age was 36 years and 55% were female. Imiglucerase therapy was stopped, and treatment with VPRIV was administered every other week at the same number of units as the patient's previous imiglucerase dose. Adjustment of dosage was allowed by study criteria if needed in order to maintain clinical parameters *[see Dosage and Administration (2.2)]*.

Hemoglobin concentrations and platelet counts remained stable on average through 12 months of VPRIV treatment. After 12 months of treatment with VPRIV the median hemoglobin concentration was 13.5 g/dL (range: 10.8, 16.1) vs. the baseline value of 13.8 g/dL (range: 10.4, 16.5), and the median platelet count after 12 months was 174 x 10^9/L (range: 24, 408) vs. the baseline value of 162 x 10^9/L (range: 29, 399). No patient required dosage adjustment during the 12-month treatment period.

In Study IV, patients who had previously been receiving imiglucerase treatment were administered VPRIV. Patients previously treated with imiglucerase maintained stability in clinical parameters (hemoglobin concentration, platelet count, liver volume, and spleen volume) compared with baseline for up to 60 months of treatment with ERT.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

VPRIV (velaglucerase alfa) for injection is a sterile, preservative free, white to off-white lyophilized powder requiring reconstitution and further dilution prior to use. It is supplied in individually packaged single-dose glass vials, which are closed with a butyl rubber stopper with a fluoro-resin coating and are sealed with an aluminum overseal with a flip-off plastic cap. VPRIV is available as: 400 units/vial (NDC 54092-701-04).

Storage

Store VPRIV refrigerated at 2ºC to 8ºC (36ºF to 46ºF) in the original carton to protect from light. Do not freeze. Do not use VPRIV after the expiration date on the vial.

17 PATIENT COUNSELING INFORMATION

- Advise patients that VPRIV is a treatment that is given intravenously every other week. The infusion typically takes up to 60 minutes.
- Advise patients that VPRIV may cause hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

VPRIV is manufactured by:

Shire Human Genetic Therapies, Inc.
300 Shire Way
Lexington, MA 02421
US License Number 1593

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For patent information: https://www.shire.com/legal-notice/product-patents