Kansas Department of Health and Environment
Division of Health Care Finance

KANSAS DRUG UTILIZATION REVIEW NEWSLETTER

Health Information Designs, LLC ***3rd Quarter 2020***

Welcome to the Quarterly edition of the "Kansas Drug Utilization Review Newsletter", published by Health Information Designs, LLC (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

Helpful Web Sites

KMAP Web Site
https://www.kmap-state-ks.us/

KDHE-DHCF Web Site
http://www.kdheks.gov/hcf/

KanCare Web Site
http://www.kancare.ks.gov/

Fee-For-Service (FFS) Helpful Numbers

Provider Customer Service (Provider Use Only)
1-800-933-6593

Beneficiary Customer Service
1-800-766-9012

KMAP PA Help Desk
1-800-285-4978

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Gene Therapy for Hemophilia A

Overview of Hemophilia A

Hemophilia A is a bleeding disorder caused by having low levels of factor VIII protein, which is needed to form blood clots. Patients with this disorder experience abnormal bleeding episodes and long term there is risk of joint, muscle and/or organ damage.[3]

It is inherited in an X-linked recessive manner and is caused by mutations in the F8 gene which is responsible for making the factor VIII protein. The F8 gene is located on the X-chromosome; so, in males, only one mutated copy of the F8 gene in each cell is enough to cause hemophilia A. In females, a mutation needs to occur in both copies of the F8 gene to cause the disorder. Because of this, hemophilia A affects males much more frequently than females. Females who have a mutation in one copy of the F8 gene are carriers, and while most carriers have no signs or symptoms, about 10% will experience some abnormal bleeding.[3]

Plasma levels of factor VIII are expressed as a percentage of a 'normal' result, which is 100%. Patients are considered to have normal levels of factor VIII if they are in the range of 50 to 150%. Patients with mild hemophilia A range from 6 to 39% plasma levels, moderate levels are 1 to 5% and in severe disease about 1%. About 50 to 60% of patients have the severe form of the disorder.[3]

Treating Hemophilia A

There is currently no cure for hemophilia A, but there are treatments available to manage the symptoms. Patients with mild or moderate hemophilia A may be treated with replacement therapy (infusion of concentrated factor VIII) as needed (when a bleeding episode occurs) or if the disease is mild, may be treated with desmopressin. Desmopressin raises the levels of factor VIII in the blood and can be given intravenously or intranasally and is given to patients with 5% or greater factor VIII levels in the plasma. Patients with severe hemophilia A generally receive regular factor VIII replacement therapy and may require infusions up to 2 to 3 times each week.[3,4]

Gene Therapy in Hemophilia A, cont.

Current Treatments

Current therapies are used for on-demand treatment and control of bleeding episodes, perioperative management of bleeding and routine prophylaxis to reduce the frequency of bleeding episodes. And while drug therapy for hemophilia A has come a long way, treatment and cost burden can still be very high. Patients with severe forms of the disease must go to infusion centers or hospitals several times a week for prophylaxis treatment and may require hospitalization or treatment for bleeding episodes several times per year. In addition to the direct costs of treatment, there are many other factors to consider; lost work/school time, transportation costs, complications associated with hemophilia A and patient adherence to treatment regimen.

Gene Therapy

Gene therapy is being explored as a new option in the treatment of hemophilia A. It is an experimental technique that treats the disorder by insertion of a gene into a patient's cells. Doing so allows for mutated genes to be replaced with a healthy copy of the gene, or for inactivation of a mutated gene that is not functioning correctly or to introduce a new gene into the body to help fight disease. Gene therapy has the potential to reduce some of the treatment burden in hemophilia, because it can be dosed much less frequently, replace the need for routine prophylaxis and significantly reduce the number of bleeding episodes that require treatment and/or hospitalization.[5]

Roctavian (valoctocogene roxaparavovec) is an investigational gene therapy treatment that is currently in phase 3 clinical trials.[2,7] It is given as a single dose treatment for hemophilia A. Roctavian consists of a harmless adeno-associated viral vector serotype 5 (AAV5) that delivers genetic material. This enables patients to increase their own production of factor VIII.[8,9] In the phase 1/2 study (NCT02576795), Roctavian demonstrated clinical improvement in patients with hemophilia A. There were 15 participants with severe hemophilia A (factor VIII levels ≤ 1 IU/dL) who were divided into 3 cohorts, each receiving a single infusion of different doses of Roctavian. After 3 years of follow-up, the 13 patients that were still participating in the study had clinically relevant benefit, as measured by a substantial reduction in annualized rates of bleeding events and a complete cessation of prophylactic factor VIII use. The patients did see the highest amount of factor VIII at the end of year 1 with the amount steadily decreasing over the next 2 years. Bleeding incidents were decreased by as much as 96% in the patient population across all treatment arms at the end of year 1. During year 3, in the 6e13vg/kg dose cohort (the high dose group, which had a total of 7 participants), 6 participants (86%) were free from bleeding events that necessitated additional factor VIII treatment as compared to 17% who had zero bleeds in the year prior to study entry. The most common adverse effect that has been reported is an increase in alanine aminotransferase (ALT). All ALT increases were mild, and no hepatocyte damage was noted. No cellular immune response, developments of factor VIII inhibitors or factor VIII antibodies have been detected at this time.[1]

The current phase 3 clinical trial (NCT03370913) has 134 participants and aims to confirm the number of doses required, evaluate the effect of exogenous FVIII on Roctavian and determine the long-term effects on the body. The trial will end in 2023, but BioMarin expects to share 1-year data in early 2021.[2]

BioMarin had been granted priority review of Roctavian and had hoped to market the drug starting late 2020; however, the FDA issued a Complete Response Letter (CRL) to the company on August 18, 2020 and recommended that the company complete the Phase 3 trial (NCT03370913) and submit 2 years of post-treatment data on the patients. This means that approval will be revisited in late 2021 or early 2022. The European Medicines Agency (EMA) review of the Marketing Authorization Application is ongoing.[6]

Gene Therapy for Hemophilia A, cont.

References:

1. Pasi KJ, Rangarajan S, Mitchell N, et al. Multiyear Follow-up of AAV5-hFVII-SQ Gene Therapy for Hemophilia A. N Engl J Med 2020;382:29-40. Available at https://www.nejm.org/doi/10.1056/NEJMoa1908490. Accessed 9/17/2020.
2. BioMarin Pharmaceuticals. Single-Arm Study to Evaluate the Efficacy and Safety of Valoctocogene Roxaparvovec in Hemophilia A Patients. (BMN 270-301). Available at https://clinicaltrials.gov/ct2/show/NCT03370913. Accessed 9/17/2020.
3. US Department of Health & Human Services, National Institutes of Health (NIH). Hemophilia A. 2020. Available at https://rarediseases.info.nih.gov/diseases/6591/hemophilia-a. Accessed 9/17/2020.
4. Blanchette VS, Key NS, Ljung LR, et al. Subcommittee on Factor VIII, Factor IX and Rare Coagulation Disorders. Definitions in hemophilia: communication from the SSC of the ISTH. Journal of Thrombosis and Haemostasis 2014;12(11):1935-1939. Available at https://onlinelibrary.wiley.com/doi/full/10.1111/jth.12672. Accessed 9/17/2020.
5. NIH, US National Library of Medicine. How does gene therapy work? 2020. Available at https://ghr.nlm.nih.gov/primer/therapy/procedures. Accessed 9/17/2020.
6. BioMarin Pharmaceuticals. BioMarin Receives Complete Response Letter (CRL) from FDA for Valoctocogene Roxaparvovec Gene Therapy for Severe Hemophilia A. Available at https://investors.biomarin.com/2020-08-19-BioMarin-Receives-Complete-Response-Letter-CRL-from-FDA-for-Valoctocogene-Roxaparvovec-Gene-Therapy-for-Severe-Hemophilia-A. Accessed 9/17/2020.
7. BioMarin Pharmaceuticals. Single-Arm Study To Evaluate The Efficacy and Safety of Valoctocogene Roxaparvovec in Hemophilia A Patients at a Dose of 4E13vg/kg. (BMN270-302). Available at https://clinicaltrials.gov/ct2/show/NCT03392974. Accessed on 9/17/2020.
8. Rangarajan S, Walsh L, Lester W, et al. AAV5-Factor VIII Gene Transfer in Severe Hemophilia A. NEJM 2017;377(26):2519-2530. Available at https://www.nejm.org/doi/full/10.1056/NEJMoa1708483. Accessed 9/17/2020.
9. Protocol for: Rangarajan S, Walsh L, Lester W, et al. AAV5-factor VIII Gene Transfer in Severe Hemophilia A. NEJM 2017;377 (26):2519-2530. Available at https://www.nejm.org/doi/suppl/10.1056/NEJMoa1708483/suppl_file/nejmoa1708483_protocol.pdf. Accessed 9/20/2020.

KDHE Website Information

New-to-market medications for Kansas Medicaid beneficiaries may be subject to Advanced Medical Hold Manual Review (AMHMR). Previously, new-to-market medications required clinical prior approval based upon package insert guidelines for coverage determination on a case-by-case basis. Effective December 1, 2018, new-to-market drugs may require a drug use review based upon the Advanced Medical Hold Manual Review (AMHMR) criteria that were approved by the Drug Utilization Review (DUR) Board in October 2018 and revised on April 10, 2019. An AMHMR PA may be in effect from the time the drug is placed on AMHMR until its review by the Kansas Medicaid DUR Board, at which time formal permanent PA criteria will be established.

The Advanced Medical Hold Manual Review process overview and drug list can be accessed via the link below:

http://www.kdheks.gov/hcf/pharmacy/AMHMR.htm

Generic Medications

Recently Approved Generic Drugs:

May 2020	June 2020	July 2020
Ivermectin lotion (Sklice®)	Meloxicam capsules (Vivlodex®)	Deferasirox oral granules (Jadenu®)
Ursodiol capsules (Actigall®)	Halobetasol lotion (Ultravate®)	
Desonide gel (Desonate®)	Betamethasone spray 0.05% (Sernivo®)	
Calcipotriene/betamethasone topical suspension (Taclonex®)	Methylphenidate ER ODT tabs (Cotempla XR ODT®)	
Esomeprazole tablets (Nexium®)	Pantoprazole granules (Protonix®)	
Icosapent Ethyl capsules (Vascepa®)		
Posaconazole 200mg/5mL suspension (Noxafil®)		
Tolvaptan tablets (Samsca®)		

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