November 2019
Issue 40

ToxUpdate

Regional Poison Control Center, Birmingham, AL
www.childrensal.org/rpcc 1-800-222-1222

Gvoke™- Ready-to-Use Glucagon

By Hope May, Samford University PharmD Candidate

Glucagon is a polypeptide hormone which consists of 29 amino acids. Glucagon is produced by alpha cells in the islets of Langerhans in the pancreas, stimulating the liver to release stored glucose, called glycogen, into the blood stream. Releasing glucose into the blood stream increases the blood glucose concentration.

Gvoke (glucagon) was approved by the FDA on September 10, 2019 as an antihypoglycemic agent indicated for the treatment of severe hypoglycemia in pediatric (two years of age and older) and adult patients with diabetes. It is packaged as an auto-injector and pre-filled syringe and is available for subcutaneous injection only. Gvoke is a liquid, stable glucagon formulation which can be stored at room-temperature.

Gvoke was evaluated in two crossover studies in adult patients aged 18 to 74 years old with type-1 diabetes mellitus. The first study was double-blinded with 80 patients and the second study was single-blinded with 81 patients. Patients were randomly assigned to receive Gvoke one milligram during one session and conventional glucose emergency kits during the other session. Treatment success was defined as plasma glucose increase from mean value at time of glucagon administration to absolute value greater than 70mg/dL or relative increase of 20mg/dL or greater, at 30 minutes after glucagon administration. In a pooled analysis of both studies, 98.7% of the patients in the Gvoke group achieved treatment success compared to 100% of the patients in the glucose emergency kit group. Gvoke was also evaluated in a study in 31 pediatric patients with type-1 diabetes mellitus. All the evaluable pediatric patients achieved a target glucose increase of at least 25mg/dL. The pediatric dosage in patients 2 to 12 years old is 0.5 mg for less than 45 kg and 1 mg for 45 kg or greater.

Gvoke is novel in its ability to be readily available for the patients who are at risk for severe hypoglycemia. The conventional glucose emergency kits are in vials of lyophilized powder. The usability of the conventional kits is not extremely ideal in an emergency; however, with Gvoke, hypoglycemic rescue can be achieved quicker and more efficiently. Gvoke as a pre-filled syringe is available in pharmacies and was launched throughout the United States in October 2019. The auto-injector formulation will be launched in 2020.

Overdose of glucagon is uncommon due to the short half-life, but there could be some cases in which patients would need observation. Signs and symptoms of mild to moderate toxicity can include nausea, vomiting, diarrhea, and gastric hypotonicity. Toxicity could also be anticipated to be an extension of a different adverse event such as hyperglycemia, hypokalemia, and increased blood pressure. (References on Page 3)

POISON Help® 1-800-222-1222

Special Interest Articles

- Gvoke
- Accrufer
- Adhansia XR

Did you know?
Patients can now have access to oral contraception through a website or smartphone app. This is known as telecontraception. Patients will complete an online questionnaire and receive a prescription for contraception at a local pharmacy or by mail.

Accrufer®: New Iron Salt Formulation for Iron Deficient Anemia in Adults

By Rachel Rusk, Auburn University PharmD Candidate

"Ferric maltol has been used for several years in Europe and Switzerland under the brand name Feraccru."

The US Food and Drug Administration recently approved a new iron replacement treatment, Accrufer (ak-roo-fer) (ferric maltol), indicated for treating iron deficiency in adults. Ferric maltol has been used for several years in Europe and Switzerland under the brand name Feraccru. Accrufer has been shown to be efficacious while having less side effects than other salt formulations.

A recent study published in March 2019 (AEGIS-H2H) showed non-inferiority over an intravenous iron replacement therapy, Ferrinject®. Two other randomized, placebo-controlled clinical trials included patients with irritable bowel syndrome, which can cause reduced iron stores in the body. Patients were randomized to receive either Ferraccru (Accrufer) for 12 weeks or placebo. After the 12 weeks, the patients from both groups could continue to take assigned therapies for an additional 40 weeks. An additional study was performed using patients with chronic kidney disease, another condition that can cause reduced iron stores in the body. This trial was performed similarly for 16 weeks. The results of these trials showed that Accrufer improved hemoglobin and iron stores at the end of treatment compared to placebo.

Accrufer remains together (iron and maltol) until it is absorbed. The iron then dissociates and enters the bloodstream to bind to transferrin. Maltol is metabolized and excreted in the urine. This is different than other salt formulations of iron supplements, which can cause more severe gastrointestinal (GI) adverse events and reduce compliance. The only other option of iron supplementation has been to use IV iron therapies. However, these are costly, invasive, inconvenient, and complex to administer. Additionally, a year's worth of Accrufer is projected to be similar to a single course of IV iron therapy. This means that using Accrufer can be beneficial in saving costs on repeat IV iron dosing and costs associated with its administration in a healthcare setting.

Side effects of Accrufer mainly involve mild GI disturbances: abdominal discomfort/pain, constipation, diarrhea, flatulence, nausea, abnormal stool color, and vomiting. Accrufer is contraindicated in patients with a history of hypersensitivity to the active ingredient or any excipients, hemochromatosis, or those that receive repeated blood transfusions (as this may also lead to iron overload). Patients should have iron parameters monitored during therapy to avoid iron overload. Accrufer has not been studied for safety or efficacy in pediatric populations. No differences were seen in safety or efficacy when used in geriatric patients.

Overdosage of Accrufer has not been reported. However, acute ingestion of 20 mg/kg of elemental iron is potentially toxic, and 200-250 mg/kg is potentially fatal (Accrufer contains 30 mg of elemental iron per capsule). Signs and symptoms of an iron overdose may include nausea, vomiting, abdominal pain, and diarrhea; with worsening, signs may include metabolic acidosis

References

1. Shield Therapeutics PLC. FDA® approves Ferracru® with a broad label of treating iron deficiency in adults. [Internet]. 2019 July [cited 2019 Oct 31]. Available from: https://www.shieldtherapeutics.com/wp-content/uploads/2019/07/STX-Feraccru-FDA-approval-26.07.19.pdf
2. Ferric Maltol. In: DRUGDEX® System (electronic version). Greenwood Village, CO: Truven Health Analytics Inc. [updated 2019 Aug 21, cited 2019 Oct 31].
3. Ferric Maltol. In: Lexi-Comp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information. [updated 2019 Oct 7 cited 2019 Oct 31].
4. Drug Trials Snapshots: ACCRUFER. FDA [Internet]. 2019 Aug [cited 2019 Oct 31]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/drug-trials-snapshots-accrufer
5. Brooks, M. FDA OKs Oral Ferric Maltol (Accrufer) for Iron Deficiency in Adults - Medscape - Aug 07, 2019. [cited 2019 Oct 31]. Available from: https://www.medscape.com/viewarticle/916601
6. Accrufer (ferric maltol) capsules, for oral use [package insert]. Shield Therapeutics, UK. July 2019. Available at: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=2ahUKEwiKg8Sp2sblAhUJVd8KHbkLDngQFjAAegQICRAC&url=https%3A%2F%2Fwww.accessdata.fda.gov%2Fdrugsatfda_docs%2Flabel%2F2019%2F212320Orig1s000lbl.pdf&usg=AOvVaw1ZKk-82hLVZKem49mDkwaP

Regional Poison Control Center attended the Homewood Senior Citizen Wellness Fair on October 25, 2019. PharmD students Rachel Rusk and Hope May, along with poison specialist, Brittany Funchess- Wilson, handed out poison control center information to the seniors attending.

PharmD students, Rachel Rusk and Hope May, visited Springville Senior Center on October 23, 2019 to teach them about Medication Safety.

References for Gvoke article

1. Valentine V, Et Al.. Human Factors Usability and Validation Studies of a Glucagon Autoinjector in a Simulated Severe Hypoglycemia Rescue Situation. *Diabetes Technol Ther*. 2019;21(9):522–530. doi:10.1089/dia.2019.0148
2. Hypoglycemia (Low Blood sugar). American Diabetes Association. https://www.diabetes.org/diabetes/medication-management/blood-glucose-testing-and-control/hypoglycemia. (Accessed October 15, 2019).
3. Gvoke™ (glucagon)—New drug approval. OptumRx. https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/drug-approvals/drugapproval_gvoke_2019-0910.pdf. 2019. (Accessed October 14, 2019).
4. Lexicomp®, (electronic version). Wolters Kluwer Clinical Drug Information, Alphen aan den Rijn, South Holland, Netherlands. https://online-lexi-com.ezproxy.samford.edu/lco/action/doc/retrieve/docid/patch_f/6983?cesid=5lWWa5KKAlV&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dgvoke%26t%3Dname%26va%3Dgvoke#use-lvl-evidence. (Accessed October 15, 2019).
5. Gvoke™ [package insert]. Xeris Pharmaceuticals, Inc., Chicago, IL. September 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212097s000lbl.pdf. (Accessed October 15, 2019).
6. FDA Approves Potentially Life Saving GVOKE: Xeris' Ready-to-Use Glucagon. The diatribe Foundation. https://diatribe.org/fda-approves-potentially-life-saving-gvoke-xeris-ready-use-glucagon. September 12, 2019. (Accessed October 15, 2019).

Adhansia XR™ - New Attention Deficit Hyperactivity Disorder Medication Targets Older Adolescents and Adults

By Laura Read, RPh, CSPI, Regional Poison Control Center, Children's of AL

Adhansia XR is a new methylphenidate capsule that may last longer than other long-acting methylphenidates. Adhansia has two distinct peaks in adults and pediatrics due to the multi-layer release technology in the beads within each capsule. The outer layer of each bead releases 20% of the methylphenidate dose and the inner layer of the bead releases 80% of the dose. Adhansia XR's formulation is ideally suited for adults and older adolescents who have commitments late into the day. Adhansia XR is approved for age 6 and above.

In adults, Adhansia XR peaks at 1.5 hours and the second peak ranges from 8.5 to 16 hours post. In pediatrics, the first peak is at 2 hours and the second peak ranges from 8- 14 hours. Adhansia XR is supplied in 25mg, 35mg, 45mg, 55mg, 70mg, and 85mg extended-release capsules. For patients who have difficulty swallowing, the contents of the capsule may be sprinkled onto a tablespoon of applesauce or yogurt. The dose of a single capsule should not be divided.

Based on the available clinical data, the most common adverse reactions for Adhansia XR were insomnia, dry mouth, and decreased appetite; however, in cases of mild overdose, symptoms may present as extensions of these common adverse reactions due to excessive adrenergic stimulation of the central nervous and cardiovascular systems. Symptoms typically associated with stimulant overdose may include tremor, nausea, tachycardia, hyperthermia, and even seizures.

References

1. Adhansia XR [package insert]. Adlon Therapeutics., Stamford, CT. 2019. https://www.adhansiaxr-hcp.com/release-profile#mlr-delivery-system. (Accessed October 14, 2019).
2. Solve Common Dilemmas with ADHD Stimulants. Pharmacist's Letter. 2019 September. Detail no. 350904 [Electronic version]. https://pharmacist.therapeuticresearch.com/Content/Articles/PL/2019/Sep/Solve-Common-Dilemmas-With-ADHD-Stimulants. (Accessed October 15, 2019).
3. Park, Brian. ADHD Treatment Adhansia XR Now Available. Monthly Prescribing Reference (MPR). https://www.empr.com/home/news/adhd-treatment-adhansia-xr-now-available/. July 30, 2019. (Accessed October 16, 2019).
4. Cutler, Andrew MD. Interview by Neal Howard. ***Health Professional Radio***, 29 March 29, 2019, https://healthprofessionalradio.com.au/adhansia-xr-for-adhd/. (Accessed October 21, 2019).
5. Methylphenidate. POISINDEX® System (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (Accessed October 17,2019).