Rixubis™ for Adults with Hemophilia B

Rixubis™ [coagulation factor IX (recombinant)] is the first and only recombinant factor IX (rFIX) product approved for routine prophylaxis in adults with hemophilia B.1,2 The approval was based on a phase I/III study which evaluated Rixubis™ in patients aged 12-65 years with severe or moderately severe hemophilia B.1,2

In the open-label efficacy segment of the study, 73 previously treated hemophilia B patients received Rixubis™ either as twice-weekly prophylaxis (n=59) or as on-demand treatment (n=14).3 Of the prophylaxis group, 56 patients received twice-weekly treatment for at least 3 months and were included in the analysis. The annualized bleeding rates (ABRs) were compared to an historical control of on-demand treated patients (the standard of therapy in many countries). The historical control included 276 hemophilia B patients treated on-demand for an average of 19.6 months. Using historical control patients was necessary to ensure an adequate sample size for statistical analysis due to the relative rarity of the disease. Baseline characteristics (including ABRs) were comparable between the prophylaxis patients and the historical controls.3

Of the 56 patients receiving prophylaxis, 24 (43%) had no bleeds during the study. ABR was reduced by 79% in the prophylaxis group compared to the on-demand historical controls (4.26 vs. 20.0, respectively; p<0.001). A total of 249 bleeds occurred during the study (115 in 32/59 prophylaxis patients and 134 in 14 on-demand patients). Most bleeds (84.7%) were controlled with 1 or 2 Rixubis™ infusions. Pain relief and improvement in signs of bleeding occurred in 96% of bleeds after a single Rixubis™ infusion.3

Rixubis™ was considered safe and well tolerated with only 2.7% of the 73 patients experiencing transient or mild adverse effects related to treatment. There were no deaths, hypersensitivity reactions, thrombotic events, or cases of inhibitory antibody formation to rFIX. Limitations included the use of a historical control group and the small study population.3

Rixubis™ is administered by intravenous injection. In adults with hemophilia B, Rixubis™ is indicated for (1) control and prevention of bleeding episodes, (2) perioperative management, and (3) routine prophylaxis to prevent or reduce the frequency of bleeding episodes.3 Rixubis™ 1 IU/kg body weight increases circulating FIX by 0.9 IU/dL. For routine prophylaxis, Rixubis™ is dosed at 40 to 60 IU/kg twice weekly. Contraindications include known hypersensitivity to Rixubis™ or hamster protein (Rixubis™ contains small amounts of hamster protein), disseminated intravascular coagulation (DIC), and signs of fibrinolysis. Adverse reactions observed in >1% of study patients were dysgeusia, extremity pain, and positive furin antibody test.4

Rixubis™ provides a rFIX treatment and routine prophylaxis option for adult patients with hemophilia B. The Medical and Scientific Advisory Council of the National Hemophilia Foundation recommends using rFIX products instead of plasma-derived FIX (pdFIX) products due to improved safety.5 This is because clotting factors made from human blood can contain viruses that need to be inactivated or filtered out, leaving the small risk of an infectious diseases like HIV/AIDS or hepatitis with pdFIX administration.6

A continuation of the study described above is currently evaluating the long-term safety and efficacy of Rixubis™.7 Rixubis™ is also being evaluated in pediatric populations and surgery patients.8,9

By Joseph Symbal, PharmD Candidate

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Questions regarding the use of over-the-counter (OTC) cough and cold medications will be on rise again during the fall and winter seasons. For the clinician and pregnant mother, it is important to weigh the risks versus the benefits of all medications taken during pregnancy as many medications may cause some risk to the baby. In addition, because the common cold is often self-limiting and non-life threatening, non-drug measures should always be used first before medications.

Possible non-drug therapies for pregnant mothers include plenty of rest, adequate fluid intake, and good nutrition. It is important to apply these lifestyle measures, even though some people with the common cold may not feel like eating or drinking. Chicken soup and hot broth are options that may be soothing while also increasing fluid intake. Tea with lemon and honey and salt water gargles may provide relief for a sore throat. Saline nasal sprays and drops, nasal strips, steamy showers, humidifiers, vaporizers may help relieve sinus congestion.

When non-drug measures are not enough and symptoms require OTC medication, a few things need to be considered when deciding on a product:

- Many OTC products are available so it is important to ask for advice from a healthcare professional when selecting a product.
- There is limited safety data on the use of OTC medications during pregnancy, and the safety of these agents often depends on pregnancy trimester.
- Read labels carefully and avoid products that are alcohol-containing, long-acting, extended-release, or maximum strength.
- Choose products with single ingredients that target specific symptoms, and avoid products with more than one ingredient.
- OTC cough and cold medications should be taken only when needed and for the shortest time possible.

OTC medications that treat symptoms of the common cold belong to drug classes called the analgesics, decongestants, antihistamines, and expectorants/antitussives and are discussed below.

### Analgesics:

Pain relievers include aspirin, acetaminophen (Tylenol®), and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Motrin®, Advil®) and naproxen (Aleve®). Of these medications, the safest to use and the pain reliever of choice in pregnant mothers is acetaminophen. The use of NSAIDs during pregnancy should be approved by the mother’s physician. NSAIDs should be used at the lowest effective dose and should not be used in the third trimester. Aspirin is not recommended during pregnancy and should never be taken without physician approval and supervision.

### Decongestants:

Nasal congestion (stuffy, runny nose) can be treated with oral decongestants which include pseudoephedrine and phenylephrine. The American College of Obstetricians and Gynecologists and the American College of Allergy, Asthma and Immunology recommend pseudoephedrine. Pseudoephedrine should not be used in the first trimester, although it may be taken in the second and third trimester. Phenylephrine is not recommended in pregnancy due to lack of efficacy and safety data.

Oxymetazoline (Afrin®) is the recommended nasal decongestant spray during pregnancy. The use of nasal decongestants should be limited to 3 days or less. Absorption of nasal decongestants may still pose some risk of exposure to the baby, although the risks are lower than with oral medications.

### Antihistamines:

Antihistamines may be used to help runny noses and sneezing, but do not help ease other symptoms associated with the common cold. Of the antihistamines, chlorpheniramine (ChlorTrimeton®) has the most safety evidence in pregnancy and is the agent of choice. However, the use of antihistamines in the last 2 weeks of pregnancy are not recommended due to the lack of information and an increase in potential risks to mother and baby.

### Expectorants/antitussives:

Available cough medications include guaifenesin (Robitussin®) and dextromethorphan (Robitussin DM®). However, these cough suppressants have not been shown to be effective for cough symptoms related to the common cold. Guaifenesin should be not be used in the first trimester in pregnancy due to potential risk of inguinal hernia in the baby. Although cough suppressants are acceptable in pregnancy, non-drug measures such as the use of a humidifier may be more effective and appropriate for pregnant women.

Non-drug measures should be tried first to help symptoms of the common cold during pregnancy. If non-drug therapies are not successful, pregnant women should discuss the risks and benefits of OTC treatments with their healthcare provider. Pregnant mothers should also choose single-ingredient products that are specific for their symptoms. Pregnant women should read labels carefully and try to avoid combination products containing more than one medication, products containing alcohol, and products that are labeled as “long-acting” or “maximum strength”. Any OTC cough and cold medications should be used only when needed and for the shortest amount of time.

By Chelsey Old Elk, PharmD Candidate

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Brintellix®—A Novel Treatment for Depression

Brintellix® (vortioxetine) is an antidepressant with a novel mechanism and was approved by the FDA in September 2013. It belongs to a new group of oral psychotropic drugs called the bis-aryl-sulfanylamines. Vortioxetine works as a 5-HT1A agonist, 5-HT1B partial agonist, 5-HT3 agonist, 5-HT7 antagonist, and 5-HT transporter protein inhibitor. The proposed additive effects of the mechanism are to raise serotonin, noradrenaline, dopamine, acetylcholine, and histamine levels in the brain, although the influence of these activities on the antidepressant effect of the mediation have not been established. Vortioxetine is approved for the treatment of major depressive disorder (MDD) and is also being evaluated for the treatment of generalized anxiety disorder (GAD), as well as relapse prevention for MDD and GAD. Because of its novel mechanism, it may be an option for patients who have failed traditional treatments in the past. Vortioxetine had mixed efficacy results when compared to placebo in clinical trials, with some studies finding benefit and others showing no benefit to treatment with vortioxetine.

A randomized, double-blind, placebo-controlled, 8-week study examined the efficacy and tolerability of vortioxetine at varying doses in 560 adults with MDD. Patients received either 1, 5, or 10 mg of vortioxetine or placebo. The primary endpoint was decline in the 24-item Hamilton Depression Rating Scale (HDRS-24) score after completing eight weeks of treatment. Other endpoints included response and remission rates of depression and the HDRS-24 score in patients with a baseline score greater than or equal to 20 for the Hamilton Anxiety Rating Scale (HARS).

Vortioxetine treatment decreased depression symptoms compared to placebo. A statistically significant reduction from baseline in the HDRS-24 score was observed for those receiving 10 mg vortioxetine versus placebo (p<0.001). Investigators also found improvements in response and remission rates and the HDRS-24 score in those with a HARS score ≥20 in all treatment groups versus placebo. Patients’ daily functioning was not affected significantly by vortioxetine at any dose. Adverse effects were also evaluated throughout the study, and the drug was found to be well tolerated. The study results are limited by the inability to determine the optimal dose of vortioxetine and the inability to apply the results to patients with comorbidities, since those patients were excluded from the study.

A second study found that vortioxetine did not decrease depressive symptoms compared to placebo. The randomized, double-blind, placebo-controlled trial consisted of 600 adults ages 18-75 years who had MDD and received either 5 mg vortioxetine or placebo daily for 6 weeks, followed by a 2-week medication-free period. The change from baseline in HDRS-24 total score was the primary endpoint, and additional endpoints included response and remission rates.

Significant differences in efficacy were not found between the two groups at week six. Those with baseline HARS scores greater than 19 had significant improvement in HDRS-24 scores at weeks 3-6 in comparison to those receiving placebo (p<0.05). The low vortioxetine dose used in this study may account for the lack of significant results. In addition, the study was conducted at multiple sites with multiple evaluators, which could have over-emphasized the response to placebo.

In the clinical trials, the most commonly reported adverse effects were nausea, vomiting, diarrhea, headache, and dizziness. The majority of side effects were dose related. Nausea was the most frequent side effect leading to discontinuation, with discontinuation rates due to an ADR ranging from 5-8% in clinical trials. As with other antidepressant medications, vortioxetine has a black box warning alerting patients and healthcare providers that antidepressants may increase risk of suicidal thoughts and behavior.

Vortioxetine is available in 5, 10, 15, and 20 mg tablets. The recommended starting dose is 10 mg orally once daily, taken with or without food. For those unable to tolerate this dose, the dose may be reduced to 5 mg daily.

The vortioxetine dose may be increased to a maximum daily dose of 20 mg as tolerated. If necessary, vortioxetine may be discontinued abruptly; however, in those receiving 15-20 mg daily, it is recommended to taper to 10 mg daily for one week before discontinuing completely.

Vortioxetine has a unique mechanism of action and differs from the currently available treatments for depression. Results from clinical trials have been mixed, as some show no benefit over placebo, while others show significant improvement in depressive symptoms. Vortioxetine appears to be well-tolerated and has an ADR profile similar to many available antidepressants. However, more studies are needed to determine its place in therapy for patients with major depressive disorder who are both treatment-naive and treatment-experienced.

By Kelsey Palmer, PharmD Candidate

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### REFERENCES:


### OTC Cough & Cold (continued from page 2)

### Vortioxetine (continued from page 3)

### REFERENCES:


### Rixubis™ (continued from page 1)

### REFERENCES:


PATIENT INFORMATION: The Affordable Care Act in 2014

Due to the Affordable Care Act, there will be several changes to how health insurance works. Most of the changes in 2014 are outlined below:

♦ The bottom line is that people need to have some sort of health insurance, such as Medicare, for example.

♦ By 2014, most people must have health coverage or pay a fee. The fee will be higher every year. In 2014, the fee will be $95 per adult, $47.50 per child, or 1% of the person’s yearly income.

♦ Starting in 2014, health insurance plans cannot refuse to cover an individual or charge more because of a pre-existing health condition. However, grandfathered individual health insurance plans (plans people buy themselves, not through an employer) do not have to cover pre-existing conditions. Insurance companies also cannot set lifetime or yearly limits for essential health benefits.

♦ People without insurance or those who want a better option can get coverage through the Health Insurance Marketplace/exchange.

♦ The Health Insurance Marketplace allows people to get lower cost insurance plans based on their income.


♦ Health Insurance Marketplace will also help people find standard price insurance and will allow people to see if they qualify for Medicaid or Children's Health Insurance Program (CHIP).

♦ Enrollment in the Health Insurance Marketplace started on October 1, 2013, and the open enrollment period ends March 31, 2014.

♦ Simply go to www.healthcare.gov and fill out an application to get started.

♦ The Health Insurance Marketplace also allows people to compare coverage options side-by-side.

♦ After filling out an application, people will be able to see all the health plans available in their area.

♦ Certain individuals can file for exemption, for example those who are uninsured for less than 3 months of the year. Other exemptions can be found on the Health Insurance Marketplace website (www.healthcare.gov).

These changes will continue until 2020 so people should become familiar with how these changes will affect them and their families.

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REFERENCE: