A Comparison of Mipomersen (Kynamro®) and Lomitapide (Juxtapid®): Medications for the Treatment of Homozygous Familial Hypercholesterolemia

Ann Marie Ruhe
Ohio Northern University

Austin Brown
Ohio Northern University

Ginny Daniels
Ohio Northern University

Kelsey Fink
Ohio Northern University

David Bright
Ohio Northern University

Follow this and additional works at: https://digitalcommons.onu.edu/paw_review

Part of the Cardiology Commons, Cardiovascular Diseases Commons, Medical Pharmacology Commons, and the Pharmaceutics and Drug Design Commons

Recommended Citation

This Article is brought to you for free and open access by DigitalCommons@ONU. It has been accepted for inclusion in Pharmacy and Wellness Review by an authorized editor of DigitalCommons@ONU. For more information, please contact digitalcommons@onu.edu.
A Comparison of Mipomersen (Kynamro®) and Lomitapide (Juxtapid®): Medications for the Treatment of Homozygous Familial Hypercholesterolemia

Ann Marie Ruhe, fifth-year pharmacy student from Cincinnati, Ohio; Austin Brown, fourth-year pharmacy student from Forest, Va.; Ginny Daniels, fourth-year pharmacy student from Dover, Ohio; Kelsey Fink, fifth-year pharmacy student from Hudson, Ohio; David Bright, PharmD, BCACP, assistant professor of pharmacy practice

Introduction
As the world’s leading cause of death, cardiovascular disease (CVD) is a fairly common diagnosis in patients, although it can manifest in different ways. There are many factors that contribute to CVD, including poor diet, lack of exercise, hypertension and dyslipidemia. In a select number of patients, poor cardiovascular outcomes can be attributed to genetic mutations. Homozygous familial hypercholesterolemia, also known as type II hyperlipoproteinemia, most frequently results from mutations in both alleles coding for LDL receptors. This mutation of the LDL receptors greatly reduces the amount of serum cholesterol absorbed by cells. There are several mechanisms by which this occurs, including inability of the receptor to be transported to the cell surface, bind to LDL when at the surface or be internalized or released upon binding the LDL cholesterol. It is estimated that HoFH affects approximately one in 1 million individuals, although it is likely that this disease is grossly under diagnosed, given the number of diagnosed cases of CVD and the number of attributable factors. Without proper lipid-lowering treatment, life expectancy is drastically reduced to before age 20 or the early 20s, with a 100 percent mortality rate by age 30. The purpose of this paper is to review HoFH and to describe two emerging pharmacological treatment options.

Overview of Homozygous Familial Hypercholesterolemia
Homozygous familial hypercholesterolemia presents with several characteristic symptoms early in life: total serum cholesterol of greater than 600mg/dL (up to 1,200mg/dL), coronary artery disease, xanthomas (a yellow-orange, lipid-filled nodule) on the skin during childhood, angina of effort (suffocating chest pain occurring during physical exertion), aortic stenosis and myocardial infarction (MI). In some patients, an MI is known to occur as young as 2 years old. Interestingly, diabetes, hypertension and obesity are not often seen in patients with HoFH. Patients who are most likely to develop HoFH are those who have parents that are diagnosed with or have a positive family history of heterozygous familial hypercholesterolemia. Clinically, it may be difficult to distinguish between severe heterozygous and normal-presenting HoFH; in homozygous familial hypercholesterolemia, the patient’s fibroblasts or lymphocytes will show a reduction of LDL receptor activity of 20 percent or more. Genetic testing will also provide a conclusive diagnosis and is useful in identifying silent cases, giving health care professionals a better understanding of the disease’s clinical presentation and prognosis, as well as providing earlier diagnoses of familial hypercholesterolemia.

Because HoFH is so rare, the best way to treat it has been with conventional methods used in treating “normal” or commonly occurring hyperlipidemia. Lifestyle changes, such
as eating a diet low in fat and cholesterol, increasing exercise, weight control, moderating alcohol intake and smoking cessation are often encouraged. There are several conventional drug options available to help treat the symptoms of HoFH. Statins and resins (such as cholestyramine; also known as bile acid sequestrants) can help to reduce serum levels of LDL cholesterol by increasing the activity of the LDL receptors; however, these drugs will not be effective in removing LDL cholesterol from the blood if the LDL receptor is absent or nonfunctional.1 Bile acid resins can also cause undesirable gastrointestinal (GI) side effects and can deplete fat-soluble vitamins (vitamins A, D, E and K).3 Fibrates, nicotinic acid (also known as niacin, a B vitamin that has shown to improve the overall lipid profile) and cholesterol absorption inhibitors like ezetimibe have also been used to improve the levels of serum LDL. The most promising nonpharmacological treatment for HoFH is LDL-apheresis. Somewhat similar to dialysis, this procedure works by passing the patient’s blood through adsorption columns to remove LDL cholesterol and then returning the blood back to the patient. The components of the columns and the process itself may vary, but the goal is to remove as much LDL cholesterol as possible.3 Treatment regimens that include a statin tend to prolong the effects of LDL-apheresis and slow the rebound rate of LDL cholesterol.1 Although this process is effective, it is fairly expensive (costing approximately $2,500 per treatment6) and inconvenient for patients, who must be treated either weekly or every other week and often spend the entire day in the hospital.3

Mipomersen (Kynamro®)

Mipomersen is a Genzyme Corporation orphan drug that has just recently been approved by the FDA in January 2013. Mipomersen is formulated as a subcutaneous injection that is indicated as an additional therapy option to supplement other lipid-lowering medications and diet in adults with HoFH. The clinical ramifications of mipomersen include reductions in low density lipoprotein-cholesterol (LDL-C), apoB, total cholesterol (TC), and non-high density lipoprotein-cholesterol (non-HDL-C). These clinical results are attributed to mipomersen’s antisense oligonucleotide inhibitor property that prevents translation of the mRNA strand that codes for apoB-100, the primary apolipoprotein in LDL and vLDL.7

In the FDA approval process, the efficacy of mipomersen was assessed primarily using one phase III clinical trial conducted by Raal et al.8 The focus of this particular study is explained, as it was the only mipomersen phase III clinical trial specific to patients with HoFH. The other phase III clinical trials involved patients with a high risk for CVD, which included heterozygous familial hypercholesterolemia.9 The Raal et al. study was a randomized, double-blind, placebo-controlled trial conducted in nine different lipid clinics in seven different countries for 26 weeks. The inclusion factors for patients were an age above 12 years and evidence that pointed to HoFH in the patient. This evidence included either genetic confirmation of HoFH, severe LDL-C concentrations from an early age or presence of heterozygous familial hypercholesterolemia in both parents of the patient. Additionally, the patients met the criteria of a consistent low-fat diet and maximum lipid-lowering medications that were continued throughout the trial. All but one patient were taking cholesterol-lowering medications. More specifically, 76 percent were taking a statin and an additional lipid-lowering medication.8

Out of patients screened, 51 patients met the inclusion criteria and were randomized in a 2:1 ratio in favor of the experimental group. Patients in the experimental group received 200 mg (160 mg if patient weighed <50 kg) mipomersen by subcutaneous injection once weekly.8 The primary outcome measure was to assess efficacy by the percent change of the LDL concentration from baseline. Secondary outcomes measured percent change from baseline for apoB, TC, and non-HDL-C concentrations. Of the 51 patients who entered the study, 45 completed the entire clinical trial. The patients who discontinued treatment did so because of adverse events, noncompliance or consent withdrawal. The results of the Raal et al. study yielded a mean percent change in LDL-C of -24.7 percent in the mipomersen group and -3.3 percent in the placebo group (p=0.0003). The results for the secondary outcomes included a mean percent change from baseline for apoB of -26.8 percent in the mipomersen group compared to -2.5 percent in the placebo group (p=0.0001), a TC change of -21.2 percent mipomersen compared to -2.0 percent placebo (p=0.0002), and a non-HDL-C change of -24.5 percent compared to -2.9 percent (p=0.0002) for mipomersen and placebo, respectively.8

The safety assessment of mipomersen included the Raal et al. study in a review of four phase III clinical trials in the FDA summary review. The Raal et al. study was specific to HoFH, but the other phase III trials involved patients with a high risk for CVD, which included heterozygous familial hypercholesterolemia. Altogether, the trials included a total of 390 patients randomized in a 2:1 ratio in the mipomersen and placebo groups respectively for six months.9

Using the pooled data of the phase III trials, the main safety issues were hepatic steatosis (fatty liver), injection site reactions, elevated serum transaminases, flu-like symptoms, immune/antibody responses and proteinuria.9 The Raal et al. study, specific to HoFH, reported hepatic steatosis, elevated transaminases, injection site reactions and flu-like symptoms, but also mentioned nausea and headache.9

In the Raal et al. study, hepatic steatosis was measured by magnetic resonance imaging (MRI) only when a patient’s aminotransferase levels reached three times their upper limit of normal (ULN). Consequently, four patients had an MRI performed, which resulted in one case of an increase in hepatic fat. Because of the few hepatic fat assessments, there is a chance that other patients experienced undetected hepatic steatosis.8 This possibility is affirmed by two other phase III clinical trials, conducted by Stein et al. and Thomas et al., in which the researchers conducted an MRI at baseline and week 28.10,11 The pooled results for these two studies showed 62 percent of the mipomersen group versus 8 percent of the placebo group had hepatic fat increases of ≥ 5 per-

February 2014 Volume 5, Issue 1 THE PHARMACY AND WELLNESS REVIEW
According to the FDA summary review, clinical significance of this adverse event has yet to be determined. A marked difference in ALT and AST elevations between groups was noted in the Raal et al. study. An ALT value ≥ three times the ULN was observed in 12 percent of the mipomersen group compared to zero in the placebo group. However, no other irregular values in liver tests were observed. Only one patient discontinued treatment due to elevated ALT. Similar results were found in the pooled studies with 16 percent in the mipomersen group versus 1 percent in the placebo.

Antibody response was an adverse event not measured in the Raal et al. study, but observed in the other phase III trials and an open-label extension study. Compiled data showed mipomersen to be very immunogenic. The percentage of mipomersen patients who developed antibodies to mipomersen increased from 4 percent in week 13 to 33 percent in week 50 of treatment. Proteinuria was also observed in 0.8 percent of the placebo group and 2.3 percent of the mipomersen group. According to the FDA summary review, clinical significance of this adverse event has yet to be determined.

Based upon the safety and efficacy studies noted earlier, mipomersen should be taken 200 mg subcutaneously once a week. Patients should also be informed that each weekly dose is priced at $4,860.4612 and that the most common side effect is injection site reactions.8,9

There are several factors that need to be considered before a patient undergoes mipomersen treatment. First, as stated previously, mipomersen is indicated specifically for adults with HoFH. Studies have yet to be conducted with a sufficient number of pediatric or geriatric patients to assess safety. Additionally, patients should undergo a full liver panel inclusive of ALT, AST, total bilirubin and alkaline phosphatase before starting mipomersen. Liver panels should be repeated every month for the first year of treatment. After the first year, tests should be conducted at a minimum of every three months. Careful monitoring of liver panels is necessary due to the increases in aminotransferases in some mipomersen patients, as noted previously. Consequently, contraindications exist with moderate to severe hepatic impairment and active liver disease. Furthermore, due to the risk of hepatotoxicity, the Risk Evaluation and Mitigation Strategy (REMS) program restricts those who can prescribe and dispense mipomersen. Thus, prescribing doctors and dispensing pharmacists must be certified in the REMS program.

The REMS program includes a prescriber training module intended to provide education about appropriate and safe prescribing practices. Each pharmacy wishing to dispense the medication must also obtain certification and implement strategies to ensure that the prescriber is certified in the REMS program and that the patient has the necessary prescription authorization form. The overarching goals of the REMS program are the education of prescribers to ensure safe medication utilization and the limitation of therapy to those with a confirmed diagnosis of HoFH.

Lomitapide (Juxtapid®), an oral alternative to mipomersen (Kynamro®), is Aegerion Pharmaceutical, Inc.'s FDA-approved orphan drug serving as an adjunct treatment for HoFH. Approved in December 2012, it is indicated exclusively as an oral lipid-lowering therapy in patients diagnosed with HoFH. When supplemented with a low-fat diet, LDL-apheresis, and other lipid-lowering therapies, lomitapide has demonstrated reduction in LDL-C, total cholesterol, apoB, and non-HDL-C. Its mechanism entails the small-molecule inhibition of the microsomal triglyceride protein (MTP). This enteric and hepatic endoplasmic reticular protein is responsible for the transfer of lipids to apoB to form a complex. Microsomal triglyceride protein inhibition ultimately precludes the synthesis and secretion of VLDL cholesterol and chylomicrons, which require apoB for assembly and subsequent function. Patients can expect a clinically significant reduction in serum LDL cholesterol when combining lomitapide therapy with both a low-fat diet and lipid-lowering therapy, as demonstrated by the clinical trials utilized for FDA approval in the subsequent discussion.

The phase II clinical trial conducted to assess the safety, tolerability, and efficacy of the novel MTP inhibitor was published in the New England Journal of Medicine in 2007. This interventional, open-label, single-group assessment of lomitapide treatment in patients with HoFH was sponsored by
Reductions from baseline in total cholesterol, apoB, and numerous others. In the 29 patients evaluated, a 40.1 percent reduction was observed in LDL cholesterol levels.

During the course of the study, patients experienced both an elevation in liver transaminases and accumulation of liver fat. This hepatic lipid accumulation is hypothesized to be a direct result of the mechanism and initiates potential progression to fibrotic liver disease. Although additional long-term studies are indicated to further assess these implications, patients should be monitored for increases in amiotransferase levels and hepatic steatosis during therapy. This study further suggests that the adverse hepatic effects may impair the clinical utility of lomitapide.

The phase III clinical assessment of the safety and efficacy of lomitapide was verified by the FDA in January 2013. It was also an interventional, open-label, intention to treat, single-group assessment conducted in 29 patients at 11 medical facilities. For six weeks prior to initiation of lomitapide therapy, patients entered a ‘run-in’ phase, during which current lipid-lowering therapies were stabilized and a low-fat diet (less than 20 percent) was initiated. Dosing was titrated from an initial oral dose of 5 mg/day for two weeks to an eventual 60 mg/day at four-week intervals.

Percentage reduction in LDL cholesterol was again pronounced as the primary outcome and was assessed through week 26 of therapy. Secondary outcomes were very similar to phase II and included percent change from baseline in total cholesterol, apoB, triglycerides, HDL, AST, ALT, and numerous others. In the 29 patients evaluated, a 40.1 ± 31.25 percent reduction was observed in LDL cholesterol levels. Reductions from baseline in total cholesterol, apoB, and triglycerides were 36.4 ± 28.2 percent, 39.4 ± 30.01 percent, and 29.0 ± 55.72 percent, respectively. Both the primary and secondary outcomes lack statistical analysis due to the trial information not yet having reached publication.

Six of the 29 initial participants failed to complete the study, and four of these discontinuations are attributed to adverse events. Both serious and more common adverse events associated with lomitapide therapy have been observed from the first dose until 28 days post-treatment. Rare yet serious adverse events included cardiac disorders (angina pectoris: chest pain secondary to ischemic cardiac muscle, coronary artery atherosclerosis: plaque accumulation in the coronary artery and acute coronary syndrome: an emergent situation in which blood supply to heart muscle is interrupted), lower respiratory tract infections and menorrhagia. More notable common adverse events, at least one of which affected 23 of the 29 participants, included gastrointestinal disorders, pain, fatigue, pyrexia, increased infection incidence and diverse pain complaints. Elevations in ALT, AST and transaminases are also under investigation for a potential patient safety risk.

After analysis of available lomitapide safety information, the primary concern during the course of therapy is the risk of hepatotoxicity. This is manifested through an increase in both AST and ALT ≥ three times the ULN. Hepatic fat increases were also noted, augmenting a patient’s risk of developing steatohepatitis and cirrhosis. Therapy should be discontinued if a patient experiences transaminase elevations concomitantly with clinical symptoms of liver injury. Elevations resolve within one to four weeks of stopping therapy in most patients.

Lomitapide therapy is contraindicated in moderate to severe hepatic impairment, active liver disease, pregnancy and concurrent therapy with moderate or strong CYP3A4 inhibitors, such as clarithromycin, ritonavir and telithromycin. A number of dose adjustments should also be considered where applicable. Dose-related myopathy has been noted with concomitant use of simvastatin (also suspected with lovastatin), and a reduction of the simvastatin dose by 50 percent is recommended upon lomitapide initiation. A maximum daily dose of 40 mg is recommended in patients with end stage renal disease (ESRD) or mild hepatic impairment (Child Pugh A).

The target population for lomitapide therapy includes those with a clinical or laboratory diagnosis of HoFH, excluding those with routine dyslipidemia. The study was a once daily oral therapy available in 5 mg, 10 mg and 20 mg capsules with an average cost per a 28 capsule bottle of $27,156. Therapy is initiated at 5 mg once daily and increased to a 10 mg daily dose after two weeks of patient tolerance. The dose may then be increased to 20 mg, 40 mg and a maximum of 60 mg at four-week intervals for peak therapeutic efficacy. Each capsule should be swallowed whole with a glass of water two hours following the evening meal.
Table 1. Clinical Comparison of Mipomersen and Lomitapide\(^7,12\)

<table>
<thead>
<tr>
<th>Basis of Comparison</th>
<th>Mipomersen (Kynamro(^\text{®}))</th>
<th>Lomitapide (Juxtapid(^\text{®}))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cost</strong></td>
<td>$4,860.46 per weekly dose</td>
<td>$27,156.00 per 28 capsules</td>
</tr>
<tr>
<td><strong>Route and Frequency of Administration</strong></td>
<td>subQ, Q week</td>
<td>oral, QD</td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
<td>Injection site reactions, flu-like symptoms, nausea, headache and elevated transaminases</td>
<td>GI upset, blood and lymphatic disorders, cardiac palpitations, chest pain, fatigue, pyrexia, headache, dizziness, weight loss and diverse musculoskeletal pain</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>Hepatotoxicity, hepatic steatosis, elevated ALT and AST, immunogenicity and proteinuria</td>
<td>Hepatotoxicity, cardiac disorders, lower respiratory tract infections and reproductive system disorders</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Baseline: ALT, AST, total bilirubin and alkaline phosphatase Test liver transaminases levels monthly for the first year and subsequently every three months. Also test before dosage increases.</td>
<td>Baseline: ALT, AST, total bilirubin, alkaline phosphatase, and pregnancy testing Test liver transaminases levels monthly for the first year and subsequently every three months. Also test before dosage increases.</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Moderate to severe hepatic impairment and active liver disease</td>
<td>Moderate to severe hepatic impairment, active liver disease, pregnancy and concurrent therapy with moderate or strong CYP3A4 inhibitors</td>
</tr>
<tr>
<td><strong>Additional Considerations</strong></td>
<td>Prescriber and pharmacy require REMS certification</td>
<td>Prescriber and pharmacy require REMS certification</td>
</tr>
</tbody>
</table>

Pharmacists need to be cognizant of both common and serious adverse events that may impact patients during the course of therapy. During the escalation of treatment doses in the safety and efficacy trial, 10.34 percent of patients experienced a serious adverse event that included cardiac disorders, lower respiratory tract infections and reproductive system disorders. More commonly, patients were at risk for a number of mild adverse effects. Gastrointestinal upset, blood and lymphatic disorders, cardiac palpitations, chest pain, fatigue, pyrexia, headache, dizziness, weight loss and diverse musculoskeletal pain are among the most notable.\(^{16}\)

Additional counseling points may be appropriate for certain patient populations. Because lomitapide is formulated with lactose, diarrhea and intestinal malabsorption may be experienced in patients with hereditary galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption. It would be appropriate to suggest supplementation with fatsoluble vitamins to all patients due to decreased absorption.\(^{18}\)

Upon initiation of therapy, baseline AST, ALT, total bilirubin, alkaline phosphatase and pregnancy testing in females of reproductive age should be recommended. Liver transaminases should subsequently be measured monthly during the first year, every three months thereafter and prior to any increase in dose.\(^{18}\)

Due to the specificity of its indication, risk of hepatotoxicity and continuous monitoring associated with therapy, lomitapide may only be prescribed and dispensed by health care professionals and pharmacies that are certified in the REMS program.\(^{20}\)

**Conclusion**

As an orphan disease, HoFH has long been treated using the standardized treatments indicated for hyperlipidemia, despite its greatly increased severity and treatment challenges. With the approval of mipomersen and lomitapide as more targeted and specialized treatments for HoFH, patients can experience greater convenience in taking an oral medication or administering a subcutaneous injection than they would experience with LDL-apheresis, an expensive and time-consuming procedure that has long been the best treatment option. These orphan drugs have been shown to improve serum cholesterol levels and may promote favorable clinical outcomes for patients with HoFH.
Assessment Questions

1. Mild adverse events associated with administration of lomitapide include all of the following EXCEPT:
   A. Blood and lymphatic disorders
   B. Chest pain
   C. GI upset
   D. Hyperkalemia

2. Which of the following are appropriate baseline monitoring parameters for a patient initiating lomitapide therapy?
   A. AST/ALT
   B. Total bilirubin
   C. Pregnancy testing
   D. Two of the above
   E. All of the above

3. In which of the following patient populations is lomitapide therapy most appropriately indicated?
   A. Monotherapy in patients diagnosed with HoFH
   B. Lipid-lowering therapy in patients with hyperlipidemia unresponsive to statin therapy
   C. As an adjunct to low-fat diet and lipid-lowering therapy in patients with HoFH diagnosis
   D. Monotherapy in patients diagnosed with heterozygous familial hypercholesterolemia

4. Health care professionals and pharmacists must be enrolled in the Risk Evaluation and Mitigation Strategy (REMS) program for which of the following reasons?
   A. Risk of hepatotoxicity
   B. Specificity of indication
   C. Need for continuous monitoring
   D. All of the above

5. What is the most common side effect associated with mipomersen treatment?
   A. Flu-like symptoms
   B. Nausea
   C. Injection site reactions
   D. Headache

6. Baseline monitoring for mipomersen is the same as lomitapide EXCEPT for:
   A. ALT/AST
   B. Pregnancy testing
   C. Total bilirubin
   D. Alkaline phosphatase

7. What is the mechanism of action associated with mipomersen?
   A. Small-molecule inhibition of microsomal triglyceride protein (MTP)
   B. Antisense oligonucleotide inhibitor
   C. HMG-CoA reductase inhibitor
   D. NPC1L1 antagonist

8. After initiation of mipomersen or lomitapide treatment, how frequently should a patient have ALT/AST tests conducted?
   A. Every six months
   B. Every month for the first year, then discontinue tests
   C. Every month during the course of treatment
   D. Every month for the first year, then every three months

9. Which of the following are characteristic symptoms of HoFH?
   A. Xanthomas
   B. Total serum cholesterol of greater than 1,300 mg/dL
   C. Early-onset cardiovascular diseases, including coronary artery disease, angina of effort, aortic stenosis and myocardial infarction
   D. A and C only
   E. All of the above

10. Which of the following conventional treatments (nonspecific for HoFH) can be used in the treatment of HoFH?
    A. Lifestyle modifications including low-fat, low-cholesterol diet, weight control, moderation of alcohol intake and smoking cessation
    B. Pharmacological therapy including statins, resins (also known as bile acid sequestrants), fibrates, nicotinic acid (also known as niacin) and cholesterol absorption inhibitors
    C. LDL-apheresis
    D. A and B only
    E. All of the above
To receive continuing education credit for this program, visit [www.onu.edu/pharmacy/CE](http://www.onu.edu/pharmacy/CE) OR fill out the form below including your indicated answers to the assessment questions and return to:

**Office of Continuing Education at the Raabe College of Pharmacy**
Ohio Northern University
525 South Main Street
Ada, Ohio 45810

---

**Ohio Northern University Continuing Education Registration & Evaluation Form**
Raabe College of Pharmacy Continuing Education Evaluation Form

**Program Title:** A Comparison of Mipomersen (Kynamro®) and Lomitapide (Juxtapid®): Medications for the Treatment of Homozygous Familial Hypercholesterolemia  
UAN: 0048-0000-14-031-H01-P  CEUs: 0.1

All information must be printed CLEARLY to ensure accurate record keeping for attendance and the awarding of continuing education credit. Certificates will be distributed as a PDF document to a valid email address.

**Name:**

**Address:**

City:  
State:  
Zip:

**Phone:**  
**Email:**

**Pharmacy License #:**  
**State:**  
**ONU Alumni?**  
Y  
N

**Program Content:**

<table>
<thead>
<tr>
<th>Strongly Disagree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

The program objectives were clear.

The program met the stated goals and objectives:

1. Describe the clinical symptoms of homozygous familial hypercholesterolemia (HoFH).
2. Identify conventional and adjunct treatments used for HoFH before the development and FDA approval of mipomersen and lomitapide.
3. Identify the mechanism of action for both mipomersen and lomitapide.
4. Identify mipomersen and lomitapide's place in therapy in the treatment of HoFH.
5. Discuss the common adverse events and appropriate monitoring parameters associated with mipomersen and lomitapide therapy.
6. The program met your educational needs.
7. Content of the program was interesting.
8. Material presented was relevant to my practice.

**Comments/Suggestions for future programs:**

---

Thank you!

**Answers to Assessment Questions—Please Circle Your Answer**

1. A  B  C  D  
2. A  B  C  D  E  
3. A  B  C  D  
4. A  B  C  D  
5. A  B  C  D  
6. A  B  C  D  
7. A  B  C  D  
8. A  B  C  D  
9. A  B  C  D  E  
10. A  B  C  D  E

Any questions/comments regarding this continuing education program can be directed to Lauren Hamman, Advanced Administrative Assistant for the Office of Continuing Education (email: l-hamman@onu.edu, phone 419-772-3280).

Ohio Northern University is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is eligible for credit until 02/25/2017.