Commercial/Healthcare Exchange PA Criteria

Effective: February 2013

Prior Authorization: Kynamro (mipomersen)

Products Affected: Kynamro (mipomersen) injection for subcutaneous use

Medication Description:

Kynamro is an oligonucleotide inhibitor of apolipoprotein B-100 synthesis indicated as an adjunct to lipid modifying therapy and diet to reduce low-density lipoprotein cholesterol (LDL-C), apolipoprotein B, total cholesterol (total-C) and non-high density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH).1 A definitive diagnosis can be made by genetic confirmation of two mutant alleles at the LDLR, APOB, PCSK9, or LDLRAP1 gene locus.

The recommended dose of Kynamro is 200 mg once weekly as a subcutaneous injection. After initiation of Kynamro therapy lipid levels should be monitored at least every 3 months for the first year and the maximal reduction of LDL-C may be seen after approximately 6 months (based on the time to steady state seen in clinical studies). The patient's LDL-C level should assessed after 6 months to determine if the LDL-C reduction achieved with Kynamro is sufficiently robust to warrant the potential risk of liver toxicity.

Kynamro has a Boxed Warning regarding the risk of hepatotoxicity and is available only through a Risk Mitigation and Strategy (REMS) Program. The most common adverse effects of Kynamro include injection-site reactions (84% of patients) and flu-like symptoms, which usually occur within 2 days after an injection (~30% of patients) and include one or more of the following: influenza-like illness, pyrexia, chills, myalgia, arthralgia, malaise, or fatigue. The safety and efficacy of Kynamro have not been established in patients with hypercholesterolemia who do not have HoFH and the effect of Kynamro on cardiovascular morbidity and mortality has not been determined.

Covered Uses:

- Homozygous Familial Hypercholesterolemia (HoFH)

Exclusion Criteria:

- Pure hypercholesterolemia or mixed hyperlipidemia
- Moderate or severe hepatic impairment (Child-Pugh B or C) or active liver disease, including unexplained persistent elevations of serum transaminases

Required Medical Information:

- Documented diagnosis of Homozygous Familial Hypercholesterolemia
- Current LDL-C (within the past 30 days)
- Previous trial of high dose statins
    - Crestor 40mg and Atorvastatin (Lipitor) 80mg
- Child-Pugh category

Age Restrictions: ≥ 18 years of age

Prescriber Restrictions: Prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders.

Coverage Duration: 12 months

Other Criteria:

Approve Kynamro if the patient meets the following criteria (A, B, C, D, E and F) **[Initial and Continuing Therapy]**:

A. The patient is aged ≥ 18 years; **AND**

B. The patient has a documented diagnosis of Homozygous Familial Hypercholesterolemia (HoFH) as defined by one of the following (i, ii, OR iii):

- **i.** The patient has had genetic confirmation of two mutant alleles at the low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), proprotein convertase subtilisin kexin type 9 (PCSK9) or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene locus [documentation required]; **OR**
- **ii.** The patient has an untreated low-density lipoprotein cholesterol (LDL-C) level > 500 mg/dL (prior to treatment with antihyperlipidemic agents) within the past 30 days; **OR**
- **iii.** The patient has a treated LDL-C level ≥ 300 mg/dL (after treatment with antihyperlipidemic agents but prior to agents such as Repatha™ [evolocumab injection for SC use] or Juxtapid [lomitapide capsules]) within the past 30 days; **AND**

C. The patient meets one of the following (i or ii):

- **i.** The patient has tried Repatha (evolocumab injection for SC use) and has had an inadequate response according to the prescribing physician; **OR**
- **ii.** The patient is known to have two LDL-receptor negative alleles; **AND**

D. The patient meets one of the following criteria (i **OR** ii):

- **i.** The patient has tried one high-intensity statin therapy (i.e., atorvastatin 80mg daily or Crestor 40mg daily) for at least 12 continuous weeks AND the LDL-C level remains ≥ 300 mg/dL; **OR**
- **ii.** The patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):
  - **a)** The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, acute renal failure and/or elevated creatine kinase [CK] levels [e.g., ≥ 10 times the upper limit of normal]) [documentation required]; **OR**
  - **b)** The patient experienced skeletal-related muscle symptoms (e.g., myopathy or myalgia and meets both of the following criteria [1. and 2.]:
    - **(1)** The skeletal-related muscle symptoms (e.g., myopathy or myalgia) occurred while receiving separate trials of both atorvastatin and Crestor [documentation required]; **AND**
    - **(2)** When receiving separate trials of both atorvastatin and Crestor the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and Crestor); A**ND**

E. Prescribed by, or in consultation with, a cardiologist, endocrinologist, or a physician who focuses in the treatment of CV risk management and/or lipid disorders; **AND**

F. If able to tolerate statins, the patient continues to receive the maximum tolerated dose of a statin while receiving Kynamro.

References:

1. Identification and management of familial hypercholesterolaemia. National Institute for Health and Clinical Excellence (NICE), Royal College of General Practitioners. Available at: http://www.nice.org.uk/cg71. Accessed July 2013
2. Kynamro (mipomersen) [prescribing information]. Cambridge, MA: Genzyme Corporation.

3. Raal FJ and Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis 2012;223:262-268.
4. Vergopoulos, Knoblauch, Schuster. DNA testing for familial hypercholesterolemia: improving disease recognition and patient care. Am J Pharmacogenomics, 2002; 2 (4); 253-62
5. Robinson. Management of Familial Hypercholesterolemia: A Review of the Recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Manag Care Pharm. 2013; 19 (2): 139-49
6. Facts & Comparisons, Online

Policy Revision history

Rev #	Type of Change	Summary of Change	Sections Affected	Date
1	New Policy	New Policy	All	2/2013
2	Policy Update	CCI to adopt EH Policy Template, CCI P&T Review History: 2/13, 10/13, 10/14, 11/15, 8/16, 8/17, 7/18 CCI Revision History: 8/16	All	7/2/2019