

Wyoming Drug Utilization Review

Monoclonal Antibody Therapy for Lipid Management

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The prevalence of hyperlipidemia necessitates continued attempts to develop therapies for treatment resistant patients while possibly reducing adverse effects. The introduction of monoclonal antibodies

for hyperlipidemia meets these requirements, at a cost. Elevated low-density lipid concentrations (LDL-C) are the result of a variety of contributing forces. Familial hyperlipidemia reflects a defect in the metabolism of LDL, whereas secondary causes range from diet choices to comorbid disease states.¹ Some data indicates that over one-half of the US population has hyperlipidemia.² Any steps taken to treat hyperlipidemia will reduce the likelihood of a patient experiencing an atherosclerotic cardiovascular disease (ASCVD) event and reduce mortality.³

Monoclonal antibodies and biologic therapies stand at the cutting edge of drug therapy and provide new thoughts about what diseases can and cannot be treated. Autoimmune diseases,

cancers, and inflammatory diseases all benefit from these new therapies. Two new agents in this class aim at treating one component of hyperlipidemia, particularly, treating elevated LDL-C. This class of drugs is called the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Two are currently available on the market, Repatha® (evolocumab) and Praluent® (alirocumab). The enzyme PCSK9 blocks a receptor that plays a role in removing LDL-C from the blood: the more PCSK9 active, the higher LDL-C. Inhibiting the PCSK9 enzyme allows active receptors to remove LDL-C from the blood, resulting in a lowering of LDL-C.⁴⁻⁶

Clinical trials of the two PCSK9 inhibitors reveal an average lowering of LDL-C of approximately 60%, when used in conjunction with maximally tolerated statin therapy.^{7,8} When taking current guidelines into consideration, these therapies may provide results above what is currently recommended and be more efficacious than high-dose statin therapy alone, which aims to reduce LDL-C by more than 50%.³

These new medications come with their own adverse effect profile.^{7,8} These are injectable medications, and injection-site reactions will occur, but in a small portion of the population, ranging from 4-6%. Clinical trials of the two agents indicate 5-6% of patients will experience myalgias or arthralgias. Neurologic changes were seen in the clinical trials, with an incidence of around 1%, including amnesia, confusion and memory impairment. This is not a comprehensive list of adverse effects, and comes from trials ranging from 1 year to 2 years long.^{7,8}

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PCSK9 therapies are not included in current treatment guidelines for dyslipidemia and are non-preferred on the Wyoming Medicaid PDL. The PDL stipulates that a therapy failure with preferred statins must occur before a non-preferred agent can be tried.⁹

Current monitoring parameters for PCSK9 inhibitors include LDL-C levels and monitoring for hypersensitivity reactions.⁶ New monitoring parameters may become evident as these therapies are further studied and find their way into the patient population. One study is currently investigating changes in neurocognition, and completion is expected sometime in February 2018.⁴ Any serious hypersensitivity to either agent is considered a contraindication.^{6,10} Signs of hypersensitivity include rash, urticaria and pruritus. The alirocumab package insert states some serious hypersensitivity events requiring hospitalization have occurred.^{11,12} Both therapies are contraindicated for use with belimumab.⁶ There are no known effects on metabolism.

The current guidelines stress the importance of lifestyle modifications; maintaining a healthy weight, getting regular exercise, and following a heart healthy diet reduce a patient's ASCVD risk.³ These lifestyle changes are effective without drug therapy but work synergistically with pharmacologic therapy that is included in a patient's treatment plan.³

The pharmacologic options for hyperlipidemia include non-statin drugs. Patients in the following categories qualify for non-statin therapy or qualify for a statin with an additional agent: high-risk patients (those with ASCVD, those with an LDL \geq 190 mg/dL, and those with diabetes), and patients unable to tolerate statins or unable to tolerate an appropriate statin dose. Non-statin therapy includes fibrates, niacin, ezetimibe, and omega-3 fatty acids.³

The current backbone of hyperlipidemia treatment remains statin therapy. These popular and effective agents represent the first line pharmacologic choice. A simple to follow decision algorithm will help

providers decide the appropriate statin intensity to achieve the necessary reduction in LDL-C. Each dosing tier, High-, Moderate-, and Low-intensity, aims to lower a patient's LDL-C by \geq 50%, 30 to $<$ 50% and $<$ 30% respectively.³

The development and marketing of biologic therapy for LDL-C lowering is an advancement in treating dyslipidemia. Current efficacy data claim these therapies may be slightly more efficacious when added to current first line therapy, but that improved efficacy comes with a significant annual cost. Considering the efficacy of current first-line therapy, guidelines stressing statin use, and the cost of these new agents, PCSK9 utility may have limited application and a limited patient population. The adverse effect profile of these agents is considerably different than statins, but it will take time and continued research to fully understand the adverse effects. Monitoring parameters may also change as research and use continues. These new agents have a favorable drug interaction profile and do not have the same metabolism constraints that are associated with statins.

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2017 P & T Committee Meeting Dates

Wednesday, May 10
Thursday, August 10
Thursday, November 9

P & T Committee meetings are held quarterly in Cheyenne at Laramie County Community College, 10 am - 1 pm. Please visit the WY-DUR website at www.uwyo.edu/DUR for meeting details. The agenda is posted approximately 2 weeks prior to a meeting.

P & T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on February 9, 2017.

Highlights of this meeting include:

The new Pharmacy Benefit Management system will be implemented May 15, 2017.

The combination of Suboxone and benzodiazepines will require prior authorization.

Nuvigil will be limited to 150 mg per day and Provigil to 200 mg per day. Nuvigil will be allowed up to 250 mg per day for those with a diagnosis of narcolepsy via prior authorization. Use of both agents concurrently will not be allowed.

Neudexta criteria will be updated to require a diagnosis of pseudobulbar affect with an underlying diagnosis of multiple sclerosis or amyotrophic lateral sclerosis.

Adlyxin and Soliqua will be non-preferred in the Diabetic GLP-1 inhibitor class pending additional safety information.

Eucrisa will be non-preferred for atopic dermatitis.

The proposed prior authorization criteria will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to April 1, 2017.

The next P&T Committee meeting will be held Wednesday, May 10, 2017 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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