MTF Formulary Management for PCSK9 Inhibitor Agent Subclass

Defense Health Agency Pharmacy Operations Division

Bottom Line

- Evolocumab (Repatha) is now designated as Uniform Formulary and step-preferred, while alirocumab (Praluent) is non step-preferred; all new users of Praluent must try Repatha first.
- Manual prior authorization applies to Repatha and Praluent; see section below.
- While the PCSK9 inhibitors offer an additional LDL-lowering option via a novel mechanism, cardiovascular outcomes trials currently underway for both agents will determine their role in cholesterol management.
- Selection of a PCSK9 inhibitor can cost approximately $10,000 per year per patient prescription.
- For the majority of Military Health System (MHS) beneficiaries, moderate-to-high intensity statins, such as generic simvastatin and atorvastatin, are appropriate first-line therapies when choosing LDL-lowering products, and provide an evidence-based choice.

Uniform Formulary Decision: The Director, DHA, approved recommendations from the November 2016 DoD P&T Committee meeting on February 2, 2017, with an implementation date of April 5, 2017.

PCSK9 Uniform Formulary (UF) Agents		**PCSK9 Nonformulary (NF) Agents**
BCF drugs — MTFs must have on formulary	**MTFs may have on formulary***	**MTFs must not have on formulary**
None*	**Step Preferred:** ** • evolocumab (Repatha) **Non Step-Preferred:** • alirocumab (Praluent)**	• None
***** Note that generic simvastatin, pravastatin, atorvastatin, and niacin ER are on the BCF as part of the Antilipidemics-1 Drug Class. **Step-preferred – Repatha must be tried first before Praluent		

Formulary Management Issues

- Repatha and Praluent are both injectable human monoclonal antibodies that provide a new mechanism of action to lower LDL; they have not been previously reviewed as a drug class for formulary placement.
- Both Repatha and Praluent have been addressed through DoD P&T Committee utilization management actions and have manual prior authorizations in place dating back to October 2015.
- The role of PCSK9 inhibitors cannot be assessed without addressing statin therapy. Recent evidence-based guidance relies on statins as the mainstay of hyperlipidemia management. The prior authorizations already in place reflect this evidence-based approach to management, and encourage statin maximization prior to considering a PCSK9 inhibitor.
- Statin intolerance, which remains ill-defined in theory and practice, should be verified prior to switching from statins to drugs that have less evidence-based support for lowering cardiovascular risk (e.g., ezetimibe/simvastatin, ezetimibe, and other non-statins including the PCSK9 inhibitors).

Clinical Summary

- While there are no head-to-head trials of the two available PCSK9 inhibitors, the results of efficacy endpoints for both drug were similar in the populations studied that led to FDA approval.
- Populations that were of special interest included homozygous familial hypercholesterolemia (HoHF), heterozygous familial hypercholesterolemia (HeFH), and patients with atherosclerotic cardiovascular disease (ASCVD) who require additional LDL lowering despite maximal lipid-lowering therapy. These are the patient populations most likely to benefit from additional LDL-lowering therapy.
- Endpoints for the various populations studied focused on LDL-lowering over various time periods, but treatment with either Repatha or Praluent consistently achieved LDL lowering from baseline ranging from 40% to 60%.

- Cholesterol management guidelines focus on statins as the foundational basis for treatment, with a shift in recent years from a target LDL to addressing cardiovascular risk. While the LDL-lowering efficacy of the PCSK9 inhibitors so far is exceptional, statins should remain the primary choice when choosing amongst available lipid-lowering therapies.
- Cardiovascular outcomes trials are still pending to determine whether the LDL-lowering benefits of the PCSK9 inhibitors will result in a significant advance in therapy, beyond that already achieved with statins.
- Repatha is administered as 140 mg every 2 weeks or 420 mg every 4 weeks, with most patients typically requiring one dose every 2 weeks. Repatha has an additional indication for HoFH in patients as young as 13 years. The Repatha once monthly 420 mg dose is only approved for patients with HoFH. Praluent similarly allows for dosing every two weeks, but also provides for titration from 75 mg to 150 mg.

Safety & Tolerability

- Both Repatha and Praluent appear safe and well tolerated over the short-term periods they have been studied. The most commonly reported adverse events include injection site and hypersensitivity reactions. Aside from hypersensitivity issues, there are no clinically significant drug-drug interactions, and no warnings or precautions for Repatha or Praluent.
- The results of the cardiovascular outcome trials with the PCSK9 inhibitors (anticipated in 2017–2018), will elucidate concerns over neurocognitive effects due to extremely low LDL levels, and risks of immunogenicity and diabetes.

Prior Authorization

- Manual prior authorization applies to new and current users of both Repatha and Praluent.
- New users of a PCSK9 inhibitor are required to try Repatha prior to Praluent. The initial prescription requires a cardiologist, lipidologist, or endocrinologist evaluation, while renewals can be completed by a primary care provider, in consultation with the initially prescribing specialist.
- Patients with HeFH and ASCVD are required to be on maximally-tolerated statin doses, unless there are contraindications or a previous history of adverse effects.
- Prior Authorization expires after one year, and renewal requires a documented positive response to therapy with an LDL less than 70 mg/dL or LDL reduction greater than 30%, and documented adherence to therapy.

References

- DoD P&T Committee minutes: http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee/Meeting-Minutes
- Current/future drug classes under review by the DoD P&T Committee: http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee
- TRICARE Formulary Search Tool: http://www.express-scripts.com/tricareformulary
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents and Executive Summaries available at: http://www.health.mil/DoDPTResources
- Point of contact for additional information: dha.jbsa.pharmacy.list.poduf@mail.mil

Antilipidemics-1/PCSK9 Inhibitors Price Comparison at MTF	
Drug	**MTF Cost/Month (November 2016)**
Basic Core Formulary	
simvastatin, pravastatin, atorvastatin	$ **Most Cost Effective**
Uniform Formulary Step Preferred	
evolocumab (Repatha)	$$$ **Less Cost-Effective**
Uniform Formulary Step Non-Preferred	
alirocumab (Praluent)	$$$$ **Least Cost-Effective**

Legend:

$ = "Most Cost-Effective" represents Rxs with the lowest cost and best clinical efficacy

$$ = "Less Cost-Effective" represents higher cost Rxs with similar clinical efficacy

$$$ = "Less Cost-Effective" represents next higher cost Rxs with similar clinical efficacy

$$$$ = "Least Cost-Effective" represents Rxs with the highest cost with similar clinical efficacy