DEPARTMENT OF DEFENSE
PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS

INTERIM MEETING

Addendum December 17, 2013

I. UNIFORM FORMULARY (UF) DRUG CLASS REVIEWS

A. Anti-Lipidemic-1s (LIP-1s)

Background—New lipid treatment guidelines were released on November 12, 2013, one day prior to the November Department of Defense (DoD) Pharmacy & Therapeutics (P&T) Committee meeting. An interim meeting was held to determine the clinical and cost-effectiveness, and UF status of the LIP-1 drugs, based on the new guidelines (found at http://content.onlinejacc.org/article.aspx?articleID=1770217). Military Treatment Facilities (MTFs) and Managed Care Support Contractors were surveyed on their opinions of the new guidelines and potential changes in statin prescribing in the Military Health System (MHS).

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (13 for, 0 opposed, 0 abstained, 3 absent) the following clinical effectiveness conclusions:

- New lipid guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) released on November 12, 2013, recommend statin therapy for patients in the following four risk categories:
  - With clinical atherosclerotic cardiovascular disease (ASCVD)
  - Low-density lipoprotein (LDL) cholesterol ≥190 mg/dL
  - Type 2 diabetic mellitus patients age 40–75 without ASCVD and with LDL between 70–189 mg/dL
  - Patients age 40–75 with 10-year cardiovascular (CV) CV risk ≥7.5% and LDL between 70–189 mg/dL but without history of ASCVD
- Based on the four risk groups, the number of patients eligible to receive statin therapy will likely increase.
- A new risk assessment scoring tool based on gender, race, age, total cholesterol, and LDL is now recommended.
- Other changes from the previous Adult Treatment Panel 3 guideline are that treatment targets based on LDL or high-density lipoprotein (HDL) are no longer recommended, dose titration based on LDL is not recommended, and there is no differentiation in statins in terms of primary and secondary prevention.
- Statins are categorized into three groups—
  - High intensity (LDL lowering ≥50%): atorvastatin 40 mg, 80 mg; rosuvastatin (Crestor) 20 mg, 40 mg

- Moderate intensity (LDL lowering between 30% to <50%): atorvastatin 10 mg, 20 mg; rosuvastatin (Crestor) 5 mg, 10 mg; simvastatin 20 mg, 40 mg; pravastatin 40 mg, 80 mg; lovastatin 40 mg; fluvastatin ER (Lescol XL) 80 mg; fluvastatin 40 mg twice daily; pitavastatin (Livalo) 2 mg, 4 mg
- Low intensity (LDL lowering <30%): simvastatin 10 mg; pravastatin 10 mg, 20 mg; lovastatin 20 mg; fluvastatin 20 mg, 40 mg; pitavastatin (Livalo) 1 mg

- Non-statin therapies (ezetimibe, niacin, fibrates, bile acid salts), whether alone or in addition to statins, do not provide acceptable ASCVD risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.
- Non-statin therapies can be considered for patients who experience adverse events from statins, less than anticipated responses, those with statin tolerability issues, or those with drug interactions.
- Based on the current guidelines, and to meet the needs of DoD beneficiaries, at least one statin from each of the statin intensity groups (low, moderate, and high intensity) is required on the Uniform Formulary.

Relative Cost-Effectiveness—Cost-effectiveness analysis (CEA) and budget impact analysis (BIA) were performed for the LIP-1s. For the BIAs, several of the model's key assumptions were varied, with corresponding sensitivity analyses conducted. The CEA was based in part on evidence and efficacy outcomes published in the 2013 ACC/AHA lipid guidelines. The CEA assessed LIP-1s based on the efficacy (i.e., intensity) of statin therapy, according to the average expected LDL lowering from low-, moderate-, or high-intensity statins. The CEA evaluated the following:

- statin monotherapy agents: atorvastatin, fluvastatin, fluvastatin ER (Lescol XL), lovastatin, lovastatin ER (Altoprev), pitavastatin (Livalo), pravastatin, rosuvastatin (Crestor), and simvastatin; and,
- fixed-dose combination therapy agents: amlodipine/atorvastatin, ezetimibe/atorvastatin (Liptruzet), ezetimibe/simvastatin (Vytorin), niacin/lovastatin (Advicor), and niacin/simvastatin (Simcor).

Relative Cost-Effectiveness Conclusion—The P&T Committee concluded (13 for, 0 opposed, 0 abstained, 3 absent) the following:

- For low-intensity statins, generic simvastatin was the most cost-effective of this subgroup of drugs, based on the weighted average cost per day of treatment across all three points of service, followed by lovastatin, pravastatin, fluvastatin, and pitavastatin (Livalo) (ranked in order from most to least cost-effectiveness)
- For moderate-intensity statins, generic simvastatin was the most cost-effective agent in this subgroup of drugs followed by generic atorvastatin 10 mg and 20 mg, lovastatin, pravastatin, rosuvastatin (Crestor) 5 mg and 10 mg, fluvastatin,

pitavastatin (Livalo), amlodipine/atorvastatin, fluvastatin ER (Lescol XL), and lovastatin ER (Altoprev).

- For high-intensity statins, generic atorvastatin 40 mg and 80 mg was the most cost-effective of this subgroup of drugs, followed by rosuvastatin (Crestor) 20 mg and 40 mg.
- For branded fixed-dose combination agents, cost analysis results showed ezetimibe/simvastatin (Vytorin) to have the lowest average cost per day in this subgroup, followed by ezetimibe/atorvastatin (Liptruzet), niacin/lovastatin (Advicor), and niacin/simvastatin (Simcor).
- Among the formulary options examined, CEA and BIA results showed the most cost-effective scenario designated all generic statins UF and step-preferred, with rosuvastatin (Crestor) as the formulary non-preferred agent (all new users required to try generic statins with equivalent intensity), and all other branded statin agents with nonformulary (NF) status and non-preferred.

1. ***COMMITTEE ACTION: UF RECOMMENDATION***—The P&T Committee recommended (12 for, 1 opposed, 0 abstained, 3 absent) the following scenario for the UF, which is the most clinically and cost-effective option for the MHS:
    - atorvastatin, atorvastatin/amlodipine, simvastatin, pravastatin, fluvastatin, and lovastatin be designated UF and step-preferred (e.g., "in front of the step");
    - rosuvastatin remain designated UF and non step-preferred (e.g., "behind the step"); and,
    - atorvastatin/ezetimibe (Liptruzet), simvastatin/ezetimibe (Vytorin), pitavastatin (Livalo), fluvastatin ER (Lescol XL), lovastatin ER (Altoprev), lovastatin/niacin (Advicor), and simvastatin/niacin (Simcor) be designated NF and non step-preferred (e.g., "behind the step").
    - This recommendation includes step therapy, which requires a trial of a generic statin at similar LDL-lowering intensity in new users of rosuvastatin (Crestor) 20mg and 40 mg and the NF statins, and manual PA criteria for new users of rosuvastatin 5 mg and 10 mg.

    Note that this recommendation does not affect the formulary status of ezetimibe (Zetia) or niacin ER (Niaspan). Ezetimibe remains UF and non step-preferred and Niaspan remains on the Basic Core Formulary (BCF).

    MTF pharmacies are highly encouraged to switch patients currently receiving Vytorin to statin monotherapy at the appropriate LDL-lowering intensity.

    MTFs are also encouraged to reserve new prescriptions for Crestor 20 mg or 40 mg for patients who are unable to tolerate atorvastatin 40 mg or 80 mg, and to consider a generic statin at the equivalent LDL-lowering intensity for new prescriptions, instead of Crestor 5 mg or 10 mg.

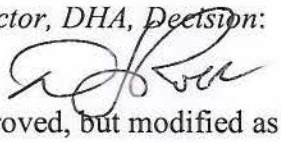
2. ***COMMITTEE ACTION: BCF RECOMMENDATION***—The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 3 absent) maintaining simvastatin 10 mg, 20 mg, and 40 mg; atorvastatin; and, pravastatin on the BCF. Simvastatin 80 mg remains UF.

3. ***COMMITTEE ACTION: MEDICAL NECESSITY (MN) CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 3 absent) MN criteria for atorvastatin/ezetimibe (Litptruzet), simvastatin/ezetimibe (Vytorin), pitavastatin (Livalo), fluvastatin ER (Lescol XL), lovastatin ER (Altoprev), lovastatin/niacin (Advicor), and simvastatin/niacin (Simcor). (See Appendix B for full criteria.)

4. ***COMMITTEE ACTION: PRIOR AUTHORIZATION (PA) CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 3 absent) automated PA criteria (step therapy) and manual PA criteria for new users of rosuvastatin (Crestor) 20 mg and 40 mg, simvastatin/ezetimibe (Vytorin), atorvastatin/ezetimibe (Liptruzet), pitavastatin (Livalo), fluvastatin ER (Lescol XL), lovastatin ER (Altoprev), lovastatin/niacin (Advicor), and (simvastatin/niacin) Simcor, requiring a trial of a step-preferred statin with similar LDL-lowering intensity. The P&T Committee also recommended (11 for, 1 opposed, 1 abstained, 3 absent) manual PA criteria for new users of rosuvastatin (Crestor) 5 mg and 10 mg, requiring a trial of atorvastatin, simvastatin, and pravastatin. (See Appendix C for full criteria.)

5. ***COMMITTEE ACTION: UF AND PA IMPLEMENTATION PERIOD***—The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 3 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service; 2) DHA send a letter to beneficiaries affected by the UF and PA decisions. Based on the P&T Committee's recommendation, the effective date is April 16, 2014.

Director, DHA, Decision: ☒ Approved ☐ Disapproved



Approved, but modified as follows:

II. UTILIZATION MANAGEMENT

A. MONTELUKAST (SINGULAIR) PA—PA criteria were recommended at the August 2011 meeting for montelukast (Singular), requiring automated PA criteria in patients with asthma, and requiring manual PA criteria for patients with seasonal allergic rhinitis or nasal polyps, based on professional treatment guidelines and cost. Generic montelukast tablets entered the market in August 2012 and, as of November 2013, there has been a significant decrease in the generic cost.

1. ***COMMITTEE ACTION: MONTELUKAST (SINGULAIR) PA***—The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 3 absent) that the PA requirements for montelukast be removed, effective upon signing of the minutes.

Director, DHA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

III. SECTION 716 NATIONAL DEFENSE AUTHORIZATION ACT FISCAL YEAR 2013 PILOT PROGRAM FOR REFILLS OF MAINTENANCE MEDICATIONS FOR TRICARE FOR LIFE BENFICIARIES THROUGH THE TRICARE MAIL ORDER PROGRAM

A. Section 716 Revised Manual PA Criteria—After the November 2013 DoD P&T Committee meeting, the Interim Final Rule for the Section 716 Maintenance Medication Program was published in the Federal Register (http://www.gpo.gov/fdsys/pkg/FR-2013-12-11/pdf/2013-29434.pdf.) The Rule is effective February 14, 2014. PA criteria were recommended at the November 2013 DoD P&T Committee meeting.

1. ***COMMITTEE ACTION: SECTION 716 MANUAL PA CRITERIA***—The P&T Committee recommended (13 for, 0 opposed, 0 abstained, 3 absent) revising the manual PA criteria for maintenance medications for the following circumstances:

    a) Patient has barriers to receiving medications by mail (e.g., no permanent address, resides in rural setting).

    b) Patient is not on a stable dose of medication; the medication is currently being titrated.

Director, DHA, Decision: ☒ Approved ☐ Disapproved

Approved, but modified as follows:

SUBMITTED BY:

John P. Kugler, M.D., MPH
DoD P&T Committee Chair

DECISION ON RECOMMENDATIONS

Director, DHA, decisions are as annotated above.

Douglas J. Robb, DO, MPH
Lieutenant General, USAF, MC, CFS
Director

10 Feb 2014
Date

Appendix B—Table of Medical Necessity Criteria

Drug / Drug Class	Medical Necessity Criteria
• Atorvastatin/ezetimibe (Liptruzet) • Simvastatin/ezetimibe (Vytorin) **Antilipidemic-1s**	• There is no alternative formulary agent: the patient requires high-intensity statin therapy (LDL lowering >50%) or moderate-intensity statin therapy (LDL lowering between 30%–50% for Vytorin 10/10 mg) and is receiving ezetimibe and atorvastatin or simvastatin therapy separately and has swallowing difficulties, requiring use of the fixed-dose combination.
• Fluvastatin ER (Lescol XL) • Pitavastatin (Livalo) **Antilipidemic-1s**	• Use of the formulary statins is contraindicated and the patient cannot take pravastatin. • The patient has experienced or likely to experience significant adverse effects from the formulary statins.
• Lovastatin ER (Altoprev) **Antilipidemic-1s**	• There is no alternative formulary agent; the patient requires treatment with lovastatin 60 mg.
• Lovastatin/niacin (Advicor) • Simvastatin/niacin (Simcor) **Antilipidemic-1s**	• There is no alternative formulary agent; the patient is receiving Niaspan and lovastatin or simvastatin separately, and has swallowing difficulties, requiring use of the fixed-dose combination.

Appendix C—Table of Prior Authorization (PA) Criteria

Drug / Drug Class	Prior Authorization Criteria
• Rosuvastatin (Crestor) 20 mg, 40 mg **Antilipidemic1-s (LIP-1s)**	All current users of Crestor are exempt from the PA criteria ("grandfathered"). New users of Crestor 20 mg, 40 mg must try a preferred statin at appropriate LDL lowering first. <u>Automated PA criteria</u> • The patient has filled a prescription for a preferred statin targeting similar LDL lowering >50% (generic atorvastatin 40 mg or 80 mg), at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days. AND <u>Manual PA criteria</u>—If automated criteria are not met, Crestor 20 mg, 40 mg is approved in new users (e.g., trial of atorvastatin 40 mg, 80 mg is NOT required) if: • The patient requires a high-intensity statin (LDL lowering >50%) and has tried atorvastatin 40 mg or 80 mg and was unable to tolerate treatment due to adverse effects. • The patient requires a high-intensity statin (LDL lowering >50%) and is on a concurrent drug metabolized by the cytochrome p450 3A4 pathway.

• Rosuvastatin (Crestor) 5 mg, 10 mg **Antilipidemic1-s (LIP-1s)**	All current users of Crestor are exempt from the PA criteria ("grandfathered"). New users of Crestor 5 mg, 10 mg must try a preferred statin at appropriate LDL lowering first. <u>Manual PA criteria</u>—For new users, Crestor 5 mg or 10 mg is approved (e.g., trial of a generic statin at appropriate LDL lowering is NOT required) if: • The patient is taking a concurrent drug that is metabolized by CYP3A4 and cannot take pravastatin. The provider must state why the patient cannot take pravastatin. • The patient requires moderate LDL lowering (LDL decrease by 30% to 50%), and has tried all 3 of the following drugs: atorvastatin ≥10 mg, simvastatin ≥20 mg, and pravastatin ≥40 mg and could not tolerate treatment due to adverse effects. • Note that the previous requirements for step therapy are removed; all new users of Crestor 5 mg and 10 mg must have a manual ("hard copy") PA.
• Atorvastatin/ezetimibe (Liptruzet) • Simvastatin/ezetimibe (Vytorin) • Fluvastatin ER (Lescol XL) • Lovastatin ER (Altoprev) • Pitavastatin (Livalo) • Lovastatin/niacin (Advicor) • Simvastatin/niacin (Simcor) **Antilipidemic1-s (LIP-1s)**	All new users of Liptruzet, Vytorin, Lescol XL, Livalo, Altoprev, Advicor, and Simcor must try a preferred statin at appropriate LDL lowering first. <u>Automated PA criteria</u> • The patient has received a prescription for a preferred agent (generic atorvastatin, simvastatin, pravastatin, fluvastatin, lovastatin, or pravastatin) targeting similar LDL reduction (LDL lowering <50%, LDL lowering between 30% to 50%, LDL lowering <30%) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days. AND <u>Manual PA criteria</u>—If automated criteria are not met, Liptruzet, Vytorin, Lescol XL, Livalo, Altoprev, Advicor, and Simcor is approved (e.g., trial of generic statin is NOT required) if: • For Vytorin: The patient requires a high-intensity statin and

Drug / Drug Class	Prior Authorization Criteria
	has tried atorvastatin ≥40 mg and was unable to tolerate treatment due to adverse effects. • For Vytorin or Liptruzet: The patient requires high-intensity therapy and is receiving ezetimibe and atorvastatin or simvastatin separately, and has swallowing difficulties (needs a fixed-dose combination product). • For Livalo, Lescol XL: o The patient has tried a preferred statin with similar LDL reduction (moderate or low intensity) and was unable to tolerate it due to adverse effects. o The patient is taking a drug that is metabolized by CYP3A4 . • For Altoprev: The patient requires treatment with lovastatin 60 mg and cannot take another statin with similar LDL lowering. • For Simcor, Advicor: The patient requires a drug that lowers LDL and raises HDL and cannot take two separate tablets (needs fixed-dose combination).

Appendix G—Table of Implementation Status of UF Recommendations/Decisions Summary

Date	DoD PEC Drug Class	Type of Action*	BCF/ECF Medications MTFs must have BCF meds on formulary	UF Medications MTFs may have on formulary	Nonformulary Medications MTFs may not have on formulary	Decision Date / Implement Date	PA and QL Issues	Comments
Dec 2013 Interim Meeting	**Antilipdemic-1s**	UF Class review Previously reviewed	▪ atorvastatin ▪ pravastatin ▪ simvastatin 10, 20, & 40 mg	▪ atorvastatin/amlodipine ▪ fluvastatin ▪ lovastatin ▪ simvastatin 80 mg ▪ rosuvastatin (Crestor) – non-step preferred – see comments	▪ simvastatin/ezetimibe (Vytorin) ▪ atorvastatin/ezetimibe (Liptruzet) ▪ fluvastatin ER (Lescol XL) ▪ lovastatin ER (Altoprev) ▪ pitavastatin (Livalo) ▪ lovastatin/niacin (Advicor) ▪ simvastatin/niacin (Simcor)	Pending signing of the minutes / 60 days	PA applies – see comments and Appendix C	▪ Step therapy applies to new users of Crestor and the 7 nonformulary drugs ▪ Current Crestor users are grandfathered (exempt from PA process) ▪ See Appendix C for details

TRICARE Formulary Search tool: http://www.pec.ha.osd.mil/formulary_search.php

Appendix H—Table of Abbreviations

ACC/AHA	American College of Cardiology/American Heart Association
ASCVD	atherosclerotic cardiovascular disease
BCF	Basic Core Formulary
BIA	budget impact analysis
CEA	cost-effectiveness analysis
CV	cardiovascular
DoD	Department of Defense
ER	extended release
HDL	high-density lipoprotein cholesterol
LDL	low-density lipoprotein cholesterol
LIP-1s	Antilipidemic-1s Drug Class
MHS	Military Health System
MN	medical necessity
MTF	Military Treatment Facility
NF	nonformulary
P&T	Pharmacy & Therapeutics
PA	prior authorization
UF	Uniform Formulary