**DOD PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS**

**INFORMATION FOR THE UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL**

# I. UNIFORM FORMULARY REVIEW PROCESS

Under 10 United States Code § 1074g, as implemented by 32 Code of Federal Regulations (CFR) 199.21, the DoD Pharmacy and Therapeutics (P&T) Committee is responsible for developing the Uniform Formulary (UF). Recommendations to the Director, TMA, on formulary status, pre-authorizations, and the effective date for a drug's change from formulary to nonformulary (NF) status receive comments from the Beneficiary Advisory Panel (BAP), which must be reviewed by the Director before making a final decision.

# II. UF CLASS REVIEWS—GASTROINTESTINAL-1s (GI-1s)

***P&T Comments***

## A. G-1s—Relative Clinical Effectiveness

*Relative Clinical Effectiveness*— The P&T Committee evaluated the relative clinical effectiveness of the GI-1 Drug Class. The class is comprised of three subclasses: aminosalicylates, GI steroids, and miscellaneous agents for irritable bowel syndrome (IBS). The aminosalicylates are comprised of sulfasalazine and the 5-aminosalicylate products (balsalazide, olsalazine, and mesalamine). The GI-1s have not been previously reviewed. There are no agents currently on the Basic Core Formulary (BCF); all drugs in the class are classified as UF drugs. The clinical review included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

The individual GI-1s are listed below:

- **Aminosalicylates:** sulfasalazine (Azulfidine, generic), sulfasalazine enteric coated (EC) (Azulfidine EN, generic), balsalazide (Colazal, generic), olsalazine (Dipentum), oral mesalamine (Asacol; Asacol HD; Pentasa; Lialda; Apriso), rectal mesalamine (Rowasa, generic enema; sulfite-free Rowasa enema; Canasa suppositories)
- **GI steroids:** budesonide (Entocort EC), rectal hydrocortisone (Colocort, Cortenema; Cortifoam)
- **Miscellaneous IBS agents:** alosetron (Lotronex), tegaserod (Zelnorm)

The GI-1 Drug Class expenditures exceed $60 million annually. In terms of overall utilization at all points of service, Asacol is the most utilized aminosalicylate and Entocort is the most utilized GI steroid. The miscellaneous

agents for IBS have restrictive distribution and limited utilization within the Military Health System (MHS).

*Relative Clinical Effectiveness Conclusion*— The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following conclusions for the GI-1Drug Class:

- **Aminosalicylates:**

1. Sulfasalazine, which is comprised of two molecules, sulfapyridine and 5-aminosalicylic acid (5-ASA), remains the first-line oral aminosalicylate recommended by the American College of Gastroenterology for extensive active ulcerative colitis. For the induction of remission in active ulcerative colitis, evidence from a systematic review by the Cochrane group found no clinically relevant differences in efficacy between sulfasalazine and the newer 5-ASA formulations.
2. For maintenance of remission in ulcerative colitis, another systematic review showed a therapeutic advantage of sulfasalazine over the 5-ASA formulations. This advantage was offset by an increase in adverse events observed with sulfasalazine, due to the sulfapyridine moiety. The 5-ASAs are better tolerated than sulfasalazine since they lack the sulfa moiety.
3. The newer 5-ASA formulations employ different release mechanisms to deliver drug at various sites in the GI tract. These differences in drug release and site of release do not confer additional benefits in terms of clinical response. All available 5-ASA formulations have shown superiority over placebo in treating ulcerative colitis. The lack of consensus in terms of efficacy measures for clinical trials makes it difficult to evaluate the comparative efficacy of the 5-ASAs.
4. The efficacy of aminosalicylates in treating Crohn's disease is questionable. Though the aminosalicylates are often used in clinical practice for induction of mild to moderate Crohn's disease, a Cochrane review showed minimal benefit over placebo and less effect compared to budesonide and conventional steroids.
5. In terms of safety, 5-ASAs, though not devoid of adverse reactions, are generally well tolerated. Olsalazine induces a secretory-type diarrhea, which largely limits its use. Otherwise, the safety profile is similar for the 5-ASA products. Concerns regarding renal toxicity, hepatotoxicity, and pancreatitis are idiosyncratic and equally projected across the 5-ASAs.
6. The choice of 5-ASA for treatment of ulcerative colitis will depend on other factors, such as location and extent of disease, as well as patient

preference in terms of ease of administration, pill burden, and frequency of dosing.

7. Rectal 5-ASAs are useful in distal colitis. The choice between the liquid enema and suppositories is based on the extent of diseased colon. Current guidelines recommend combination of oral and rectal therapy for treating mild to moderate distal ulcerative colitis since it is more effective than either therapy alone.

- **GI steroids:**

1. Budesonide delayed-release capsules (Entocort EC) are the only oral steroid preparation available in the GI-1 Drug Class. Budesonide has fewer systemic effects than the other oral corticosteroids (e.g., prednisone) and is delivered directly to the colon. For induction of remission in Crohn's disease, a systematic review found oral budesonide was more effective than placebo and mesalamine, but corticosteroids were more effective than budesonide.
2. For the maintenance of remission in Crohn's disease, another systematic review found budesonide was no more effective than placebo after 6-12 months, and budesonide was no more effective than glucorticoids (which are not effective for maintaining remission). Budesonide was more effective at maintaining remission in Crohn's disease compared to mesalamine. The package labeling for Entocort EC limits treatment to 3 months.
3. Budesonide is not effective for maintenance of remission in ulcerative colitis, based on a systematic review comparing budesonide with placebo, oral mesalamine, and corticosteroids.
4. The rectally-administered topical steroids include the hydrocortisone enema (Colocort, Cortenema) and foam (Cortifoam) preparations, which are effective and safe for the treatment of distal ulcerative colitis.
5. Treatment choice depends on the location of disease and tolerability of the preparation.

- **Miscellaneous IBS agents:**

1. Due to severe adverse effects, including death due to bowel obstruction, alosetron (Lotronex) is restricted to women with severe refractory diarrhea-predominant IBS under a U.S. Food and Drug Administration (FDA) mandated risk evaluation and mitigation strategy program.
2. Due to severe adverse cardiovascular effects, tegaserod (Zelnorm) is available only for emergency use in cases of severe constipation-

predominant IBS after application to the FDA. Upon approval, the manufacturer sends the medication to the patient.

## B. G-1s—Relative Cost-Effectiveness

*Relative Cost-Effectiveness*—The P&T Committee evaluated the relative cost-effectiveness of the GI-1 Drug Class. Cost minimization analyses (CMAs) and budget impact analyses (BIAs) were performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

- **Aminosalicylates:** CMA and BIA were used to assess the potential impact of cost scenarios where sulfasalazine (Azulfidine, generic), sulfasalazine EC (Azulfidine EN, generic), balsalazide (Colazal, generic), olsalazine (Dipentum), oral mesalamine (Asacol, Asacol HD, Apriso, Lialda, Pentasa), and rectal mesalamine (Canasa, Rowasa, sfRowasa) were designated with formulary or NF status on the UF. Cost scenarios evaluating the impact of designating selected agents with BCF status were also considered. BIA results showed that all investigated scenarios resulted in lower cost estimates compared to current MHS expenditures. Overall, cost analyses indicated that the placement of all agents on the UF was the most cost-effective scenario.
- **GI steroids and Miscellaneous IBS agents:** Cost analysis and budget estimates were used to assess the potential impact of designating budesonide (Entocort EC), and rectal hydrocortisone (Colocort, Cortenema, and Cortifoam) with formulary or NF status on the UF. Cost analysis results and budget estimates indicated that the placement of all agents on the UF was the most cost-effective scenario.

*Relative Cost-Effectiveness Conclusion*— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee voted to accept the relative cost-effectiveness of the aminosalicylates (17 for, 0 opposed, 0 abstained, 1 absent) and GI Steroids and Miscellaneous IBS agents (17 for, 0 opposed, 0 abstained, 1 absent) in the GI-1 Drug Class.

## C. G-1s—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended the following:

1. **Aminosalicylates:** sulfasalazine, balsalazide, olsalazine (Dipentum), mesalamine (Asacol, Asacol HD, Pentasa, Lialda, Apriso, Canasa, sulfite-free Rowasa, and mesalamine enema) remain classified with formulary status on the UF (15 for, 1 opposed, 1 abstained, 1 absent).

2. **GI steroids and Miscellaneous IBS Agents:** budesonide (Entocort EC), hydrocortisone enema, hydrocortisone foam (Cortifoam) and alosetron (Lotronex) remain classified with formulary status on the UF (16 for, 0 opposed, 1 abstained, 1 absent). Tegaserod (Zelnorm) is only available from the FDA under a treatment investigational new drug application.
3. As a result of the above recommendations, there are no GI-1 agents designated with NF status on the UF.

## III. UF CLASS REVIEWS—GI-1s

### *BAP Comments*

### A. GI-1s—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended the following:

1. **Aminosalicylates:** sulfasalazine, balsalazide, Dipentum, Asacol, Asacol HD, Pentasa, Lialda, Apriso, Canasa, sulfite-free Rowasa, and mesalamine enema remain classified with formulary status on the UF.
2. **GI steroids and Miscellaneous IBS Agents:** Entocort EC, hydrocortisone enema, Cortifoam and Lotronex remain classified with formulary status on the UF. Zelnorm is only available from the FDA under a treatment investigational new drug application.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## IV. UF CLASS REVIEWS—ANTILIPIDEMIC-2s (LIP-2s)

### *P&T Comments*

### A. LIP-2s—Relative Clinical Effectiveness

The P&T Committee evaluated the relative clinical effectiveness of the LIP-2 Drug Class, which was previously reviewed at the May 2007 P&T Committee meeting. The clinical review for the LIP-2s included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

The LIP-2 Drug Class accounted for $111 million in MHS expenditures in FY 2010. This class is comprised of three subclasses: fibric acid derivatives, omega-3 fatty acids, and bile acid sequestrants (BAS). For the omega-3 fatty acids (fish oil products), there are a number of nutritional supplement products available over-the-counter (OTC); they are not eligible for inclusion on the UF. The individual drugs are outlined, below.

- **Fibric acid derivatives:** Gemfibrozil (Lopid, generics) and several formulations of fenofibrate (Tricor; Lofibra, generics; Antara, Lipofen and Triglide), fenofibrate acid (Fibricor), and choline fenofibrate acid (Trilipix)
- **Omega-3 fatty acids:** Lovaza (formerly known by the brand name Omacor)
- **BAS:** Cholestyramine/sucrose (Questran, generics), cholestyramine/aspartame (Questran Light, generics), colestipol (Colestid, generics), and colesevelam (Welchol)

Gemfibrozil is the current BCF LIP-2. The prescription omega-3 fatty acid product Lovaza, the BAS colesevelam (Welchol), and several fenofibrate formulations (including Tricor and Trilipix) are nonformulary.

Fenofibrate meltdose (Fenoglide) was removed from the BCF in November 2010 due to manufacturing problems. Subsequently, it was not covered by TRICARE® based on the manufacturer's refusal to sign a Master Agreement with the Veterans Administration and participate in the drug discount program required by 38 United States Code 8126. Additionally, the manufacturer voluntarily removed Fenoglide from the TRICARE Pharmacy Benefits Program.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the LIP-2s:

- **Fibric acid derivatives:**
    1. Both gemfibrozil and fenofibrate reduce triglycerides (TG) 20%–50% and raise high density lipoprotein (HDL) 10%–20%. There is insufficient

evidence to conclude that gemfibrozil and fenofibrate differ in their ability to reduce TG and raise HDL.

2. In terms of clinical outcomes, there are no head-to-head trials comparing gemfibrozil with fenofibrate. Gemfibrozil was shown in two trials (HHS and VA-HIT trials) to reduce nonfatal myocardial infarction (MI) and coronary heart disease (CHD) death. Mixed results have been shown with fenofibrates. A reduction in nonfatal MI was seen with fenofibrates in the FIELD trial, but there was a nonsignificant increase in CHD death. In the ACCORD trial when fenofibrate was used in combination with a statin, there was a trend for a reduction in nonfatal MI, nonfatal stroke or death from cardiovascular (CV) causes in individuals with TG > 204 mg/dl and HDL < 34 mg/dl.
3. The newer fenofibrate formulations [nanocrystallized (Tricor), micronized (Antara and Lofibra), insoluble drug-delivery particle (IDD-P) (Triglide), meltdose (Fenoglide), and lidose (Lipofen)] utilize distinct technologies to enhance absorption. The fenofibric acid products (Trilipix and Fibricor) are prodrugs which are water soluble. In terms of efficacy, these newer fenofibrate formulations do not offer a clinical advantage over the original Tricor fenofibrate formulation. Despite differences in dosage strength, particle technology, or active ingredient, the fenofibrates are bioequivalent to the original Tricor 200 mg formulation approved in 1988. The newer fenofibrate formulations do offer patient convenience of administration without regard to meals and once daily dosing, which compares with gemfibrozil.
4. Fenofibrate acid (Trilipix) is the only fenofibrate indicated for combination use with a statin, but other fenofibrate formulations are frequently given concurrently with a statin.
5. Gemfibrozil and the fenofibrates have similar drug-drug interaction profiles and contraindications. Tolerability issues that may affect patient compliance include GI distress (abdominal pain, constipation, nausea, etc.). Gemfibrozil must be taken twice daily prior to meals.
6. The ACCORD trial demonstrated the combination of a fenofibrate with a statin was well tolerated. Although pharmacokinetic and FDA spontaneous adverse event reporting data suggest that gemfibrozil is more likely to interact with statins than fenofibrates, there is a lack of clinical evidence to support that the incidence of myopathy/rhabdomyolysis is lower with fenofibrates. Current guidelines from the American Heart Association and the American College of Cardiology conclude there is a risk with all fibric acid and statin combinations that is not limited to just gemfibrozil.

7. For MHS patients requiring a fibric acid derivative, gemofibrozil and at least one fenofibrate formulation would be expected to meet the needs of the majority of the patient population.

- **Omega-3 fatty acids:**

1. Lovaza is the only prescription omega-3 fatty acid product approved by the FDA. It is indicated for use as an adjunct to diet in patients with very high TG levels (>500 mg/dL).
2. FDA oversight of the manufacturing process for Lovaza offers increased assurance of its omega-3 fatty acid content and purity, in contrast to some fish oil supplements.
3. Overall, Lovaza decreases TG 20%–45%. However, Lovaza has also been associated with increases in low density lipoprotein (LDL), which may offset the beneficial reductions in TG.
4. Lovaza's TG-lowering effects are slightly lower than those achieved with fibric acid derivatives or niacin. Lovaza is associated with similar increases in HDL compared to fibric acid derivatives and niacin. Niacin and gemfibrozil both have clinical trial evidence supporting long-term benefits on cardiovascular outcomes.
5. There are no head-to-head trials comparing Lovaza with fish oil supplements to evaluate lipid profile changes. Trials with fish oil supplements show they are effective at reducing TG levels at doses ranging between 2–4 grams/day.
6. The Lovaza product marketed in the United States does not have outcomes studies showing beneficial effects of reducing death, MI, or stroke, and is not indicated to prevent CHD. The evidence of fish oil supplements or dietary fish consumption for reducing CHD risk is supportive but not conclusive.
7. There is insufficient evidence to support the use of Lovaza for non-CV conditions, including behavioral health/psychiatric conditions. The results of small clinical trials have been conflicting, and used formulations of fish oil different than that found in the Lovaza product.
8. GI disturbances and taste perversions are the most commonly reported adverse effects of Lovaza.
9. There are a few OTC fish oil supplements available from reputable manufacturers that contain the equivalent ingredients per capsule as Lovaza, which should yield similar clinical results. But concerns remain regarding issues such as potency, capsule counts, batch-to-batch consistency, and purity/ truth in labeling with the fish oil supplements.

10. Lovaza provides an alternative therapy in patients with elevated TGs who are not candidates for niacin or fibrates due to a history of adverse effects.

- **BAS:**

1. The BAS reduce LDL 15%–30%. This subclass has largely been replaced by the statins, which reduce LDL 18%–55%. There is insufficient evidence to conclude that BAS differ in their ability to lower LDL. Cholestyramine is the only BAS to show beneficial effects on cardiovascular outcomes.
2. In terms of lipoprotein effects, colesevelam (Welchol) has no major efficacy advantages compared to cholestyramine or colestipol, despite manufacturer claims of enhanced bile acid binding capacity. It has a more favorable pregnancy category rating than the older products (B versus C) and may cause less constipation, which may be clinically relevant in patients with a previous history of GI obstruction.
3. Colesevelam (Welchol) is now FDA-approved for glycemic control in patients with Type 2 diabetes mellitus, when used as adjunctive therapy with other glucose-lowering drugs. Colesevelam only provides a modest HbA1c reduction and other noninsulin diabetes drugs reduce HbA1c more than 0.5%.
4. Issues with palatability of powder formulations and/or large daily tablet burdens are a concern with the class as a whole and may affect compliance.

## B. LIP-2s—Relative Cost-Effectiveness

*Relative Cost-Effectiveness*—The P&T Committee evaluated the relative cost-effectiveness of LIP-2 Drug Class. CMAs and BIAs were performed based on findings that there were no clinically relevant differences in efficacy, safety, tolerability, and other factors among the LIP-2 subclasses. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

- **Fibric acid derivatives:** BIA was used to assess the potential impact of cost scenarios where selected fibric acid derivatives were designated with formulary or NF status on the UF. Cost scenarios evaluating the impact of designating selected agents with BCF and step-preferred statuses were also considered. BIA results for the fibric acid derivatives subclass showed that all investigated scenarios resulted in lower cost estimates than current MHS expenditures. Overall, scenarios where fenofibrate nanocrystallized (Tricor), generic gemfibrozil, and generic fenofibrate micronized/nonmicronized were selected as step-preferred agents, while designating all other fibric acids as UF, were the most cost-effective scenarios. A sensitivity analysis was performed regarding

the date of generic competition for fenofibrate nanocrystallized (Tricor) and fenofibric acid choline (Trilipix). Sensitivity analysis results supported the above conclusion.

- **Omega-3 fatty acids:** BIA was used to assess the potential impact of cost scenarios where Lovaza was designated with formulary or NF status on the UF. Cost scenarios evaluating the impact of implementing prior authorization (PA) were also considered. Overall, scenarios where Lovaza was subject to a prior authorization, which would apply to all current and new users were the most cost-effective. Results from a sensitivity analysis performed supported the above conclusion.
- **BAS:** Results from CMAs performed showed colesevelam (Welchol) was less cost effective than generic BAS currently available on the UF.

*Relative Cost-Effectiveness Conclusion*— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee voted to accept the relative cost-effectiveness of the fibric acid derivatives (17 for, 0 opposed, 0 abstained, 1 absent), omega-3 fatty acids (Lovaza) (16 for, 0 opposed, 0 abstained, 2 absent), and BAS (17 for, 0 opposed, 0 abstained, 1 absent) in the LIP-2 Drug Class.

## C. LIP-2s—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended the following:

1. **Fibric Acid Derivatives:**
    a) Gemfibrozil (Lopid, generics), fenofibrate nanocrystallized (Tricor), fenofibrate IDD-P (Triglide), fenofibrate micronized/nonmicronized (Lofibra, generics), and fenofibrate lidose (Lipofen) remain designated with formulary status on the UF; and that fenofibrate micronized (Antara) fenofibrate nanocrystallized (Tricor), fenofibric acid (Fibricor), and choline fenofibric acid (Trilipix) be designated with formulary status on the UF (16 for, 0 opposed, 0 abstained, 2 absent).
    b) Prior authorization for the fenofibrate acid derivatives would require a trial of gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra), or fenofibrate nanocrystallized (Tricor) (step-preferred drugs) for new patients (16 for, 0 opposed, 0 abstained, 2 absent).

2. **Omega-3 fatty acids**: Lovaza be designated with formulary status on the UF (12 for, 4 opposed, 1 abstained, 1 absent) and subject to PA criteria that allows use in all current and new users (patients will not be grandfathered) only for FDA-approved indications. The dissenting votes reflected information considered by the P&T Committee that shows Lovaza is not cost-effective relative to OTC fish oil supplements and has not been shown to improve CHD outcomes.
3. **Bile Acid Sequestrants:** Cholestyramine/sucrose (Questran, generics), cholestyramine/aspartame (Questran Light, generics), and colestipol (Colestid, generics) remain formulary on the UF; and, colesevelam (Welchol) remain designated with NF status on the UF (14 for, 2 opposed, 1 abstained, 1 absent).

## D. LIP-2s—Fibric Acid Derivatives PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) the following PA criteria should apply to the nonpreferred fibric acid derivatives, fenofibrate micronized (Antara), fenofibrate IDD-P (Triglide), fenofibrate micronized (Lipofen), fenofibric acid (Fibricor), and fenofibric acid choline (Trilipix). Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:
    a) The patient has received a prescription for gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra) or fenofibrate nanocrystallized (Tricor) (MTFs, retail network pharmacies, or mail order) during the previous 180 days.
2. Manual (paper) PA criteria, if automated criteria are not met:
    a) The patient has a contraindication to the preferred fibric acid derivatives that is not expected to occur with the nonpreferred fibric acid derivatives.

## E. LIP-2s—Fibric Acid Derivatives PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 0 abstained, 2 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service; and 2) TMA send a letter to beneficiaries affected by this UF decision.

## F. LIP-2s—Lovaza PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to the prescription omega-3 fatty acid product, Lovaza. Lovaza would be approved only for the FDA-approved indications. All current

and new users of Lovaza must meet one of the following criteria to pass through the PA process.

1. Patients with TG > 500 mg/mL who are receiving statins AND have had an inadequate TG-lowering response to a therapeutic trial of niacin (1-2 g/day) or fibrates, are unable to tolerate niacin or fibrates, or are not candidates for niacin or fibrate therapy.
2. Patients with TG > 500 mg/mL who are not receiving statins AND who have had an inadequateTG-lowering response to a therapeutic trial of monotherapy with both a fibrate and niacin, are unable to tolerate niacin and fibrates, or are not candidates for niacin and fibrate therapy.
3. Coverage is not approved for Lovaza for use in non-FDA approved conditions, including the following: Attention Deficit Hyperactivity Disorder, Alzheimer's disease, bipolar disease, Crohn's disease, cystic fibrosis, dementia, depression, inflammatory bowel disease, intermittent claudication, metabolic syndrome, osteoporosis, post-traumatic stress disorder, renal disease (immunoglobulin A nephropathy), rheumatoid arthritis, schizophrenia, Type 2 diabetes mellitus, and ulcerative colitis.

### G. LIP-2s—Lovaza PA Implementation Plan

The P&T Committee recommended (13 for, 3 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service; and 2) TMA send a letter to beneficiaries affected by this UF decision.

### H. LIP-2s—Colesevelam (Welchol) Medical Necessity (MN) Criteria

Based on the clinical evaluation of the BAS and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) maintaining the current MN criteria for colesevelam (Welchol).

## V. UF CLASS REVIEWS—LIP-2s

***BAP Comments***

### A. LIP-2s—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended the following:

1. **Fibric Acid Derivatives:**
    a) Gemfibrozil, Tricor, Triglide, generic fenofibrate micronized/nonmicronized, and Lipofen remain designated with formulary status on the UF; and that Antara, Tricor, Fibricor, and Trilipix be designated with formulary status on the UF.
    b) Prior authorization for the fenofibrate acid derivatives would require a trial of gemfibrozil, generic fenofibrate micronized/nonmicronized, or Tricor as step-preferred drugs for new patients.

2. **Omega-3 fatty acids**: Lovaza be designated with formulary status on the UF and subject to PA criteria that allows use in all current and new users only for FDA-approved indications.
3. **Bile Acid Sequestrants:** Generic Questran, generic Questran light, and generic Colestid remain formulary on the UF; and, Welchol remain designated with NF status on the UF.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**B. LIP-2s—Fibric Acid Derivatives PA Criteria**

The P&T Committee recommended the following PA criteria should apply to the nonpreferred fibric acid derivatives, Antara, Triglide, Lipofen, Fibricor, and Trilipix. Coverage would be approved if the patient met any of the following criteria:

1. Automated PA criteria:
    a) The patient has received a prescription for gemfibrozil, generic fenofibrate micronized/nonmicronized formulations (including Lofibra) or Tricor (at the MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:
    a) The patient has a contraindication to the preferred fibric acid derivatives that is not expected to occur with the nonpreferred fibric acid derivatives.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**C. LIP-2s—Fibric Acid Derivatives PA Implementation Plan**

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service; and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**D. LIP-2s—Lovaza PA Criteria**

The P&T Committee recommended PA criteria should apply to the prescription omega-3 fatty acid product, Lovaza. Lovaza would be approved only for the FDA-approved indications. All current and new users of Lovaza must meet one of the criteria outlined previously in section 4, subsection F on page 11, to pass through the PA process.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

### E. LIP-2s—Lovaza PA Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60-day implementation period in all points of service; and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

### F. LIP-2s—Colesevelam (Welchol) MN Criteria

Based on the clinical evaluation of the BAS and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended maintaining the current MN criteria for Welchol.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## VI. UF REVIEWS—PANCREATIC ENZYME PRODUCTS (PEPs)

***P&T Comments***

### A. PEPs—Relative Clinical Effectiveness

*Relative Clinical Effectiveness*— The P&T Committee evaluated the relative clinical effectiveness of the PEPs. There are three drugs in the class, which all contain the same active ingredient of lipase, protease, and amylase in different amounts. Creon and Zenpep were approved for marketing in 2009 and Pancreaze was approved in April 2010. There is one authorized generic PEP formulation, pancrelipase delayed-release capsules, which is equivalent to Zenpep 5,000. All previously marketed non-FDA approved PEPs have been discontinued.

The PEP Drug Class has not previously been reviewed; all the drugs are currently designated with formulary status on the UF. This class is designated as an ECF

drug class. Creon has the highest utilization, with about 500,000 units dispensed monthly in the MHS, followed by Zenpep and Pancreaze at an estimated 100,000 units each dispensed monthly. The clinical review focused on use of the PEPs for exocrine pancreatic insufficiency (EPI) and included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(1).

*Relative Clinical Effectiveness Conclusion*—The P&T Committee recommended (17 for, 0 opposed, 0 abstained, 1 absent) the following clinical effectiveness conclusions for the PEPs:

1. There are no head-to-head trials comparing the PEPs. Based on indirect studies comparing each agent to placebo, Creon, Pancreaze, and Zenpep are superior to placebo for improving fat malabsorption associated with EPI due to cystic fibrosis (CF).
2. For patients with EPI due to CF, the endpoint of the average coefficient of fat absorption (CFA) for Creon, Pacnreaze, and Zenpep ranged between 83%–88% in the placebo-controlled trials used to obtain FDA approval. A CFA > 80% is considered clinically relevant for improving fat malabsorption.
3. Creon was superior to placebo for improving fat malabsorption (measured by CFA) as compared to placebo in one study conducted in 44 patients with chronic pancreatitis or following pancreatectomy. Creon is the only PEP approved for use in patients with chronic pancreatitis. In contrast, Zenpep did not meet primary endpoint for improving fat malabsorption in 72 patients with chronic pancreatitis in one unpublished study.
4. With regards to safety, the available evidence suggests there are no clinically relevant differences between Creon, Pancreaze, and Zenpep.
5. With regards to other factors such as microsphere size and storage requirements/stability, there are no clinically relevant differences between the PEPs. Zenpep has unpublished information for enteral administration via G-tube administration, but this route of administration is currently under FDA review.
6. With regard to special populations, Pancreaze is the only PEP which has efficacy and safety data in children as young as 6 months. Pediatric dosing should follow Cystic Fibrosis Foundation Consensus Conferences guidelines.

## B. PEPs—Relative Cost-Effectiveness

*Relative Cost-Effectiveness*—The P&T Committee evaluated the relative cost-effectiveness of the PEPs. Based on clinical findings that efficacy, safety, tolerability, and other factors found among the PEPs were similar at equipotent

doses, CMA and BIA were performed. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

*Relative Cost-Effectiveness Conclusion*—Based on the results of the cost-minimization analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) that Pancreaze was the most cost-effective PEP, followed by Zenpep. Creon was the least cost-effective agent based on weighted average cost per day of therapy. BIA results indicated the scenario that placed all PEPs on the UF was the most cost-effective formulary scenario.

### C. PEPs—Uniform Formulary Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) Creon, Pancreaze, and Zenpep be designated with formulary status on the UF. As a result of this action, no PEPs are designated NF.

## VII. UF REVIEWS—PEPs

***BAP Comments***

### A. PEPs—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Creon, Pancreaze, and Zenpep be designated with formulary status on the UF. As a result of this action, no PEPs are designated NF.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## VIII. RECENTLY APPROVED U.S. FDA AGENTS—RENIN ANGIOTENSIN ANTIHYPERTENSIVE AGENTS (RAAs)

### *P&T Comments*

### A. Aliskiren/Amlodipine Tablets (Tekamlo)—Relative Clinical Effectiveness

*Relative Clinical Effectiveness*—Tekamlo is a fixed-dose combination product containing the direct renin inhibitor (DRI) aliskiren (Tekturna) and amlodipine (Norvasc, generics), a dihydropyridine (DHP) calcium channel blocker (CCB). Aliskiren is also available in a fixed-dose combination tablet containing the diuretic hydrochlorothiazide (HCTZ).

Aliskiren and aliskiren/HCTZ are currently designated with formulary status on the UF, non-step-preferred, requiring prior authorization. Amlodipine is designated with BCF status. Tekamlo is included in the RAAs Drug Class, which is comprised of several subclasses: angiotensin receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, and direct renin inhibitors (DRIs) and their combinations with CCBs or diuretics. The RAAs Drug Class was reviewed at the August 2010 P&T Committee meeting. The clinical evaluation for Tekamlo included, but was not limited to, the requirements stated in 32 Code of Federal Regulations (CFR) 199.21(e)(1).

Tekamlo is indicated for treating hypertension. No positive clinical outcomes have been reported for Tekamlo or any aliskiren-containing product, though outcomes trials with aliskiren remain underway. Current national guidelines [Joint National Committee (JNC-7)] for treating hypertension have not yet addressed the place in therapy for DRIs, although updated guidelines (JNC-8) are anticipated later this year. The American Society of Hypertension does not list the Tekamlo (or any aliskiren-containing) combination as either preferred or acceptable in their recent position statement. Tekamlo does not contain a thiazide-type diuretic, which is considered first-line for most patients.

Treatment with Tekamlo was shown in one randomized trial to significantly reduce blood pressure (BP) compared to placebo. The adverse reaction profile for Tekamlo reflects that of the individual components.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) that although aliskiren/amlodipine (Tekamlo) has a unique mechanism of action due to the DRI component and offers the potential for increased medication persistence, it did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other RAAs included on the UF.

## B. Aliskiren/Amlodipine Tablets (Tekamlo)—Relative Cost-Effectiveness

The P&T Committee evaluated the cost of aliskiren/amlodipine (Tekamlo) in relation to the efficacy, safety, tolerability, and clinical outcomes of the other RAAs, as well as the individual components, aliskiren and amlodipine. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Tekamlo compared to other UF agents. Results from the CMA showed the projected weighted average cost per day for Tekamlo is higher than the other formulary RAAs, including the triple fixed-dose combination drug valsartan/amlodipine/HCTZ (Exforge HCT) and the individual components, Tekturna and amlodipine.

*Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent) aliskiren/amlodipine (Tekamlo) is not cost-effective relative to the other RAAs in this class.

## C. Aliskiren/Amlodipine Tablets (Tekamlo)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (16 for, 0 opposed, 1 abstained, 1 absent) aliskiren/amlodipine (Tekamlo) be designated with NF status on the UF.

## D. Aliskiren/Amlodipine Tablets (Tekamlo)—PA Criteria

As a result of UF action, Tekamlo is designated as a non-preferred RAAs. Prior Authorization for the RAAs class requires a trial of one of the following step-preferred drugs for new patients: losartan (Cozaar, generics), losartan/HCTZ (Hyzaar, generics), telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), and valsartan/amlodipine/HCTZ (Exforge HCT). The other RAAs are non-preferred.

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the following PA criteria should apply to aliskiren/amlodipine (Tekamlo):

1. Automated PA criteria:

a) The patient has received a prescription for losartan, losartan/HCTZ, telmisartan (Micardis), telmisartan/HCTZ (Micardis HCT), telmisartan/amlodipine (Twynsta), valsartan (Diovan), valsartan/HCTZ (Diovan HCT), valsartan/amlodipine (Exforge), or valsartan/amlodipine/HCTZ (Exforge HCT) at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.

b) The patient has tried one of the preferred RAAs and has had an inadequate response.

c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

**E. Aliskiren/Amlodipine Tablets (Tekamlo)—MN Criteria**

Based on the clinical evaluation of aliskiren/amlodipine (Tekamlo) and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Tekamlo.

**F. Aliskiren/Amlodipine Tablets (Tekamlo)—UF and PA Implementation Plan**

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

## IX. RECENTLY APPROVED U.S. FDA AGENTS—RAAs

***BAP Comments***

### A. Aliskiren/Amlodipine Tablets (Tekamlo)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Tekamlo be designated with NF status on the UF.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**B. Aliskiren/Amlodipine Tablets (Tekamlo)—PA Criteria**

As a result of UF action, Tekamlo is designated as a non-preferred RAAs. Prior Authorization for the RAAs class requires a trial of one of the following step-preferred drugs for new patients: generic losartan, generic losartan/HCTZ, Micardis, Micardis HCT, Twynsta, Diovan, Diovan HCT, Exforge, and Exforge HCT. The other RAAs are non-preferred.

The P&T Committee recommended the following PA criteria should apply to aliskiren/amlodipine (Tekamlo):

1. Automated PA criteria:
    a) The patient has received a prescription for a step-preferred RAAs at any MHS pharmacy point of service (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual (paper) PA criteria, if automated criteria are not met:

    a) The patient has tried one of the preferred RAAs and was unable to tolerate treatment due to adverse effects.
    b) The patient has tried one of the preferred RAAs and has had an inadequate response.
    c) The patient has a contraindication to the preferred RAAs, which is not expected to occur with the non-preferred RAAs (e.g., history of angioedema).

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**C. Aliskiren/Amlodipine Tablets (Tekamlo)—MN Criteria**

Based on the clinical evaluation of Tekamlo and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended MN criteria for Tekamlo.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**D. Aliskiren/Amlodipine Tablets (Tekamlo)—UF and PA Implementation Plan**

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## X. RECENTLY APPROVED U.S. FDA AGENTS—RAAs

***P&T Comments***

**A. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—Relative Clinical Effectiveness**

*Relative Clinical Effectiveness*—Tribenzor is a fixed-dose combination product containing olmesartan (Benicar), amlodipine (Norvasc, generics), and HCTZ. It is the second three-drug combination product containing an ARB (olmesartan; Benicar), a DHP CCB (amlodipine), and thiazide-type diuretic (HCTZ) to reach the market. Exforge HCT [valsartan (Diovan)/amlodipine/HCTZ] was the first three-drug entrant on the market.

Olmesartan is currently designated with formulary status on the UF, non-step-preferred, requiring prior authorization; amlodipine and HCTZ are designated as BCF. Tribenzor is included in the RAAs Drug Class, which was reviewed at the

August 2010 P&T Committee meeting. The clinical evaluation for Tribenzor included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1).

Tribenzor is solely indicated for treating hypertension; it can be substituted for the individual titrated components or used as add-on therapy in patients not adequately controlled on two of the component drugs. It is not approved for initial therapy to control BP. Each of the component drugs is consistent with first-line therapy choices per current national guidelines (JNC-7).

Treatment with Tribenzor was shown in one randomized trial to significantly reduce BP when compared to baseline and to each two-drug combination of the component drugs. There are no trials evaluating clinical outcomes of mortality or morbidity with Tribenzor, although outcomes trials are available with the individual components.
The adverse reaction profile for Tribenzor reflects that of the individual components. Although no studies are available specifically addressing the potential for increased compliance with Tribenzor over the individual components administered together, other studies have shown an increase in persistence with fixed-dose antihypertensive combination products.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) that although olmesartan/amlodipine/HCTZ (Tribenzor) offers the potential for increased medication persistence, it did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over other RAAs included on the UF.

## B. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—Relative Cost-Effectiveness

The P&T Committee evaluated the cost of olmesartan/ amlodipine/HCTZ (Tribenzor) in relation to the efficacy, safety, tolerability, and clinical outcomes of the RAAs as well as the individual components, olmesartan, amlodipine, and HCTZ. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was used to evaluate the relative cost-effectiveness of Tribenzor relative to other UF agents in this class. Results from the CMA showed the projected weighted average cost per day for Tribenzor is higher than the other formulary fixed-dose combination RAAs, including the triple-therapy drug amlodipine/valsartan/hydrochlorothiazide (Exforge HCT) and the individual components olmesartan (Benicar), amlodipine, and HCTZ.

*Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for,

0 opposed, 0 abstained, 2 absent) olmesartan/amlodipine/HCTZ (Tribenzor) is not cost- effective relative to the other RAAs in this class.

### C. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent) olmesartan/amlodipine/HCTZ (Tribenzor) be designated NF on the UF.

### D. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—PA Criteria

As a result of the UF action, Tribenzor is designated as a non-preferred RAAs. The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) the same automated and manual PA criteria as outlined above for aliskiren/amlodipine (Tekamlo) should apply to olmesartan/amlodipine/HCTZ (Tribenzor). (See VIII, D for full PA criteria.)

### E. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—MN Criteria

Based on the clinical evaluation of olmesartan/amlodipine/HCTZ (Tribenzor) and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Tribenzor.

### F. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

## XI. RECENTLY APPROVED U.S. FDA AGENTS—RAAs

***BAP Comments***

### A. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Tribenzor be designated NF on the UF.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**B. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—PA Criteria**

As a result of the UF action, Tribenzor is designated as a non-preferred RAAs. The P&T Committee recommended the same automated and manual PA criteria as outlined in section 8, subsection D on page 21, for Tekamlo should apply to Tribenzor.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**C. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—MN Criteria**

Based on the clinical evaluation of Tribenzor and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended MN criteria for Tribenzor.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

### D. Olmesartan/Amlodipine/HCTZ Tablets (Tribenzor)—UF and PA Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## XII. RECENTLY APPROVED U.S. FDA AGENTS—ANTIEMICS

***P&T Comments***

### A. Ondansetron Oral Soluble Film (Zuplenz)—Relative Clinical Effectiveness

*Relative Clinical Effectiveness*—Ondansetron oral soluble film (Zuplenz) is a serotonin subtype 3 (5-HT3) receptor antagonist. It is the only newer antiemetic available in an oral soluble film dosage form. Ondansetron (Zofran, generics) is also available in tablets, orally disintegrating tablets (ODTs), and an oral solution; these formulations are included on the UF. The Newer Antiemetics Drug Class was reviewed at the May 2006 P&T Committee meeting. There are no newer antiemetics designated as BCF; the older antiemetic promethazine is the only BCF antiemetic. The clinical evaluation included, but was not limited to, the requirements sated in 32 CFR 199.21(e)(1).

Ondansetron oral soluble film (Zuplenz) obtained FDA approval via section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act using efficacy and safety data submitted from the ondansetron ODT (Zofran) submission. Bioequivalence studies demonstrated that a single dose of ondansetron oral soluble film 8 mg, taken with or without water and in underfed and fasting conditions, was comparable to ondansetron ODT 8 mg. There are no head-to-head clinical trials comparing ondansetron oral soluble film to the other newer antiemetics. Zuplenz's safety profile reflects that of the other ondansetron products.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) there is no evidence to suggest ondansetron oral soluble film (Zuplenz) has a compelling clinical advantage over ondansetron

products currently included on the UF.

### B. Ondansetron Oral Soluble Film (Zuplenz)—Relative Cost-Effectiveness

CMA was performed that evaluated the cost of ondansetron oral soluble film (Zuplenz) in relation to other currently available newer antiemetics. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

*Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) ondansetron oral soluble film (Zuplenz) was more costly than all other oral comparators in the newer antiemetic class.

### C. Ondansetron Oral Soluble Film (Zuplenz)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (17 for, 0 opposed, 1 abstained, 0 absent) ondansetron oral soluble film (Zuplenz) be designated NF on the UF.

### D. Ondansetron Oral Soluble Film (Zuplenz)—MN Criteria

Based on the clinical evaluation of ondansetron oral soluble film (Zuplenz) and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) MN criteria for Zuplenz.

### E. Ondansetron Oral Soluble Film (Zuplenz)—UF Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

## XIII. RECENTLY APPROVED U.S. FDA AGENTS—ANTIEMICS

***BAP Comments***

### A. Ondansetron Oral Soluble Film (Zuplenz)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Zuplenz be designated NF on the UF.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**B. Ondansetron Oral Soluble Film (Zuplenz)—MN Criteria**

Based on the clinical evaluation of Zuplenz and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended MN criteria for Zuplenz.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**C. Ondansetron Oral Soluble Film (Zuplenz)—UF Implementation Plan**

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## XIV. RECENTLY APPROVED U.S. FDA AGENTS—ALZHEIMER'S DRUGS

### *P&T Comments*

### A. Donepezil 23 mg Tablets (Aricept 23 mg)—Relative Clinical Effectiveness

*Relative Clinical Effectiveness*—Donepezil 23 mg (Aricept 23 mg) is a formulation of donepezil (Aricept) in a higher dosage than previously available (5, 10 mg). The Alzheimer's Drug Class was previously reviewed in November 2005; donepezil 5 and 10 mg tablets are the current Extended Core Formulary (ECF) drugs. Generic formulations of donepezil 5 and 10 mg tablets and ODTs entered the market in November 2010.

The pharmacokinetic profile of one donepezil 23 mg tablet shows a delayed and lower peak concentration compared to giving two of the 10 mg tablets. The 23 mg formulation is not an extended-release preparation; the 5 mg, 10 mg, and 23 mg tablets are administered once daily.

The one clinical trial used to gain FDA approval, which compared donepezil 23 mg with 10 mg, showed statistically significant improvement in measures of cognition, but no benefit in improving global functioning. An indirect comparison suggests efficacy of 23 mg donepezil appears similar to giving 10 mg donepezil with memantine (Namenda).

Tolerability of the donepezil 23 mg formulation will be limited by the increased incidence of adverse events, particularly gastrointestinal (GI) effects, compared with donepezil 10 mg.

*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) donepezil 23 mg (Aricept 23 mg) did not have a significant, clinically meaningful therapeutic advantage in terms of safety, effectiveness, or clinical outcomes over donepezil 10 mg.

### B. Donepezil 23 mg Tablets (Aricept 23 mg)—Relative Cost-Effectiveness

*Relative Cost-Effectiveness*— CMA was performed that evaluated the cost of donepezil 23 mg (Aricept 23 mg) in relation to other currently available agents in the Alzheimer's Drug Class. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

*Relative Cost-Effectiveness Conclusion*— Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (18 for,

0 opposed, 0 abstained, 0 absent) donepezil 23 mg (Aricept 23 mg) tablets are currently cost competitive with all other comparators in the Alzheimer's Drug Class. However, the current generic manufacturer enjoys exclusive marketing rights until spring 2011. Once other generic manufacturers enter the market, donepezil 23 mg (Aricept 23 mg) tablets will be more costly than all other drugs in the Alzheimer's Drug Class.

### C. Donepezil 23 mg Tablets (Aricept 23 mg)——UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (13 for, 4 opposed, 1 abstained, 0 absent) donepezil 23 mg tablets (Aricept 23 mg) be designated NF on UF. The reasons given for the dissenting votes were that some patients could potentially benefit from the drug.

### D. Donepezil 23 mg Tablets (Aricept 23 mg)—MN Criteria

Based on the clinical evaluation of donepezil 23 mg tablets and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Aricept 23 mg.

### E. Donepezil 23 mg Tablets (Aricept 23 mg)—UF Implementation Plan

The P&T Committee recommended (15 for, 0 opposed, 1 abstained, 2 absent) 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

## XV. RECENTLY APPROVED U.S. FDA AGENTS—ALZHEIMER'S DRUGS

***BAP Comments***

### A. Donepezil 23 mg Tablets (Aricept 23 mg)—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended Aricept 23 mg be designated NF on UF.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**B. Donepezil 23 mg Tablets (Aricept 23 mg)—MN Criteria**

Based on the clinical evaluation of Aricept 23 mg tablets and the conditions for establishing MN for a nonformulary medication, the P&T Committee recommended MN criteria for Aricept 23 mg.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

**C. Donepezil 23 mg Tablets (Aricept 23 mg)—UF Implementation Plan**

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## XVI. RECENTLY APPROVED U.S. FDA AGENTS—SELF-MONITORING BLOOD GLUCOSE SYSTEM (SMBGS) TEST STRIPS

### *P&T Comments*

### A. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—Relative Clinical Effectiveness

*Relative Clinical Effectiveness*—The SMBGS test strips were reviewed at the August 2008 P&T Committee meeting. SMBGS test strips designated with formulary status on the UF include Accu-Chek Aviva, Precision Xtra (the BCF SMBGS test strip), Freestyle Lite, Contour and TRUEtest. The clinical evaluation for Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips included, but was not limited to, the requirements stated in 32 CFR 199.21(e)(1). Glucocard 01, Glucocard Vital, Embrace, and Nova Max SMBGS test strips met the previously determined minimum technical requirements, which were approved at the May 2007 P&T Committee meeting, and met the operational limitations of the existing Mail Order and Retail contracts, and Federal Government contracting regulations.

The following did not meet the minimum technical requirements: Advocate Redi-code, EasyMax, EZ Smart Plus, Fifty50, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate. The following were not in compliance with the Buy American/Trade Agreement Acts: Blood Sugar Diagnostic, Liberty, Wavesense Jazz, Wavesense Presto.

The Glucocard 01, Glucocard Vital, Embrace, and Nova Max SMBGS test strips meet the requirements for accuracy by the FDA and the International Standard for Organization, do not require manual coding, require only a 0.3–0.6 microliter blood sample size, are approved for at least one alternate testing site, and provide results in 5 to 7 seconds. The Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips utilize glucose oxidase instead of glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) as the reagent. Test strips with GDH-PQQ have rarely been associated with falsely high blood glucose readings and potential patient harm when used concurrently with products containing maltose (e.g., dialysis patients receiving icodextrin dialysate solutions).

*Relative Clinical Effectiveness Conclusion*—The P&T Committee concluded (17 for, 0 opposed, 0 abstained, 1 absent): 1) Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips are similar to the other test strips included on the UF, in terms of meeting the minimum technical requirements; 2) Nova Max test strips offer ketone testing on the Nova Max Plus meter (ketone testing is also available with the Precision Xtra meter); 3) Nova Max test strips offer wireless communication with insulin pumps on the Nova Max Link meter; and 4) Embrace

test strips used in the Embrace meters offers a talking feature that speaks blood glucose results and instructions for testing.

## B. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—Relative Cost-Effectiveness

*Relative Cost-Effectiveness*—The P&T Committee evaluated the relative cost-effectiveness of Glucocard 01, Glucocard Vital, Embrace, and Nova Max test strips in relation to efficacy, safety, tolerability, and clinical outcomes of the other test strips in the SMBGS test strip class. Information considered by the P&T Committee included, but was not limited to, sources of information listed in 32 CFR 199.21(e)(2).

CMA was performed to evaluate the cost-effectiveness of the Glucocard 01, Glucocard Vital, Embrace, and Nova Max SMBGS test strips. The cost-effectiveness of each new test strip was evaluated relative to the following agents: Accu-chek Aviva, Contour, OneTouch Ultra, Precision Xtra, and TRUEtest. CMA results showed the following, in order from most to least cost-effective: Glucocard Vital > Glucocard 01 > TRUEtest > Contour > Precision Xtra > Accu-Chek Aviva > One Touch Ultra > Nova Max.

*Relative Cost-Effectiveness Conclusion*—Based on the results of the cost analysis and other clinical and cost considerations, the P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) 1) Glucocard Vital is the most cost-effective strip in all points of service, 2) Glucocard 01 is the second most cost-effective strip, 3) Embrace test strips fall in the middle of the price range for UF products and 4) Nova Max is the least cost-effective SMBGS test strip.

## C. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—UF Recommendation

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended (15 for, 0 opposed, 1 abstained, 2 absent):

1. Glucocard 01, Glucocard Vital, and Embrace test strips be designated with formulary status on the UF;

2. Nova Max be designated with NF status on the UF; and

3. Advocate Redi-code, Blood Sugar Diagnostic, EasyMax, EZ Smart Plus, Fifty50, Liberty, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate, Wavesense Jazz, and Wavesense Presto be designated with NF status on the UF because they do not meet the minimum technical standards

required for inclusion on the UF or Federal Government contracting regulations.

**D. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—MN Criteria**

Based on the clinical evaluation of the SMBGS and the conditions for establishing medical necessity for a nonformulary medication provided for in the UF rule, the P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) MN criteria for Nova Max SMBGS test strips.

**E. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—UF Implementation Plan**

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

## XVII. RECENTLY APPROVED U.S. FDA AGENTS—SMBGS TEST STRIPS

***BAP Comments***

**A. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—UF Recommendation**

Taking into consideration the conclusions from the relative clinical effectiveness and relative cost-effectiveness determinations, and other relevant factors, the P&T Committee, based upon its collective professional judgment, recommended:

1. Glucocard 01, Glucocard Vital, and Embrace test strips be designated with formulary status on the UF;

2. Nova Max be designated with NF status on the UF; and

3. Advocate Redi-code, Blood Sugar Diagnostic, EasyMax, EZ Smart Plus, Fifty50, Liberty, Microdot, Rightest GS100, Rightest GS300, Ultratrak Ultimate, Wavesense Jazz, and Wavesense Presto be designated with NF status on the UF because they do not meet the minimum technical standards required for inclusion on the UF or Federal Government contracting regulations.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

### B. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—MN Criteria

Based on the clinical evaluation of the test strips and the conditions for establishing medical necessity for a nonformulary medication provided for in the UF rule, the P&T Committee recommended MN criteria for Nova Max test strips.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

### C. Glucocard 01, Glucocard Vital, Embrace, and NovaMax Test Strips—UF Implementation Plan

The P&T Committee recommended 1) an effective date of the first Wednesday after a 60 days implementation period in all points of service, and 2) TMA send a letter to beneficiaries affected by this UF decision.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## XVIII. UTILIZATION MANAGEMENT—MODIFICATION OF PRIOR AUTHORIZATION

***P&T Comments***

### A. Quinine Sulfate (Qualaquin) PA

Quinine sulfate, under the trade name Qualaquin, is FDA-approved only for the treatment of malaria. Qualaquin's product labeling states it is not approved for malaria prophylaxis or for persistent malaria. Recommended dosing for treatment of malaria is 2 capsules, 3 times daily, for 7 days. Center for Disease Control

recommendations for quinine use include co-administration with tetracycline, doxycycline, or clindamycin, dependent on the type of plasmodium species and the resistance patterns in each malaria-endemic country. In May 2010, the P&T Committee recommended a prior authorization requirement for Qualaquin, limited to treatment of malaria, due to severe adverse events, including death. The PA took effect on October 6, 2010.

**B. Quinine Sulfate (Qualaquin) PA Modification—Recommendation for Quantity Limits**

To ensure the appropriate use of Qualaquin, consistent with the product labeling, the P&T Committee recommended (16 for, 2 opposed, 0 abstained, 0 absent) implementing a quantity limit of 42 capsules per fill, one fill per prescription, with no refills, which will allow quinine (Qualaquin) use in patients who have a documented diagnosis of malaria.

**B. Quinine Sulfate (Qualaquin) PA—Modification of PA Implementation**

The quantity limits for Qualaquin become effective the first Wednesday after a 60-day implementation period in all points of service.

## XIX. UTILIZATION MANAGEMENT—MODIFICATION OF PRIOR AUTHORIZATION

***BAP Comments***

**A. Quinine Sulfate (Qualaquin) PA Modification—Recommendation for Quantity Limits**

To ensure the appropriate use of Qualaquin, consistent with the product labeling, the P&T Committee recommended implementing a quantity limit of 42 capsules per fill, one fill per prescription, with no refills, which will allow Qualaquin use in patients who have a documented diagnosis of malaria.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

### C. Quinine Sulfate (Qualaquin) PA—Modification of PA Implementation

The quantity limits for Qualaquin become effective the first Wednesday after a 60-day implementation period in all points of service.

*BAP Comment:* □ Concur □ Non-concur

Additional Comments and Dissentions:

## XX. ITEMS FOR INFORMATION

**A. Propoxyphene Withdrawal from the Market—**Propoxyphene has been available since the late 1950s, but concerns regarding adverse events, including prolongation of the QT interval have persisted. All propoxyphene products (Darvon, Darvocet, generics) were voluntarily withdrawn from the market in November 2010.