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 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—ANTIPLATELET AGENTS

P&T Comments

A. Antiplatelet Agents

Background Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the antiplatelet drugs, which are used for treating acute coronary syndromes, stroke, and peripheral artery disease. The Antiplatelet Drug Class is comprised of the following: clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta), ticlopidine (Ticlid, generics), aspirin/dipyridamole extended release (ER; Aggrenox), dipyridamole (Persantine, generics), cilostazol (Pletal, generics), and pentoxifylline (Trental, generics). Aspirin is available over-the-counter and is not part of the TRICARE® benefit.

Clopidogrel was designated with Basic Core Formulary (BCF) status on the UF in 2002, prior to implementation of the UF Rule. Generic formulations of clopidogrel are expected in May 2012. Military Health System (MHS) expenditures for antiplatelet agents exceed $260 million annually.

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

1. With regard to efficacy, the following conclusions were made:
    - Acute coronary syndrome (ACS):

- Several large clinical trials have shown the effectiveness of clopidogrel in decreasing the incidence of major cardiovascular (CV) events in patients with ACS.
- Prasugrel and ticagrelor have a faster onset of action and exhibit more complete platelet inhibition, compared to clopidogrel.
- Guidelines from professional cardiology groups recommend clopidogrel, prasugrel, or ticagrelor as first-line options for treating ACS patients requiring percutaneous coronary intervention (PCI).
- Prasugrel and ticagrelor are approved solely for ACS; however, prasugrel is limited to patients whose coronary anatomy is known and suitable for PCI.
- In the TRITON-TIMI 38 trial, prasugrel was more effective than clopidogrel in reducing the composite endpoint of cardiovascular death, non-fatal myocardial infarction (MI), and stroke in ACS patients undergoing PCI. There was no significant difference between prasugrel and clopidogrel for the single endpoint of CV death.
- In the TRITON-TIMI 38 trial, a subgroup analysis showed prasugrel was superior to clopidogrel in patients who are diabetic, those with prior stent thrombosis, and those younger than 65 years.
- In the PLATO trial, ticagrelor was more effective than clopidogrel in reducing the composite endpoint of CV death, non-fatal MI, and stroke in ACS. Ticagrelor was more effective than clopidogrel in reducing the single endpoints of CV death and non-fatal MI, although the trial was not designed to assess differences in mortality.
- In the PLATO trial, a subgroup analysis of the 1,413 U.S. patients found no significant difference between ticagrelor and clopidogrel for major coronary events. This was attributed to the higher aspirin dose utilized in North America versus the rest of the world. Ticagrelor should only be used with aspirin doses lower than 100 mg.
- Definitive statements about comparative clinical effectiveness between prasugrel and ticagrelor are difficult to make because there are no head-to-head studies.

- Stroke

- A systematic review from the Oregon Drug Effectiveness Review Project (DERP) concluded there was no significant difference between aspirin/dipyridamole ER and clopidogrel for all-cause mortality, CV mortality, and recurrent stroke, in patients with ischemic stroke, based on the PROFESS trial.
- The DERP review concluded there was no significant difference between ticlopidine and clopidogrel on outcomes of all-cause mortality, CV death, or cerebral infarction in stroke patients.

- Peripheral artery disease (PAD)
  - Cilostazol is the recommended first-line agent to improve walking distance in patients with PAD, while pentoxifylline is the second-line alternative, based on professional guidelines.
  - Clopidogrel and aspirin are recommended to reduce the risk of MI, stroke or vascular death in patients with symptomatic PAD.

2. With regards to safety/tolerability, the following conclusions were made:
   - In the TRITON-TIMI 38 trial, prasugrel had a significantly higher rate of bleeding, including non-coronary artery bypass grafting (CABG) related bleeding and fatal bleeding, compared to clopidogrel. Additional risk factors that increase the bleeding risk with prasugrel include low weight (<60 kg), age greater than 75 years, and prior history of stroke and transient ischemic attack (TIA).
   - In the PLATO trial, ticagrelor had a similar rate of major and fatal bleeding compared to clopidogrel; however, the rate of non-CABG-related major bleeding was significantly higher with ticagrelor than clopidogrel. Ticagrelor was associated with a higher rate of non-hemorrhagic adverse events (AEs), including dyspnea, and increases in serum creatinine and uric acid levels.
   - Unlike clopidogrel and ticagrelor, prasugrel is contraindicated in patients with previous stroke or TIA.
   - Ticlopidine's therapeutic use is greatly limited by its AE profile, including risk of neutropenia and aplastic anemia.
   - In stroke patients, clopidogrel had a lower rate of major bleeding and withdrawal due to AEs, compared with aspirin/dipyridamole ER.
3. With regards to other factors
   - Prasugrel and ticagrelor are less susceptible to genetic variation and drug-drug interactions with proton pump inhibitors (PPIs), compared to clopidogrel.

- The Pharmacy Outcomes Research Team (PORT) conducted an analysis to define a typical MHS Aggrenox user. A total of 13,341 users with an average age of 76 years were identified. Over 82% of patients had received Aggrenox in the last 180 days, with a new user rate of 13%–18%, suggesting that patients had been on Aggrenox for extended periods.

B. Antiplatelet Agents—Relative Cost-Effectiveness

The P&T Committee evaluated the relative cost-effectiveness of the antiplatelet agents for secondary prevention in ACS, for secondary prevention in stroke, and for PAD. Cost minimization analyses (CMAs) were performed for the antiplatelet drugs used for stroke and PAD (aspirin/dipyridamole ER, ticlopidine, cilostazol, dipyridamole, and pentoxifylline). Cost-effectiveness analyses (CEAs) and CMAs were used to analyze antiplatelet agents for ACS (clopidogrel, prasugrel, and ticagrelor), as efficacy differences between the agents were noted in the clinical review.

- CMA and budget impact analysis (BIA) were used to assess the potential impact of cost scenarios where selected antiplatelet agents were designated with formulary or NF status on the UF. The impact of generic clopidogrel availability was modeled in the BIA scenarios.

- For the antiplatelet drugs prescribed following ACS, CEAs and CMAs were used to assess the potential impact of the occurrence rates of CV and bleeding events, based on differences highlighted in the clinical review.

Two separate cost-effectiveness models were constructed in the analyses of antiplatelet agents for ACS secondary prevention: prasugrel (Effient) versus clopidogrel and ticagrelor (Brilinta) versus clopidogrel. Analysis was based on direct comparisons of relevant trial data. The models compared the annual cost per CV event avoided (the composite of nonfatal MI, nonfatal stroke, and death from CV cause).

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 against, 0 abstained, 2 absent) the following:

- **Antiplatelet agents for ACS—**CEA results showed that prasugrel (Effient) and ticagrelor (Brilinta) provide reasonable clinical benefit for the increase in treatment cost, as shown by their incremental cost-effectiveness ratios (ICERs) of $28,083 and $58,358 per cardiovascular event avoided, respectively.

- **Antiplatelet agents for stroke—**CMA results showed that aspirin/dipyridamole ER (Aggrenox) was the least cost-effective agent, based on analysis of the average weighted price per day of therapy at all three points of service (POS).

- **Antiplatelet agents for PAD—**CMA results showed that pentoxifylline and cilostazol are similarly cost-effective therapy options.

- **All antiplatelet agents—**BIA results showed the scenario where all current BCF agents were retained on the BCF, all current UF agents were retained on the UF, and aspirin/dipyridamole ER (Aggrenox) and ticagrelor (Brilinta) were designated NF resulted in the lowest projected cost compared to current MHS expenditures.

C. Antiplatelet Agents—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 (14 for, 3 opposed, 0 abstained, 1 absent) clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta), ticlopidine (Ticlid, generics), aspirin/dipyridamole ER (Aggrenox), dipyridamole (Persantine, generics), cilostazol (Pletal, generics) and pentoxifylline (Trental, generics) remain formulary on the UF. Although the cost-effectiveness review showed aspirin/dipyridamole ER was the least cost-effective drug for stroke, the P&T Committee recommended that it remain formulary on the UF due to the low new user rate and the advanced age of the patient population. Ticagrelor was also recommended to remain formulary on the UF due its ICER, compared to clopidogrel.

III. UF CLASS REVIEWS—ANTIPLATELET AGENTS

BAP Comments

A. Antiplatelet Agents—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 clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta), ticlopidine (Ticlid, generics), aspirin/dipyridamole ER (Aggrenox), dipyridamole (Persantine, generics), cilostazol (Pletal, generics) and pentoxifylline (Trental, generics) remain formulary on the UF. Although the cost-effectiveness review showed aspirin/dipyridamole ER was the least cost-effective drug for stroke, the P&T Committee recommended that it remain formulary on the UF due to the low new

user rate and the advanced age of the patient population. Ticagrelor was also recommended to remain formulary on the UF due its ICER, compared to clopidogrel.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

IV. UF CLASS REVIEWS—DIPEPTIDYL PEPTIDASE-4 (DPP-4) INHIBITORS

P&T Comments

A. DPP-4 Inhibitors

Relative Clinical Effectiveness: The P&T Committee evaluated the relative clinical effectiveness of the DPP-4 inhibitors, which include:

- sitagliptin (Januvia), sitagliptin/metformin (Janumet), sitagliptin/simvastatin (Juvisync);
- saxagliptin (Onglyza), saxagliptin/metformin ER (Kombiglyze XR);
- linagliptin (Tradjenta).

Two new products, sitagliptin/metformin ER (Janumet XR) and linagliptin/ metformin (Jentadueto) will be reviewed at an upcoming meeting. The DPP-4 inhibitors were previously reviewed in November 2010 as a subclass of the Non-insulin Diabetes Drug Class. Prior Authorization (PA) criteria and step therapy require a trial of metformin or sulfonylurea (SU) prior to using a DPP-4 inhibitor.

MHS expenditures exceed $119 million annually for DPP-4 inhibitors. In terms of overall utilization at all POS, sitagliptin and sitagliptin/metformin are the most utilized agents and are currently designated with BCF status on the UF.

Relative Clinical Effectiveness Conclusion—The P&T Committee recommended (18 for, 0 opposed, 0 abstained, 0 absent) the following clinical effectiveness conclusions for the DPP-4 inhibitors:

1. Clinical practice guidelines, including the DoD/Veterans Affairs guidelines for diabetes mellitus, do not currently recommend DPP-4 inhibitors for a specific place in therapy but list the class as alternative agents. Metformin remains the recommended first line agent for most patients who do not have a contraindication for metformin therapy.
2. There are no completed long-term studies assessing CV outcomes with sitagliptin, saxagliptin, and linagliptin, although three studies are under way, with results expected in 2014–2018.
3. One head-to-head trial did not show clinically relevant differences in efficacy or safety between sitagliptin and saxagliptin.
4. Sitagliptin, saxagliptin, and linagliptin show similar effects of lowering hemoglobin A1c when used as monotherapy, ranging from 0.4% to 0.9%. When a DPP-4 inhibitor is combined with metformin, the mean decrease in A1c from baseline ranges from 0.4% to 2.5%; when combined with a thiazolidinedione (TZD), the mean decrease in A1c ranges from 0.7% to 1.06%; and when combined with a SU, the mean decrease in A1c ranges from 0.5% to 0.6%.
5. DPP-4 inhibitors are weight neutral, lipid neutral, and have minimal impact on blood pressure.
6. Linagliptin has not been directly compared with saxagliption or sitagliptin in a clinical trial. A meta-analysis showed the A1c-lowering effect of linagliptin plus metformin was non-inferior to sitagliptin plus metformin. Linagliptin is the only DPP-4 inhibitor that does not require dose adjustments due to renal or hepatic impairment.
7. Juvisync is a fixed-dose combination product containing sitagliptin with the cholesterol-lowering drug simvastatin. There are no clinical trials evaluating Juvisync; it obtained FDA approval based on bioequivalence with the individual components. Juvisync may provide a dosing convenience in patients who require both sitagliptin and a statin.
8. In terms of commonly reported adverse events, there are no clinically relevant differences between sitagliptin, saxagliptin, and linagliptin. Drug interaction profiles are also similar between agents. Pancreatitis has been reported with both sitagliptin and saxagliptin. Acute renal failure has been reported with sitagliptin.
9. There is a high degree of therapeutic interchangeability between sitagliptin, saxagliptin, and linagliptin.
10. The PORT conducted an analysis of the changes in DPP-4 inhibitor utilization following the November 2010 P&T Committee Meeting. At that meeting, sitagliptin and sitagliptin/metformin were designated BCF and step therapy (automated PA) was implemented, requiring a trial of

metformin or a SU prior to use of a DPP-4 inhibitor. An increase in DPP-4 utilization has been noted at the MTF and Mail Order POS. Utilization increase at the Mail Order POS may also be due to the change in co-pay structure implemented in October 2011. There has also been a concurrent decline in TZD utilization, which is likely due to safety concerns.

11. The PORT also examined the effects of step therapy at the three POS.
    - **MTFs**—Out of 48,097 patients receiving their first DPP-4 prescription in the period from December 2010 to November 2011, 32% were new users of DPP-4 inhibitors; of these new users, 19%–21% had no evidence of prior use of metformin or SU.
    - **Retail and Mail Order**—In the 8-month evaluation period, 848 DPP-4 inhibitor prescriptions were rejected due to no evidence of prior metformin or SU use. However, 67% of these rejected prescriptions did show that a DPP-4 inhibitor prescription was received within 240 days of the reject, and 52% showed a later prescription for metformin of SU. There was no evidence of a prescription fill for any oral non-insulin diabetes drug in 12% of the rejected claims ("no fill" rate).

B. DPP-4 Inhibitors—Relative Cost-Effectiveness

CMAs and BIA were used to evaluate the relative cost-effectiveness of the DPP-4 inhibitors. Based on the results of the cost analyses and other clinical and cost considerations, the P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) the following:

- BIA was used to assess the potential impact of cost scenarios where selected DPP-4 inhibitors were designated with formulary, BCF, or NF status on the UF. The analysis included an evaluation of the potential impact of cost scenarios where DPP-4 inhibitors were designated with preferred product status (step therapy) on the UF; i.e., a trial of a preferred DPP-4 inhibitor would be required before using other DPP-4 inhibitors on the UF.
- BIA results showed the scenario where sitagliptin (Januvia), sitagliptin/ metformin (Janumet), and sitagliptin/simvastatin (Juvisync) are step-preferred on the UF, linagliptin (Tradjenta) is non-preferred on the UF, and saxagliptin (Onglyza) and saxagliptin/metformin (Kombiglyze XR) are non-preferred and NF was determined to be the most cost-effective.

C. DPP-4 Inhibitors—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, 1 opposed, 1 abstained, 0 absent):

- sitagliptin (Januvia), sitagliptin/metformin (Janumet), and sitagliptin/simvastatin (Juvisync) be designated step-preferred and formulary on the UF;
- linagliptin (Tradjenta) be designated non-preferred and formulary on the UF;
- saxagliptin (Onglyza) and saxagliptin/metformin ER (Kombiglyze XR) be designated non-preferred and NF.

This recommendation implements step therapy, which requires a trial of Januvia, Janumet, or Juvisync (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors would require a trial of metformin or SU for new patients.

D. DPP-4 Inhibitors—PA Criteria

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) the following PA criteria should apply to the DPP-4 inhibitors subclass. 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 metformin or SU at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

    b) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Onglyza, Kombiglyze XR, or Tradjenta) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria for Januvia, Janumet, Juvisync, Onglyza, Kombiglyze XR, or Tradjenta, if automated criteria are not met:

    a) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.

    b) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

    c) The patient has a contraindication to both metformin and a SU.

3. In addition to the above criteria regarding metformin and SU, the following PA criteria would apply specifically to saxagliptin (Onglyza), saxagliptin/ metformin ER (Kombiglyze XR), and linagliptin (Tradjenta):
    a) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with saxagliptin- or linagliptin-containing products.
    b) The patient has had an inadequate response to a sitagliptin-containing product.
    c) The patient has a contraindication to sitagliptin.

E. DPP-4 Inhibitors—UF and PA Implementation Plan

The P&T Committee recommended (17 for, 0 opposed, 1 abstained, 0 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS.

V. UF CLASS REVIEWS—DPP-4 INHIBITORS

BAP Comments

A. DPP-4 Inhibitors—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:

- sitagliptin (Januvia), sitagliptin/metformin (Janumet), and sitagliptin/simvastatin (Juvisync) be designated step-preferred and formulary on the UF;
- linagliptin (Tradjenta) be designated non-preferred and formulary on the UF;
- saxagliptin (Onglyza) and saxagliptin/metformin ER (Kombiglyze XR) be designated non-preferred and NF.

This recommendation implements step therapy, which requires a trial of Januvia, Janumet, or Juvisync (the preferred drugs) prior to using other DPP-4 inhibitors. Prior authorization for the DPP-4 inhibitors would require a trial of metformin or SU for new patients.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. DPP-4 Inhibitors—PA Criteria

The P&T Committee recommended the following PA criteria should apply to the DPP-4 inhibitors subclass. 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 metformin or SU at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

    b) The patient has received a prescription for a DPP-4 inhibitor (Januvia, Janumet, Juvisync, Onglyza, Kombiglyze XR, or Tradjenta) at any MHS pharmacy POS (MTFs, retail network pharmacies, or mail order) during the previous 180 days.

2. Manual PA criteria for Januvia, Janumet, Juvisync, Onglyza, Kombiglyze XR, or Tradjenta, if automated criteria are not met:

    a) The patient has experienced any of the following adverse events while receiving metformin: impaired renal function that precludes treatment with metformin or history of lactic acidosis.

    b) The patient has experienced the following adverse event while receiving a SU: hypoglycemia requiring medical treatment.

    c) The patient has a contraindication to both metformin and a SU.

3. In addition to the above criteria regarding metformin and SU, the following PA criteria would apply specifically to saxagliptin (Onglyza), saxagliptin/ metformin ER (Kombiglyze XR), and linagliptin (Tradjenta):

    a) The patient has experienced an adverse event with sitagliptin-containing products, which is not expected to occur with saxagliptin- or linagliptin-containing products.

    b) The patient has had an inadequate response to a sitagliptin-containing product.

    c) The patient has a contraindication to sitagliptin.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. DPP-4 Inhibitors—UF and PA Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday after a 60-day implementation period in all POS.

BAP Comment: □ Concur □ Non-concur Additional Comments and Dissentions:

VI. UF CLASS REVIEWS—ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)/WAKEFULNESS-PROMOTING AGENTS

P&T Comments

A. ADHD/Wakefulness-Promoting Agents

Relative Clinical Effectiveness—The P&T Committee evaluated the relative clinical effectiveness of the ADHD and Wakefulness-Promoting Agents Class, which was previously reviewed in November 2006. The drugs in this class are comprised of the following three subclasses: 1) ADHD stimulants, 2) ADHD non-stimulants, and 3) wakefulness-promoting agents.

The ADHD stimulants include lisdexamphetamine (Vyvanse), and long- and short-acting formulations of methylphenidate, amphetamine, and mixed amphetamine salt products. (Refer to the BAP Handout, Table 3 for the full list of the drugs in the subclass and the classification of long- and short-acting stimulants.) Since the November 2006 review, dexmethylphenidate immediate release (IR; Focalin), mixed amphetamine salts ER and IR (Adderall XR; Adderall), and methylphenidate long-acting (LA) (Ritalin LA) are now available in generic formulations. There is one authorized generic for methylphenidate osmotic-controlled release oral delivery system (OROS), which is produced by the manufacturer of Concerta.

The ADHD non-stimulants subclass is comprised of atomoxetine (Strattera), clonidine ER (Kapvay), and guanfacine ER (Intuniv). The wakefulness-promoting subclass includes modafinil (Provigil), armodafinil (Nuvigil), and sodium oxybate (Xyrem). Generic formulations of modafinil are expected in the 2nd quarter of 2012. Prior Authorization is currently required for modafinil and armodafinil.

The current BCF agents include mixed amphetamine salts ER (Adderall XR, generics), methylphenidate IR (Ritalin, generic), and methylphenidate OROS (Concerta). The current NF products include dexmethylphenidate ER (Focalin XR), dexmethylphenidate IR (Focalin), lisdexamfetamine (Vyvanse), and methylphenidate transdermal system (Daytrana).

Relative Clinical Effectiveness Conclusion

1. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) on the following conclusions regarding the ADHD stimulants and non-stimulants:

    a) Methylphenidate IR is more effective than placebo in improving ADHD symptoms in preschool-aged children (4–5 years of age) who do not respond to parental behavior training.

    b) Based on a DERP systematic review, the following conclusions apply in children and adolescents aged 6–17 years:

        - There are no clinically relevant differences between the IR stimulant formulations.
        - There are no clinically relevant differences between IR and sustained release (SR) stimulants (Ritalin SR, Metadate CD).
        - There is conflicting evidence when methylphenidate IR is compared with methylphenidate OROS (Concerta). Two double-blinded studies showed no difference in efficacy, while two open-label studies favored methylphenidate OROS.
        - There are no clinically relevant differences when SR stimulant formulations are compared to other SR formulations. Minor differences include that methylphenidate CD (Metadate CD) and dexmethylphenidate ER (Focalin XR) show greater response in the morning, while methylphenidate OROS (Concerta) shows greater response in the evening.
        - Lisdexamphetamine (Vyvanse) treatment resulted in similar scores on AHDH rating scales when compared to mixed amphetamine salts ER (Adderall XR).
        - Transdermal methylphenidate (Daytrana) produced similar scores on investigator, teacher, and parent rating scales when compared to methylphenidate OROS (Concerta) over a 7-week period.

c) In adults (18 years of age and older), there are no clinically relevant differences in efficacy when switching to methylphenidate OROS (Concerta) versus continuing with methylphenidate IR.

d) With regards to safety, package labeling for all stimulants contains a black box warning for potential abuse and dependency.

e) Use of mixed amphetamine salts (Adderall IR, generic) is associated with a higher incidence of weight loss and insomnia than methylphenidate IR.

f) One large randomized controlled trial, the Multimodal Therapy Study of ADHD, reported stimulants caused a decrease in growth velocity in children at 36 months.

g) Stimulants do not significantly increase the risk of serious cardiovascular events in children, adolescents, or adults (up to age 64), based on two large cohort studies.

h) The stimulants with the lowest potential for abuse/diversion are Vyvanse, Daytrana, and Concerta. In adolescents, American Academy of Pediatrics guidelines recommend prescribing non-stimulants or stimulants with the lowest potential for abuse/ diversion, compared to the other stimulant products.

i) For patients with swallowing difficulties, lisdexamfetamine (Vyvanse) is dissolvable in water. Ritalin LA, Metadate CD, Adderall XR, and Focalin XR are formulated in capsules that can be opened and sprinkled on food.

j) The PORT analyzed ADHD prescription use in the MHS for the first 4 months of the school year.

(1) Use of any ADHD medication is highest among 6–12 year olds (33%) and 13–17 year olds (20%), and declines with age. Use of a specific long-acting stimulants varies by age group, with Concerta predominating in patients younger than 18, and Adderall XR or its generic predominating in patients older than 18.

(2) Overall, 62% of usage is for a long-acting stimulant alone without another ADHD drug. About 14% of ADHD prescriptions were for a long-acting stimulant with a short-acting stimulant, which varied from 9% with Vyvanse, 11% with Concerta, and up to 27% with Ritalin LA.

2. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) on the following conclusions regarding the ADHD non-stimulants:

a) The DERP systematic review concluded atomoxetine (Strattera) is associated with efficacy outcomes similar to methylphenidate IR. Methylphenidate OROS (Concerta) and mixed amphetamine salts ER (Adderall XR, generic) are superior to atomoxetine in terms of response rates.

b) There are no head-to-head trials comparing clonidine ER (Kapvay) or guanfacine ER (Intuniv) with other ADHD drugs. Placebo-controlled studies with clonidine ER showed modest benefit when used as add-on or monotherapy. Placebo-controlled studies with guanfacine ER (Intuniv) showed modest benefit up to 8 hours after dosing.

c) With regards to safety, the package labeling for atomoxetine (Strattera) contains a black box warning for suicidal ideation. Atomoxetine has a higher incidence of vomiting, nausea, and somnolence compared to stimulants.

d) Clonidine ER (Kapvay) and guanfacine ER (Intuniv) are associated most commonly with somnolence and fatigue, although there are no comparative data with other ADHD drugs.

3. The P&T Committee agreed (17 for, 0 opposed, 0 abstained, 1 absent) on the following conclusions regarding the wakefulness-promoting drugs:

a) A large percentage (estimated 90%) of modafinil (Provigil) and armodafinil (Nuvigil) MHS prescriptions are for non-FDA approved indications.

b) There is one head-to-head trial comparing modafinil 200 mg with armodafinil 150 mg in patients with excessive sleepiness due to shift work sleep disorder. There was no significant difference between the two drugs in terms of percentage of responders at 12 weeks.

c) There are no head-to-head trials comparing modafinil with armodafinil in patients with narcolepsy or obstructive sleep apnea.

d) The manufacturer of armodafinil (Nuvigil) submitted data to the FDA requesting approval for patients with jet lag, but the application was denied.

e) The manufacturer of sodium oxybate (Xyrem) sought FDA approval for use in fibromyalgia, but was denied due to abuse potential and safety concerns.

f) With regards to safety and tolerability, there are no clinically relevant differences in the safety profiles between modafinil and armodafinil.

g) Sodium oxybate (Xyrem) has a black box warning for abuse/misuse/ diversion potential. A restricted distribution program limits dispensing to one centralized pharmacy.

h) The PORT analyzed usage of modafinil (Provigil) and armodafinil (Nuvigil) in the MHS. For the patients who received armodafinil, 32% were new users; of these new users, only 6% of patients had a previous prescription for modafinil in the previous 180 days, suggesting that the majority of new armodafinil users do not first receive a trial of modafinil.

B. ADHD/Wakefulness-Promoting Agents—Relative Cost-Effectiveness

The P&T Committee evaluated the relative cost-effectiveness of ADHD long-acting stimulants, short-acting stimulants, non-stimulants, and the wakefulness-promoting agents. CMAs were performed to compare the average daily cost of therapy for all branded and generic drugs within each of the respective subclasses. BIAs of varying formulary scenarios where various agents moved between BCF, UF, and NF status were performed for the long-acting stimulants, the non-stimulants, and the wakefulness-promoting drugs.

- *ADHD*—BIA was used to evaluate the long-acting stimulants, with corresponding sensitivity analyses. For relative comparison with the long-acting stimulants, a composite average daily cost for the short-acting stimulants was also calculated.

- *Wakefulness-promoting agents*—CMA and BIAs were used to evaluate the drugs in this subclass, with corresponding sensitivity analyses. BIAs also considered the potential impact of cost scenarios where current armodafinil (Nuvigil) users were grandfathered (and prior authorization would only apply to new users) versus a no-grandfathering scenario with prior authorization applicable to all users. Sodium oxybate (Xyrem) was not included in the CMA or BIAs due to restricted distribution from one pharmacy. Generic pricing estimates for modafinil (Provigil) were used in the cost analyses based on its anticipated generic availability.

Relative Cost-Effectiveness Conclusion—Based on the results of the economic analysis and other clinical and cost considerations, the P&T Committee concluded the following for the ADHD and wakefulness-promoting agents:

1. The P&T Committee agreed (17 for, 0 opposed, 1 abstained, 0 absent) on the following conclusions regarding the long-acting stimulants: CMA results showed the following ranking, from least costly to most costly: mixed amphetamine salts ER < Ritalin LA < Vyvanse < Focalin XR < Concerta < Daytrana. BIAs results showed that scenarios where the current

branded NF long-acting stimulants remained NF generated greatest cost avoidance.

2. The P&T Committee agreed (17 for, 0 opposed, 1 abstained, 0 absent) on the following conclusions regarding the short-acting stimulants: CMA results showed the following ranking, from least costly to most costly: methylphenidate IR (Ritalin generic) < dextroamphetamine tablets (Dexedrine generic) < mixed amphetamine salts (Adderall generic) < dexmethylphenidate (Focalin generic) < methylphenidate SR (Ritalin SR generic) < Metadate CD < Methylin chewable tablet < dextroamphetamine spansules (Dexedrine, generic) < Procentra liquid < Desoxyn. Composite costs results showed the short-acting stimulants were more cost-effective than the long-acting stimulants.
3. The P&T Committee agreed (18 for, 0 opposed, 0 abstained, 0 absent) on the following: for the non-stimulants, Strattera was most cost-effective, followed by Intuniv; Kapvay was least cost-effective. BIAs results showed minimal differences in cost-avoidance between branded NF and UF non-stimulants.
4. The P&T Committee agreed (18 for, 0 opposed, 0 abstained, 0 absent) on the following: for the wakefulness-promoting agents, CMA showed the estimated generic modafinil was most cost-effective, followed by Provigil; Nuvigil was least cost-effective. BIAs results showed that scenarios where Nuvigil changes to NF status and all current and new users of Nuvigil undergo the PA process (e.g., not grandfathered) generated greatest cost-avoidance; this scenario also included maintaining the existing PA for Provigil.

C. ADHD/Wakefulness-Promoting Agents—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:

For Stimulants: The Committee voted 15 for, 1 opposed, 1 abstain, 1absent that dextroamphetamine (Dexedrine, Dextrostat, Procentra solution, generics), methamphetamine HCl (Desoxyn, generic), methylphenidate CD (Metadate CD), methylphenidate IR (Ritalin, generic), methylphenidate LA (Ritalin LA, generic), methylphenidate ER (Metadate ER, Methylin ER, generics), methylphenidate chewable tablets, solution (Methylin, generic), methylphenidate OROS (Concerta), methylphenidate SR (Ritalin SR, generic), mixed amphetamine salts IR (Adderall, generic), mixed amphetamine salts ER (Adderall XR, generic), dexmethylphenidate IR (Focalin, generic) be designated with formulary status on UF and that desmethylphenidate ER (Focalin XR), lisdexamphetamine (Vyvanse), methylphenidate transdermal system (Daytrana) be designated with NF status on UF.

For Non-stimulants: The Committee voted 16 for, 0 opposed, 1 abstain, 1 absent that atomoxetine (Strattera), clonidine ER (Kapvay), guanfacine ER (Intuniv) be designated with formulary status on UF. Clonidine IR tablets and transdermal system (Catapress, Catapress patch, generic) and guanfacine IR (Tenex, generics) are designated UF in the Miscellaneous Anti-hypertensive Agents Drug Class.

For Wakefulness agents: The Committee voted 16 for, 0 opposed, 1 abstain, 1 absent modafinil (Provigil), sodium oxybate (Xyrem) be designated with formulary status on UF and that armodafinil (Nuvigil) designated with NF status on UF.

D. ADHD/Wakefulness-Promoting Agents—PA Criteria

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) PA criteria should apply to modafinil (Provigil), armodafinil (Nuvigil), and sodium oxybate (Xyrem). The current PA criteria for modafinil (Provigil) were recommended to be continued without modification. The P&T Committee recommended maintaining the current PA criteria for armodafinil, with one modification; jet lag would be added to the list of uses not provided. Additionally, the recommendation was that all current and new users of Nuvigil must undergo the PA process. The P&T Committee recommended PA criteria for sodium oxybate, which would be provided only for the current FDA-approved indications. Prior authorization is not intended to apply to modafinil or armodafinil use in active duty operational/readiness situations based on established protocols; MTFs should make necessary allowances for such use. (Refer to the Table 1 on page 29 for full PA criteria.)

E. ADHD/Wakefulness-Promoting Agents—UF and PA Implementation Plan

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) an effective date of the first Wednesday after a 60-day implementation period in all POS.

VII. UF CLASS REVIEWS—ADHD/WAKEFULNESS-PROMOTING AGENTS

BAP Comments

A. ADHD/Wakefulness-Promoting Agents—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:

For Stimulants: The Committee voted 15 for, 1 opposed, 1 abstain, 1absent that dextroamphetamine (Dexedrine, Dextrostat, Procentra solution, generics), methamphetamine HCl (Desoxyn, generic), methylphenidate CD (Metadate CD), methylphenidate IR (Ritalin, generic), methylphenidate LA (Ritalin LA, generic), methylphenidate ER (Metadate ER, Methylin ER, generics), methylphenidate chewable tablets, solution (Methylin, generic), methylphenidate OROS (Concerta), methylphenidate SR (Ritalin SR, generic), mixed amphetamine salts IR (Adderall, generic), mixed amphetamine salts ER (Adderall XR, generic), dexmethylphenidate IR (Focalin, generic) be designated with formulary status on UF and that desmethylphenidate ER (Focalin XR), lisdexamphetamine (Vyvanse), methylphenidate transdermal system (Daytrana) be designated with NF status on UF.

For Non-stimulants: The Committee voted 16 for, 0 opposed, 1 abstain, 1 absent that atomoxetine (Strattera), clonidine ER (Kapvay), guanfacine ER (Intuniv) be designated with formulary status on UF. Clonidine IR tablets and transdermal system (Catapress, Catapress patch, generic) and guanfacine IR (Tenex, generics) are designated UF in the Miscellaneous Anti-hypertensive Agents Drug Class.

For Wakefulness agents: The Committee voted 16 for, 0 opposed, 1 abstain, 1 absent modafinil (Provigil), sodium oxybate (Xyrem) be designated with formulary status on UF and that armodafinil (Nuvigil) designated with NF status on UF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

B. ADHD/Wakefulness-Promoting Agents—PA Criteria

The P&T Committee recommended PA criteria should apply to modafinil (Provigil), armodafinil (Nuvigil), and sodium oxybate (Xyrem). The current PA criteria for modafinil (Provigil) were recommended to be continued without modification. The P&T Committee recommended maintaining the current PA criteria for armodafinil, with one modification; jet lag would be added to the list of uses not provided. Additionally, the recommendation was that all current and new users of Nuvigil must undergo the PA process. The P&T Committee recommended PA criteria for sodium oxybate, which would be provided only for the current FDA-approved indications. Prior authorization is not intended to apply to modafinil or armodafinil use in active duty operational/readiness situations based on established protocols; MTFs should make necessary allowances for such use. (Refer to appendix 1 on page 28 for full PA criteria.)

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

C. ADHD/Wakefulness-Promoting Agents—UF and PA Implementation Plan

The P&T Committee recommended an effective date of the first Wednesday after a 60-day implementation period in all POS.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

VIII. RECENTLY APPROVED U.S. FDA AGENTS—OPHTHALMIC-1 CLASS

P&T Comments

A. Alcaftadine Ophthalmic Solution 0.25% (Lastacaft)

Alcaftadine (Lastacaft) is a dual action ophthalmic antihistamine/mast cell stabilizer. It is dosed once daily to prevent symptoms associated with allergic conjunctivitis (AC). The Ophthalmic-1 Class was evaluated for UF placement in February 2010. The current BCF product is olopatadine 0.1% (Patanol); there are no NF Ophthalmic-1 drugs.

There are no head-to-head trials with alcaftadine and the other dual action ophthalmic antihistamines. Alcaftadine was superior to placebo in preventing ocular itching associated with AC, but was not superior in relieving conjunctival redness. Alcaftadine's safety profile appears similar to the other ophthalmic antihistamines.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (16 for, 0 opposed, 0 abstained, 2 absent) there is no evidence to suggest alcaftadine ophthalmic solution has a compelling clinical advantage over the other dual action agents for AC on the UF.

B. Alcaftadine Ophthalmic Solution 0.25% (Lastacaft)—Relative Cost-Effectiveness and Relative Cost-Effectiveness Conclusion

CMA was performed. The weighted average cost per day at all three POS was evaluated for alcaftadine ophthalmic solution in relation to other currently available Ophthalmic-1 agents. 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) that alcaftadine ophthalmic solution was cost-effective when compared to other agents on the UF.

C. Alcaftadine Ophthalmic Solution 0.25% (Lastacaft)—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, 1abstained, 2 absent) alcaftadine ophthalmic 0.25% solution (Lastacaft) remain designated with formulary status on the UF.

IX. RECENTLY APPROVED U.S. FDA AGENTS—OPHTHALMIC-1 CLASS

BAP Comments

A. Alcaftadine Ophthalmic Solution 0.25% (Lastacaft)—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 alcaftadine ophthalmic 0.25% solution (Lastacaft) remain designated with formulary status on the UF.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

X. RECENTLY APPROVED U.S. FDA AGENTS—NARCOTIC ANALGESICS

P&T Comments

A. Tapentadol ER Tablets (Nucynta ER)

Tapentadol ER (Nucynta ER) is an opioid analgesic with dual modes of action; it is a mu receptor agonist with norepinephrine reuptake inhibition properties. Tapentadol ER is a Schedule II narcotic, and is classified as a high potency analgesic in the Narcotic Analgesics Drug Class. The class was last reviewed for UF placement in February 2007. Tapentadol IR (Nucynta) was reviewed in November 2009 and is currently NF. Tapentadol ER is indicated for moderate to severe pain when continuous, around-the-clock opioid analgesia is needed chronically. In two trials, tapentadol ER demonstrated greater reductions in pain scores compared to placebo, and produced similar reductions in pain scores as oxycodone ER (Oxycontin).

The safety profile of tapentadol ER is typical of the other high potency long-acting opioids. The adrenergic properties of the drug create additional safety concerns

with respect to serotonin syndrome and interactions with monoamine oxidase inhibitors. When indirectly compared to oxycodone ER in clinical trials, the frequency of gastrointestinal (GI) adverse events (constipation, nausea, and vomiting) was observed less frequently in the Nucynta ER treatment groups. However, there were more central nervous system (CNS) disorders seen in the Nucynta ER groups.

Relative Clinical Effectiveness Conclusion—The P&T Committee concluded (18 for, 0 opposed, 0 abstained, 0 absent) that tapentadol extended release (Nucynta ER) offers another long-acting, high-potency narcotic analgesic treatment option that may have less GI adverse events but more CNS adverse events than oxycodone ER. There is no evidence that pain control with tapentadol ER is superior to oxycodone ER.

B. Tapentadol ER Tablets (Nucynta ER)—Relative Cost-Effectiveness and Relative Cost-Effectiveness Conclusion

CMA was performed. 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) that tapentadol ER (Nucynta ER) was more costly on an average weighted cost per day of therapy basis than several other comparators in the high potency narcotic analgesics currently on the UF, including generic morphine sulfate IR and fentanyl patches. Tapentadol ER was less costly than morphine sulfate ER (Avinza and Kadian), oxymorphone ER (Opana ER), oxycodone ER (OxyContin), and hydromorphone ER (Exalgo).

C. Tapentadol ER Tablets (Nucynta ER)—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 (9 for, 8 opposed, 1abstained, 0 absent) tapentadol ER (Nucynta ER) remain formulary on the UF. UF status was designated due to the potential for decreased GI intolerance as compared to oxycodone ER, despite the concerns of potential undesirable drug interactions due to norepinephrine reuptake inhibition properties.

XI. RECENTLY APPROVED U.S. FDA AGENTS—NARCOTIC ANALGESICS

BAP Comments

A. Tapentadol ER Tablets (Nucynta ER)—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 tapentadol ER (Nucynta ER) remain formulary on the UF. UF status was designated due to the potential for decreased GI intolerance as compared to oxycodone ER, despite the concerns of potential undesirable drug interactions due to norepinephrine reuptake inhibition properties.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XII. UTILIZATION MANAGEMENT

P&T Comments

A. Crizotinib (Xalkori)—PA

Crizotinib (Xalkori) is an oral anaplastic lymphoma kinase (ALK) inhibitor indicated for the treatment of patients with ALK-positive non-small cell lung cancer (NSCLC) as detected by a FDA-approved diagnostic test. The FDA has approved a new molecular diagnostic test (Vysis ALK FISH Probe test) designed to identify ALK-positive NSCLC patients for treatment with Xalkori.

The P&T Committee recommended (16 for, 0 opposed, 1 abstained, 1 absent) the following PA criteria should apply to Xalkori capsules, consistent with the FDA-approved product labeling:

1. Coverage would be approved for the treatment of patients with documented diagnosis of ALK-positive NSCLC, detected by a FDA- approved test such as Vysis ALK FISH Probe test.

XIII. UTILIZATION MANAGEMENT

BAP Comments

A. Crizotinib (Xalkori)—PA

The P&T Committee recommended the PA criteria as noted above should apply to crizotinib (Xalkori), consistent with the FDA-approved product labeling. Coverage would be approved for the treatment of patients with documented diagnosis of ALK-

positive NSCLC, detected by a FDA- approved test such as Vysis ALK FISH Probe test.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XIV. UTILIZATION MANAGEMENT

P&T Comments

A. Vermurafenib (Zelboraf)—PA

Vermurafenib (Zelboraf) is an oral kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with $BRAF^{v600E}$ mutation. Zelboraf is not recommended for use in wild-type BRAF melanoma. The FDA also approved a new molecular diagnostic test (Cobas 4800) designed to detect the $BRAF^{v600E}$ mutation and identify patients likely to respond to Zelboraf therapy.

1. The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) the following PA criteria should apply to Zelboraf tablets, consistent with the FDA-approved product labeling.
    a) Coverage will be approved for the treatment of patients with documented diagnosis of unresectable or metastatic melanoma with $BRAF^{v600E}$ mutation, detected by a FDA-approved test such as Cobas 4800.
    b) Coverage will not be approved for patients with wild-type BRAF melanoma.

XV. UTILIZATION MANAGEMENT

BAP Comments

A. Vermurafenib (Zelboraf)—PA

The P&T Committee recommended the PA criteria as noted above should apply to vermurafenib (Zelboraf) tablets, consistent with the FDA-approved product labeling. Coverage will be approved for the treatment of patients with documented diagnosis of unresectable or metastatic melanoma with $BRAF^{v600E}$ mutation, detected by a FDA-approved test such as Cobas 4800. Coverage will not be approved for patients with wild-type BRAF melanoma.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

XVI. UTILIZATION MANAGEMENT

P&T Comments

A. Ivacaftor (Kalydeco)—PA

Ivacaftor (Kalydeco) is a new oral agent that targets a specific subgroup of patients with Cystic Fibrosis (CF). It is a potentiator of the cystic fibrosis transmembrane conductance regulator (CFTR). Kalydeco is indicated for the treatment of CF in patients aged 6 years of age and older who have a G551D mutation in the CFTR gene. This rare mutation occurs in about 4% of CF patients. In patients for whom the genotype is unknown, a FDA-approved test should be used to detect the presence of the G551D mutation. Kalydeco is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene, which occurs in about 90% of CF patients. There are several FDA-approved in-vitro molecular diagnostic tests designed to simultaneously detect and identify mutations in the CFTR gene.

1. The P&T Committee recommended (16 for, 0 opposed, 1 abstain, 1 absent) the following PA criteria should apply to Kalydeco tablets, consistent with the FDA-approved product labeling:
    a) Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D mutation in the CFTR gene, detected by a FDA-approved test.
    b) Coverage will not be approved for patients who are homozygous for the F508del mutation in the CFTR gene.

XVII. UTILIZATION MANAGEMENT

BAP Comments

A. Ivacaftor (Kalydeco)—PA

The P&T Committee recommended the PA criteria as noted above should apply to Kalydeco tablets, consistent with the FDA-approved product labeling. Coverage will be approved for the treatment of CF patients aged 6 years and older who have a G551D mutation in the CFTR gene, detected by a FDA-approved test. Coverage will not be approved for patients who are homozygous for the F508del mutation in the CFTR gene.

BAP Comment: □ Concur □ Non-concur

Additional Comments and Dissentions:

Appendix 1: Wakefulness-Promoting Drugs – Prior Authorization Criteria

Prior Authorization for Modafinil (Provigil)

Coverage provided for the treatment of:

- Excessive daytime sleepiness associated with narcolepsy, as diagnosed by polysomnogram or MSLT objective testing
- Excessive daytime sleepiness associated with OSAHS, only after adequate titration of CPAP treatment
- Excessive sleepiness associated with SWSD, only in patients who work night shifts
- Excessive fatigue associated with multiple sclerosis, only after secondary causes of fatigue have been addressed
- Excessive fatigue associated with myotonic dystrophy
- Depression, only after primary therapy has failed and if the use of other stimulant augmentation is contraindicated
- Idiopathic hypersomnia diagnosed by a sleep specialist
- Fatigue associated with traumatic brain injury

Coverage NOT provided for the treatment of other conditions not listed above, including the following:

- Chronic fatigue syndrome
- Stroke rehabilitation
- Appetite suppression
- Parkinson's disease

Prior Authorization for Armodafinil (Nuvigil)

Coverage provided for the treatment of:

- Excessive daytime sleepiness associated with narcolepsy, as diagnosed by polysomnogram or MSLT objective testing
- Excessive daytime sleepiness associated with OSAHS, only after adequate titration of CPAP treatment
- Excessive sleepiness associated with SWSD, only in patients who work night shifts

Coverage NOT provided for the treatment of other conditions not listed above, including the following:

- Jet lag
- Excessive fatigue associated with multiple sclerosis
- Excessive fatigue associated with myotonic dystrophy
- Depression
- Idiopathic hypersomnia
- Fatigue associated with traumatic brain injury
- Chronic fatigue syndrome
- Stroke rehabilitation
- Appetite suppression
- Parkinson's disease

Prior Authorization for Sodium Oxybate

- Treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy, diagnosed by polysomnogram and MSLT
- Excessive sleepiness associated with narcolepsy without cataplexy, if the patient has previously tried modafinil (Provigil)

Coverage NOT provided for the treatment of other conditions not listed above or any non-FDA approved use, including the following:

- Fibromyalgia
- Insomnia
- Excessive sleepiness not associated with narcolepsy