

Reimbursement Cut for Fast In-Office HbA_{1c} Test

BY JANE ANDERSON
Contributing Writer

The Centers for Medicare and Medicaid Services will cut reimbursement for physicians who provide their diabetic patients with point-of-care hemoglobin A_{1c} testing using a “glycosylated Hb home device” from about \$21 a test to about \$13.50 a test on April 1, a coding expert from the American Academy of Family Physicians said.

The reimbursement cut was mandated by a provision in the Medicare, Medicaid, and SCHIP Extension Act of 2007, enacted at the end of last year. That provision reverses a decision by CMS in late 2006 to increase reimbursement for the HbA_{1c} test, said AAFP coding specialist Cynthia Hughes, who noted that AAFP had lobbied hard for several years for the increase in reimbursement. “It was slipped into SCHIP,” Ms. Hughes said. “It would take another act of Congress to reverse it.”

The language added to the SCHIP legislation states that point-of-care HbA_{1c} testing using the kit and billed under CPT code 83037 should be paid at the same rate as HbA_{1c} testing done with an in-office analyzer in a physician’s office or laboratory setting and billed with CPT code 83036.

Ms. Hughes said that the average cost to physicians’ offices for each test kit is about \$13, but that costs also include shipping and handling of the kits themselves, staff time to administer the test, supplies, and

additional overhead expenses. AAFP has suggested to CMS that an appropriate payment—one that takes into account all the costs of purchasing and administering the test—would be more than \$34.

Providing the test at the point of care is more convenient for the patient and augments care because the test results are available in just a few minutes, in time for the physician to counsel the patient about those results, Ms. Hughes said.

The decreased reimbursement for the test kits could lead to fewer patients receiving the HbA_{1c} test at the point of care, Ms. Hughes said.

PROVIGIL® (modafinil) TABLETS [C-IV]

BRIEF SUMMARY: Consult Package Insert for Complete Prescribing Information
INDICATIONS AND USAGE: PROVIGIL is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder. In OSAS, PROVIGIL is indicated as an adjunct to standard treatment(s) for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating PROVIGIL. If PROVIGIL is used adjunctively with CPAP, the encouragement of and periodic assessment of CPAP compliance is necessary. In all cases, careful attention to the diagnosis and treatment of the underlying sleep disorder(s) is of utmost importance. Prescribers should be aware that some patients may have more than one sleep disorder contributing to their excessive sleepiness.

CONTRAINDICATIONS: Known hypersensitivity to modafinil, amodafinil (the R-enantiomer of PROVIGIL) or its inactive ingredients.
WARNINGS: Serious Rash, including Stevens-Johnson Syndrome

Serious rash requiring hospitalization and discontinuation of treatment has been reported in adults and children in association with the use of PROVIGIL. PROVIGIL is not approved for use in pediatric patients for any indication. In clinical trials of PROVIGIL, the incidence of rash resulting in discontinuation was approximately 0.8% (13 per 1,585) in pediatric patients (age <17 years); these rashes included 1 case of possible Stevens-Johnson Syndrome (SJS) and 1 case of apparent multi-organ hypersensitivity reaction. Several of the cases were associated with fever and other abnormalities (e.g., vomiting, leukopenia). The median time to rash that resulted in discontinuation was 13 days. No serious skin rashes were observed among 380 pediatric patients who received placebo. No serious skin rashes have been reported in adult clinical trials (0 per 4,254) of PROVIGIL. Rare cases of serious or life-threatening rash, including SJS, Toxic Epidermal Necrolysis (TEN), and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) have been reported in adults and children in worldwide post-marketing experience. The reporting rate of TEN and SJS associated with PROVIGIL use, which is generally accepted to be an underestimate due to underreporting, exceeds the background incidence. Estimates of the background incidence rate for these serious skin reactions in the general population range between 1 to 2 cases per million-person-years. There are no factors that are known to predict the risk of occurrence or the severity of rash associated with PROVIGIL. Nearly all cases of serious rash associated with PROVIGIL occurred within 1 to 5 weeks after treatment initiation. However, isolated cases have been reported after prolonged treatment (e.g., 3 months). Accordingly, duration of therapy cannot be relied upon as a means to predict the potential risk heralded by the first appearance of a rash. Although benign rashes also occur with PROVIGIL, it is not possible to reliably predict which rashes will prove to be serious. Accordingly, PROVIGIL should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug-related. Discontinuation of treatment may not prevent a rash from becoming life-threatening or permanently disabling or disfiguring.

Angioedema and Anaphylactoid Reactions: One serious case of angioedema and one case of hypersensitivity (with rash, dysphagia, and bronchospasm), were observed among 1,595 patients treated with amodafinil. No such cases were observed in PROVIGIL clinical trials. Angioedema has been reported in postmarketing experience with PROVIGIL. Patients should be advised to discontinue therapy and immediately report to their physician any signs or symptoms suggesting angioedema or anaphylaxis (e.g., swelling of face, eyes, lips, tongue or larynx; difficulty in swallowing or breathing; hoarseness).
Multi-organ Hypersensitivity Reactions: Multi-organ hypersensitivity reactions, including at least one fatality in postmarketing experience, have occurred in close temporal association (median time to detection 13 days; range 4-33) to the initiation of PROVIGIL. Although there have been a limited number of reports, multi-organ hypersensitivity reactions may result in hospitalization or be life-threatening. There are no factors that are known to predict the risk of occurrence or the severity of multi-organ hypersensitivity reactions associated with PROVIGIL. Signs and symptoms of this disorder were diverse; however, patients typically, although not exclusively, presented with fever and rash associated with other organ system involvement. Other associated manifestations included myocarditis, hepatitis, liver function test abnormalities, hematological abnormalities (e.g., eosinophilia, leukopenia, thrombocytopenia), pruritus, and asthenia. Because multi-organ hypersensitivity is variable in its expression, other organ system symptoms and signs, not noted here, may occur. If a multi-organ hypersensitivity reaction is suspected, PROVIGIL should be discontinued. Although there are no case reports to indicate cross-sensitivity with other drugs that produce this syndrome, the experience with drugs associated with multi-organ hypersensitivity would indicate this to be a possibility.

Persistent Sleepiness: Patients with abnormal levels of sleepiness who take PROVIGIL should be advised that their level of wakefulness may not return to normal. Patients should be frequently reassessed for their degree of sleepiness and, if appropriate, advised to avoid driving or any other potentially dangerous activity.
Psychiatric Symptoms: Psychiatric adverse experiences have been reported in patients treated with PROVIGIL. Postmarketing adverse events associated with the use of PROVIGIL have included mania, delusions, hallucinations, and suicidal ideation, some resulting in hospitalization. Many, but not all, patients had a prior psychiatric history. In the adult PROVIGIL controlled trial database, psychiatric symptoms resulting in treatment discontinuation (at a frequency ≥0.3%) and reported more often in patients treated with PROVIGIL compared to those treated with placebo were anxiety (1%), nervousness (1%), insomnia (<1%), confusion (<1%), agitation (<1%), and depression (<1%). Caution should be exercised when PROVIGIL is given to patients with a history of psychosis, depression, or mania. Consideration should be given to the possible emergence or exacerbation of psychiatric symptoms in patients treated with PROVIGIL. If psychiatric symptoms develop in association with PROVIGIL administration, consider discontinuing PROVIGIL.

PRECAUTIONS: Diagnosis of Sleep Disorders: PROVIGIL should be used only in patients who have had a complete evaluation of their excessive sleepiness, and in whom a diagnosis of narcolepsy, OSAS, and/or SWSD has been made in accordance with ICSD or DSM diagnostic criteria. **General:** Although PROVIGIL has not been shown to produce functional impairment, a drug affecting the CNS may alter judgment, thinking or motor skills. Patients should be cautioned about operating an automobile or other hazardous machinery until they are reasonably certain that PROVIGIL therapy will not adversely affect their ability to engage in such activities. **CPAP Use in Patients with OSAS:** If PROVIGIL is used adjunctively with CPAP, the encouragement of and periodic assessment of CPAP compliance is necessary. **Cardiovascular System:** PROVIGIL has not been evaluated in patients with a recent history of myocardial infarction or unstable angina, and such patients should be treated with caution. It is recommended that PROVIGIL tablets not be used in patients with a history of left ventricular hypertrophy or in patients with mitral valve prolapse who have experienced the mitral valve prolapse syndrome when previously receiving CNS stimulants. Such signs may include but are not limited to ischemic ECG changes, chest pain, or arrhythmia. If new onset of any of these symptoms occurs, consider cardiac evaluation. Increased monitoring of blood pressure may be appropriate in patients on PROVIGIL. **Patients Using Steroidal Contraceptives:** The effectiveness of steroidal contraceptives may be reduced when used with PROVIGIL tablets and for one month after discontinuation of therapy (See **PRECAUTIONS, Drug Interactions**). Alternative or concomitant methods of contraception are recommended for patients treated with PROVIGIL tablets, and for one month after discontinuation of PROVIGIL. **Patients Using Cyclosporine:** The blood levels of cyclosporine may be reduced when

used with PROVIGIL (See **PRECAUTIONS, Drug Interactions**). Monitoring of circulating cyclosporine concentrations and appropriate dosage adjustment for cyclosporine should be considered when these drugs are used concomitantly. **Patients with Severe Hepatic Impairment:** In patients with severe hepatic impairment, with or without cirrhosis, PROVIGIL should be administered at a reduced dose. **Patients with Severe Renal Impairment:** There is inadequate information to determine safety and efficacy of dosing in patients with severe renal impairment. **Elderly Patients:** In elderly patients, elimination of PROVIGIL and its metabolites may be reduced as a consequence of aging. Therefore, consideration should be given to the use of lower doses in this population. **Information for Patients:** Physicians are advised to discuss the following with patients for whom they prescribe PROVIGIL. PROVIGIL is indicated for patients who have abnormal levels of sleepiness. PROVIGIL has been shown to improve, but not eliminate this abnormal tendency to fall asleep. Therefore, patients should not alter their previous behavior with regard to potentially dangerous activities (e.g., driving, operating machinery) or other activities requiring appropriate levels of wakefulness, until and unless treatment with PROVIGIL has been shown to produce levels of wakefulness that permit such activities. Patients should be advised that PROVIGIL is not a replacement for sleep. Patients should be informed that it may be critical that they continue to take their previously prescribed treatments. Patients should be informed of the availability of a patient information leaflet, and they should be instructed to read the leaflet prior to taking PROVIGIL. Patients should be advised to contact their physician if they experience chest pain, rash, depression, anxiety, or signs of psychosis or mania. **Pregnancy:** Patients should notify their physician if they become pregnant or intend to become pregnant during therapy. **Nursing:** Patients should notify their physician if they are breastfeeding. **Concomitant Medication:** Patients should be advised to inform their physician if they are taking or plan to take any prescription or over-the-counter drugs, because of the potential for drug interactions.

Alcohol: Patients should be advised that it is prudent to avoid alcohol while taking PROVIGIL. **Allergic Reactions:** Patients should be advised to stop taking PROVIGIL and notify their physician if they develop a rash, hives, mouth sores, blisters, peeling skin, trouble swallowing or breathing or a related allergic phenomenon. **Drug Interactions:** **CNS Active Drugs:** Concomitant administration of PROVIGIL with methyphenidate or dextroamphetamine produced no significant alterations on the pharmacokinetic profile of PROVIGIL or either stimulant, even though the absorption of PROVIGIL was delayed by approximately one hour. The coadministration of a single dose of clomipramine (50 mg) on the first three days of treatment with PROVIGIL (200 mg/day) in healthy volunteers did not show an effect on the pharmacokinetics of either drug. However, one incident of increased levels of clomipramine and its active metabolite desmethylclomipramine has been reported in a patient with narcolepsy during treatment with PROVIGIL. In the drug interaction study between PROVIGIL and ethinyl estradiol (EE), on the same days as those for the plasma sampling for EE, pharmacokinetics, a single dose of triazolam (0.125 mg) was also administered. Mean C_{max} and AUC_{0-∞} of triazolam were decreased by 42% and 59%, respectively, and its elimination half-life was decreased by approximately 1 hour after the PROVIGIL treatment. Interaction studies with monoamine oxidase (MAO) inhibitors have not been performed. Therefore, caution should be used when concomitantly administering MAO inhibitors and PROVIGIL. **Other Drugs:** More frequent monitoring of prothrombin times/INR is advised when PROVIGIL is coadministered with warfarin. Administration of PROVIGIL to female volunteers once daily at 200 mg/day for 7 days followed by 400 mg/day for 21 days resulted in a mean 11% decrease in C_{max} and 18% decrease in AUC_{0-∞} of ethinyl estradiol. One case of an interaction between PROVIGIL and cyclosporine, a substrate of CYP3A4, has been reported in a 41 year old woman who had undergone an organ transplant. After one month of PROVIGIL 200 mg/day, cyclosporine blood levels were decreased by 50%. Dosage adjustment for cyclosporine may be needed.

Potential Interactions with Drugs That Inhibit, Induce, or are Metabolized by Cytochrome P-450 Isoenzymes and Other Hepatic Enzymes: In vitro studies using primary human hepatocyte cultures, PROVIGIL was shown to slightly induce CYP1A2, CYP2B6 and CYP3A4 in a concentration-dependent manner. Caution needs to be exercised when PROVIGIL is coadministered with drugs that depend on these three enzymes for their clearance, since lower blood levels of such drugs could result (See **Other Drugs** above). The exposure of human hepatocytes to PROVIGIL in vitro produced an apparent concentration-related suppression of expression of CYP2C9 activity (also via CYP2C9) or S-mephenytoin may have prolonged elimination upon coadministration with PROVIGIL and may require dosage reduction and monitoring for toxicity. CYP2C19 also provides an ancillary pathway for the metabolism of certain tricyclic antidepressants (e.g., clomipramine and desipramine) that are primarily metabolized by CYP2D6. In tricyclic-treated patients deficient in CYP2D6, the amount of metabolism by CYP2C19 may be substantially increased. PROVIGIL may cause elevation of the levels of the tricyclics in this subset of patients. Physicians should be aware that a reduction in the dose of tricyclic agents might be needed in these patients. In addition, due to the partial involvement of CYP3A4 in the metabolic elimination of PROVIGIL, coadministration of potent inducers of CYP3A4 (e.g., carbamazepine, phenobarbital, rifampin) or inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole) could alter the plasma levels of PROVIGIL.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis: Carcinogenicity studies were conducted in which PROVIGIL was administered in the diet to mice for 78 weeks and to rats for 104 weeks. The highest dose studied is 1.5 (mouse) or 3 (rat) times greater than the recommended adult human daily dose of PROVIGIL (200 mg) on a mg/m² basis. There was no evidence of tumorigenesis associated with PROVIGIL administration in these studies. However, since the mouse study used an inadequate high dose that was not representative of a maximum tolerated dose, a subsequent carcinogenicity study was conducted in the TgAC transgenic mouse. Doses evaluated in the TgAC assay were 125, 250, and 500 mg/kg/day, administered orally. There was no evidence of tumorigenicity associated with PROVIGIL administration; however, this dermal model may not adequately assess the carcinogenic potential of an orally administered drug. **Mutagenesis:** PROVIGIL demonstrated no evidence of mutagenic or clastogenic potential in a series of in vitro assays in the absence or presence of metabolic activation, or in vivo assays. PROVIGIL was also negative in the unscheduled DNA synthesis assay in rat hepatocytes. **Impairment of Fertility:** Oral administration of PROVIGIL (doses of up to 480 mg/kg/day) to male and female rats prior to and throughout mating, and continuing in females through day 7 of gestation produced an increase in the time to mate at the highest dose; no effects were observed on other fertility or reproductive parameters. The no-effect dose of 240 mg/kg/day was associated with a plasma modafinil exposure (AUC) approximately equal to that in humans at the recommended dose of 200 mg. **Pregnancy: Pregnancy Category C:** In studies conducted in rats and rabbits, developmental toxicity was observed at clinically relevant exposures. There are no adequate and well-controlled studies in pregnant women. Two cases of intrauterine growth retardation and one case of spontaneous abortion were reported in association with amodafinil and modafinil. Whether the cases reported are drug-related is unknown. PROVIGIL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Labor and Delivery:** The effect of PROVIGIL on labor and delivery in humans has not been systematically investigated. **Nursing Mothers:** It is not known whether PROVIGIL or its metabolites are excreted in human milk. Caution should be exercised

when PROVIGIL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients, below age 16, have not been established. Serious skin rashes, including erythema multiforme major (EMM) and Stevens-Johnson Syndrome (SJS) have been associated with PROVIGIL use in pediatric patients (See **WARNINGS, Serious Rash, including Stevens-Johnson Syndrome**). In the controlled and open-label clinical studies, treatment emergent adverse events of the psychiatric and nervous system included Tourette’s syndrome, insomnia, hostility, increased cataplexy, increased hypnagogic hallucinations and suicidal ideation. Transient leukopenia, which resolved without medical intervention, was also observed. In the controlled clinical study, 3 of 38 girls, ages 12 or older, treated with PROVIGIL experienced dysmenorrhea compared to 0 of 10 girls who received placebo.

Geriatric Use: Safety and effectiveness in individuals above 65 years of age have not been established. Experience in a limited number of patients who were greater than 65 years of age in clinical trials showed an incidence of adverse experiences similar to other age groups.

ADVERSE REACTIONS: PROVIGIL has been evaluated for safety in over 3500 patients, of whom more than 2000 patients with excessive sleepiness associated with primary disorders of sleep and wakefulness were given at least one dose of PROVIGIL. In clinical trials, PROVIGIL has been found to be generally well tolerated and most adverse experiences were mild to moderate. The most commonly observed adverse events (≥5%) associated with the use of PROVIGIL more frequently than placebo-treated patients in the placebo-controlled clinical studies in primary disorders of sleep and wakefulness were headache, nausea, nervousness, rhinitis, diarrhea, back pain, anxiety, insomnia, dizziness, and dyspepsia. In the placebo-controlled clinical trials, 8% of the 934 patients who received PROVIGIL discontinued due to an adverse experience. The most frequent reasons for discontinuation that occurred at an adverse rate for PROVIGIL than placebo patients were headache (2%), nausea, anxiety, dizziness, insomnia, chest pain, and nervousness (each <1%). **Incidence in Controlled Trials:** The incidence of adverse experiences that occurred at a rate of ≥1% and were more frequent in adult patients treated with PROVIGIL than in placebo-treated patients in the principal trials are listed below. Consult full prescribing information on adverse events. **Body as a Whole:** Headache, back pain, flu syndrome, chest pain, chills, neck rigidity **Cardiovascular:** Hypertension, tachycardia, palpitation, vasodilatation **Digestive:** Nausea, diarrhea, dyspepsia, dry mouth, anorexia, constipation, abnormal liver function, flatulence, mouth ulceration, throat **Hemic/Lymphatic/Immune:** Eosinophilia **Metabolic/Nutritional:** Edema **Nervous:** Nervousness, insomnia, anxiety, dizziness, depression, paresthesia, somnolence, hyperkinesia, dyskinesia, hyperkinesia, agitation, confusion, tremor, emotional lability, vertigo **Respiratory:** Rhinitis, pharyngitis, lung disorder, epistaxis, asthma **Skin/Appendages:** Sweating, herpes simplex **Special Senses:** Amblyopia, abnormal vision, taste perversion, eye pain **Urogenital:** Urine abnormality, hematuria, pyuria **Dose Dependency of Adverse Events:** In the adult placebo-controlled clinical trials which compared doses of 200, 300, and 400 mg/day of PROVIGIL and placebo, the only adverse events that were clearly dose related were headache and anxiety. **Vital Sign Changes:** The requirement for antihypertensive medication was slightly greater in patients on PROVIGIL compared to placebo. **Weight Changes:** There were no clinically significant differences in body weight change in patients treated with PROVIGIL compared to placebo-treated patients. **Laboratory Changes:** Clinical chemistry, hematology, and urinalysis parameters were monitored in Phase 1, 2, and 3 studies. In these studies, mean plasma levels of gamma glutamyltransferase (GGT) and alkaline phosphatase (AP) were found to be higher following administration of PROVIGIL, but not placebo. Few subjects, however, had GGT or AP elevations outside of the normal range. Shifts to higher, but not clinically significantly abnormal, GGT and AP values appeared to increase with time on PROVIGIL. No differences were apparent in alanine aminotransferase, aspartate aminotransferase, total protein, albumin, or total bilirubin. **ECG Changes:** No treatment-emergent pattern of ECG abnormalities was found in placebo-controlled clinical trials which compared doses of 200, 300, and 400 mg/day of PROVIGIL and placebo, the only adverse events that were clearly dose related were headache and anxiety. **Vital Sign Changes:** The requirement for antihypertensive medication was slightly greater in patients on PROVIGIL compared to placebo. **Weight Changes:** There were no clinically significant differences in body weight change in patients treated with PROVIGIL compared to placebo-treated patients. **Laboratory Changes:** Clinical chemistry, hematology, and urinalysis parameters were monitored in Phase 1, 2, and 3 studies. 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