

**Regence BlueCross BlueShield of Oregon • Regence BlueShield  
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**Medication Policy Manual**

**Policy No:** dru058

**Topic:** Provigil<sup>®</sup>, modafinil

**Date of Origin:** April 22, 2002

**Revised/Effective Date:** July 17, 2009

**Next Review Date:** July 2010

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Modafinil (Provigil<sup>®</sup>) is a medication used to treat excessive sleepiness. Modafinil has wake promoting actions like amphetamines and caffeine, although the exact way armodafinil works in the body is unknown.

## **Policy/Criteria**

**I.** Most contracts require prior authorization approval of modafinil prior to coverage. Modafinil may be considered medically necessary in patients when criteria A, B, or C below are met.

**A.** Excessive sleepiness associated with narcolepsy (diagnosed by the criteria of DSM-IV-TR, Appendix 1) when at least one formulary/preferred treatment, such as methylphenidate or dextroamphetamine, has been ineffective or not tolerated.

**OR**

**B.** Excessive daytime sleepiness associated with obstructive sleep apnea/hypopnea syndrome when both criteria 1 and 2 below are met:

**1.** There is documentation of residual excessive daytime sleepiness associated with obstructive sleep apnea/hypopnea syndrome.

**AND**

**2.** There is documentation that the patient has been compliant with CPAP or BiPAP for at least 2 months.

**OR**

**C.** Excessive sleepiness associated with shift-work sleep disorder (circadian rhythm sleep disorder) when all criteria 1 through 4 below are met.

**1.** Diagnosis is made using the criteria from International Classification of Sleep Disorders (ICSD; Appendix 2).

**AND**

**2.** Sleep disturbance causes specific measurable functional impairment in social, occupational, or other important areas of functioning that has persisted at least 3 months.

**AND**

**3.** Sleep disturbance is not due to otherwise reversible conditions. Other reversible conditions may include, but are not limited to, another sleep disorder, mental disorder, or physiological effects of another substance.

## AND

4. Non-pharmacologic therapies have been inadequate in improving functional impairments. Examples of non-pharmacologic therapies include, but are not limited to, planned sleep schedules and timed light exposure.

## II. Administration, Quantity Limitations, and Authorization Period

A. Regence considers modafinil to be a self-administered medication.

### B. Quantity Limitations

#### 1. Narcolepsy and obstructive sleep apnea/hypopnea syndrome:

- a. When prior authorization is approved, modafinil may be authorized in quantities of 200 mg per day.
- b. Doses up to 400 mg per day may be considered medically necessary when there is documentation showing that 200mg daily does not provide adequate response.

2. Shift-work sleep disorder: When prior authorization is approved, modafinil may be authorized in quantities of 200 mg per day.

C. Authorization shall be reviewed in the timeframes defined below to confirm that current medical necessity criteria are met and that the medication is effective.

1. **Narcolepsy:** Authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

#### 2. **Obstructive Sleep Apnea/Hypopnea:**

- a. **Initial authorization:** Authorization shall be reviewed at 6 months to confirm that the patient continues to be adherent on CPAP while on modafinil.

**b. Continued authorization:** After initial approval, authorization shall be reviewed at least annually to confirm that the patient continues to be adherent on CPAP while on modafinil.

**3. Shift-work Sleep Disorder:** Authorization shall be renewed at least annually confirm that current medical necessity criteria are met and that the medication is effective.

**III.** Modafinil is considered not medically necessary when used for treatment of attention deficit/hyperactivity disorder (ADHD) (pediatric or adult).

**IV.** Modafinil is considered investigational when used for all other conditions, including, but not limited to, the following:

- A.** Fatigue, including fatigue associated with any other condition (other than above) or medication adverse event.
- B.** Idiopathic hypersomnia.
- C.** Augmentation in patients with major depressive disorder.

## **Position Statement**

### *Summary*

- Modafinil and armodafinil are both used to improve alertness, reduce tiredness, and improve memory in patients with narcolepsy, obstructive sleep apnea treated with continuous positive airway pressure (CPAP) therapy, and for patients who work nights and are tired during waking hours despite adequate sleep (shift-work sleep disorder).<sup>[40,53]</sup>

The studies for both medications have flaws that result in uncertainty about their conclusions.

The quality of the evidence for modafinil and armodafinil is comparable to other treatments, such as amphetamine and methylphenidate.

- Modafinil (Provigil) and armodafinil (Nuvigil) contain the same active ingredient, but in different amounts. A 300 mg tablet of Provigil delivers the same amount of armodafinil as 150 mg of Nuvigil.<sup>[40,53]</sup>

- Neither modafinil nor armodafinil correct the underlying reason for the patient's lack of restorative sleep. Rather, both medications help treat the symptoms of tiredness and fatigue. When possible, correcting the source of the sleep problems is the preferred approach, though for some diseases (e.g. narcolepsy), this may not be possible. <sup>[40,53]</sup>

### *Clinical Efficacy*

#### NARCOLEPSY/SLEEP APNEA/HYPOPNEA

- Modafinil improves daytime wakefulness in patients with narcolepsy and obstructive sleep apnea/hypopnea. <sup>[1, 21-24]</sup>
- There is no evidence that modafinil has superior clinical benefit over other treatment alternatives, such as methylphenidate or dextroamphetamine in narcolepsy.
- There is not conclusive evidence of additional benefit with 400 mg modafinil daily compared to 200 mg daily in patients with narcolepsy or sleep/apnea hypopnea. <sup>[1, 21-24]</sup>

In the management of obstructive sleep apnea/hypopnea, modafinil and armodafinil should be used in ADDITION to standard treatment(s) for the underlying obstruction. If the appropriate treatment is continuous positive airway pressure (CPAP), then treatment with CPAP should be optimized before initiating either medication.

- There are no well-designed trials of adequate power to support additional clinical benefits of doses above 400 mg per day for the treatment of narcolepsy or sleep apnea/hypopnea.
  - \* A split-dosing modafinil regimen (400 mg in the morning; 200 mg at midday) has been evaluated in a small study (n=24) of limited duration. <sup>[18]</sup>
  - \* Another trial evaluated 4 regimens including 400 mg (200 mg am, 200 mg noon) and 600 mg (400 mg am, 200 mg noon) split dose regimens. <sup>[31]</sup> Both the 400 mg and 600 mg regimens were more effective than 200 mg once daily (p<0.01), but were not significantly different from each other. <sup>[31]</sup>

#### SHIFT-WORK SLEEP DISORDER

- Planned sleep schedules and timed-light exposure are non-drug therapies deemed as indicated for the treatment of shift-work sleep disorder by the American Academy of Sleep Medicine. <sup>[46]</sup>

- Modafinil modestly improves sleep latency and subjective reports of sleepiness when administered to patients with shift-work sleep disorder diagnosed according to criteria stipulated in the International Classification of Sleep Disorders. <sup>[40, 45-47]</sup>
  - \* After receiving modafinil 200 mg each work day for 3 months, sleep latency (measured in a sleep lab) was increased by 1.3 minutes from baseline compared to those patients receiving placebo. <sup>[46]</sup>
  - \* Of the patients taking modafinil, 74% were rated as at least minimally improved on the Clinical Global Impression of Change test at the final visit, as compared with 36 % in the placebo group. <sup>[46]</sup>
- There have been no reliable clinical trials evaluating modafinil in patients with shift-work sleep disorder that have demonstrated improved efficacy or safety with doses higher than 200 mg daily.
- Preliminary studies have suggested that modafinil 200 mg to 400 mg has about the same effect on sleep latency in patients with shift-work sleep disorder as caffeine 600 mg, though larger, well controlled trials are needed to confirm these results. <sup>[46, 48-51]</sup>

## MULTIPLE SCLEROSIS

- Although initial studies with modafinil were promising, <sup>[7,13]</sup> new data show modafinil 100-400 mg daily is not effective in improving fatigue associated with multiple sclerosis. <sup>[14]</sup>

## DEPRESSION

- Modafinil did not achieve study endpoints to determine its overall clinical benefit in augmenting antidepressant treatment in partial responders to selective serotonin reuptake inhibitors with persistent fatigue and sleepiness. <sup>[16]</sup>
  - \* There was significant improvement in CGI-I (Clinical Global Impressions-Improvement). (p=0.02)
  - \* There were no significant differences between modafinil and placebo in improving fatigue (based on Fatigue Severity Score, Brief Fatigue Inventory) or depression (HAM-D scores, MADRS scores) after 8 weeks of treatment.

- The effectiveness of modafinil in excessive sleepiness and fatigue after SSRI treatment in patients with major depression was evaluated in a 12-week, open-label, extension study. The study experienced a high rate of drop-outs (24%) making the results of the trial unreliable. [30]
- There are no randomized, controlled trials that evaluate the safety or effectiveness of modafinil used to treat manic-depressive (bipolar) disorder. Long-term safety of modafinil in this condition is unknown.
- The use of modafinil in 66 patients with DSM-IV atypical major depression was assessed over 12 weeks of open-label treatment followed by a 12 week double-blind, randomized, placebo-controlled relapse phase. A significant improvement in HAM-D-29 was noted at the end of the open-label phase, but no statistically significant difference was noted at the end of the relapse phase, casting doubt on the overall efficacy of modafinil in this indication. [43]

#### ATTENTION DEFICIT/HYPERACTIVITY DISORDER

- Data from randomized, placebo-controlled trials indicate that treatment with modafinil in doses of 325 mg and 425 mg once daily (some dosage strengths not yet available) may improve ADHD symptoms in children ages 6 to 17 over a study period of up to 9 weeks. [10, 35-39]
- There is no evidence that differentiates safety and efficacy of modafinil from other traditional medications used for ADHD in children (such as methylphenidate or dextroamphetamine).
- While small preliminary trials have shown potential efficacy of modafinil in adults with attention deficient hyperactivity disorder [3], positive results have not been demonstrated in larger, adequately-powered studies. [10]
- On March 25, 2006, the Psychopharmacologic Drugs Advisory Committee voted unanimously that modafinil (to be marketed under the trade name of Sparlon<sup>®</sup>) is effective for its intended use but recommended that Cephalon collect additional data to support the safety of the drug in children and adolescents with ADHD. [25]
  - \* The committee noted that in the safety database submitted by Cephalon, there were two cases of confirmed erythema multiforme, Stevens-Johnson, and 10 other possible cases of a significant rash. This would indicate a total range of risk of between 0.2% and 1.3%. [25]

## IDIOPATHIC HYPERSOMNIA

- Only one trial has been published to date evaluating modafinil in patients with idiopathic hypersomnia. <sup>[52]</sup>
  - \* Following treatment with modafinil at 200 to 500 mg/day in two divided doses, 18 subjects with idiopathic hypersomnia experienced a statistically significant improvement in subjective drowsiness and number of sleep attacks per day. <sup>[52]</sup>
  - \* This study had no comparator group, no placebo control, and no evaluation of functional status after treatment. This study is suggestive, but a blinded, randomized controlled trial is needed to establish efficacy in this disorder.

## OTHER INDICATIONS

- The use of modafinil (400 mg per day) in 36 patients with post-polio syndrome did not produce statistically significant changes to fatigue or quality of life when compared to placebo over a period of 6 weeks. <sup>[41]</sup>
- The use of modafinil (100 mg to 200 mg per day) in 20 subjects with DSM-IV schizophrenia or schizoaffective disorder did not produce a statistically significant change in the negative symptoms of schizophrenia when compared with placebo over a period of 8 weeks. <sup>[42]</sup>

### *Safety*

- The most commonly observed adverse events (>5%) associated with the use of modafinil 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. The adverse event profile was similar across these studies. <sup>[40]</sup>
- Rare but severe skin disorders such as erythema multiforme and Stevens-Johnson syndrome have been reported in patient receiving modafinil (see above). <sup>[25]</sup>
- The abuse potential of modafinil (200, 400, and 800 mg) was assessed relative to methylphenidate (45 mg and 90 mg) in an inpatient study in individuals experienced with drugs of abuse. Results from this clinical study demonstrated that modafinil produced psychoactive and euphoric effects and feelings consistent with other scheduled CNS stimulants (methylphenidate). <sup>[40, 53]</sup>

## Appendix 1: Diagnostic criteria for Narcolepsy <sup>[44]</sup>

**A.** Irresistible attacks of refreshing sleep that occur daily over at least 3 months.

**AND**

**B.** The presence of one or both of the following:

- 1.** Cataplexy (i.e., brief episodes of sudden bilateral loss of muscle tone, most often in association with intense emotion).

**OR**

- 2.** Recurrent intrusions of elements of rapid eye movement (REM) sleep into the transition between sleep and wakefulness, as manifested by either hypnopompic (i.e., the intermediate consciousness that precedes complete awakening from sleep) or hypnagogic (i.e., the state of intermediate consciousness preceding onset of sleep) hallucinations or sleep paralysis at the beginning or end of sleep episodes.

**AND**

**C.** The disturbance is not due to the direct physiological effects of substance (e.g., a drug of abuse, a medication) or another general medical condition.

## Appendix 2: Diagnostic Criteria: Shift Work Sleep Disorder <sup>[45]</sup>

**A.** There is a complaint of insomnia or excessive sleepiness that is temporally associated with a recurring work schedule that overlaps the usual time for sleep.

**AND**

**B.** The symptoms are associated with the shift-work schedule over the course of at least one month.

**AND**

**C.** Sleep log or other monitoring (with sleep diaries) for at least seven days demonstrates disturbed circadian and sleep-time misalignment.

**AND**

**D.** The sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

### References

1. Kingshott RN, Vennelle M, Coleman EL, et al. "Randomized, double-blind, placebo controlled crossover trial of modafinil in the treatment of residual excessive daytime sleepiness in the sleep/apnea/hypopnea syndrome." *Am J Resp Crit Care Med* 2001;163:918-23.
2. Labellarte MJ. "Pharmacokinetics and safety of modafinil in children with attention deficit hyperactivity disorder (ADHD)." Poster presentation.
3. Taylor FB, Russo J. "Efficacy of modafinil compared to dextroamphetamine for the treatment of attention deficit hyperactivity disorder in adults." *J Child Adol Psychopharm* 2000;10:311-20.
4. Rugino TA, Copley TC. "Effects of modafinil in children with attention deficit/hyperactivity disorder: an open-label study." *J Am Acad Child Adol Psych* 2001;40:230-5.

5. Anon. "US modafinil in narcolepsy multicenter study group. Randomized trial of modafinil for the treatment of pathological somnolence in narcolepsy." *Annals of Neurology* 1998;43:88-97.
6. Schwartz JRL, Schwartz ER, Veit CA, Blakely EA. "Modafinil for the treatment of excessive daytime sleepiness associated with narcolepsy." *Today's therapeutic trends* 1998;16:287-308.
7. Rammohan KW, Rosenberg JH, Lynn DJ, et al. "Efficacy and safety of modafinil (Provigil) for the treatment of fatigue in multiple sclerosis: a two centre phase 2 study." *J Neurol Neurosurg Psychiatry* 2002;72:179-83.
8. McDonald WI, et al. "Recommended diagnostic criteria for multiple sclerosis: Guidelines from the international panel on the diagnosis of multiple sclerosis." *Ann Neurol* 2001;50(1):121-7.
9. Pack AI, Black JE, Schwartz RL, Matheson JK. "Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea." *Am J Respir Crit Care Med* 2001;164:1675-81.
10. Data on File. Cephalon, Inc.
11. Adler CH, Caviness JN, Hentz JG, Lind M, Tied J. "Randomized trial of modafinil for treating subjective daytime sleepiness in patients with Parkinson's disease." *Mov Disord* 2003 Mar;18(3):287-93.
12. Hogl B, Saletu M, Brandauer E, et al. "Modafinil for the treatment of daytime sleepiness in Parkinson's disease: a double-blind, randomized, crossover, placebo-controlled polygraphic trial." *Sleep* 2002 Dec;25(8):905-9.
13. Zifko UA, Rupp M, Schwarz S, Zipko HT, Maida EM. Modafinil in treatment of fatigue in multiple sclerosis. Results of an open-label study. *J Neurol* 2002;249:983-7.
14. Stankoff B, Waubant E, Confavreux C, Edan G, Debouverie M, Rumbach L, Moreau T, Pelleier J, et al. Modafinil for fatigue in MS. A randomized placebo-controlled double-blind study. *Neurology* 2005;64:1139-43.
15. Dackis CA, Kampman KM, Lynch KG, Pettinati HM, O'Brien CP, et al. A double-blind, placebo-controlled trial of modafinil for cocaine dependence. *Neuropsychopharmacology* 2005;30:205-11.

16. Fava M, Thase ME, DeBattista C. A multicenter, placebo-controlled study of modafinil augmentation in partial responders to selective serotonin reuptake inhibitors with persistent fatigue and sleepiness. *J Clin Psych* 2005;6:85-93.
17. Taneja I, Bruehl S, Robertson D. Effect of modafinil on acute pain. A randomized double-blind cross-over study. *J Clin Pharmacol* 2004;44:1425-7.
18. Schwartz JRL, Nelson MT, Schwartz ER, Hughes RJ. Effects of modafinil on wakefulness and executive function in patients with narcolepsy experiencing late-day sleepiness. *Clin Neuropharmacol* 2004;74-9.
19. MacDonald JR, Hill JD, Tarnopolsky MA. Modafinil reduces excessive somnolence and enhances mood in patients with myotonic dystrophy. *Neurology* 2002;59:1876-80.
20. US Modafinil in Narcolepsy Multicenter Study Group. Randomized trial of modafinil as a treatment for the excessive daytime somnolence of narcolepsy. *Neurology* 2000;54:1166-75.
21. Broughton RJ, Fleming JAE, George CFP, Hill JD, Kryger MH, Moldosfsky H, et al. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of excessive daytime sleepiness in narcolepsy. *Neurology* 1997;49:444-51.
22. US Modafinil in Narcolepsy Multicenter Study Group. Randomized trial of modafinil for the treatment of pathological somnolence in narcolepsy. *Ann Neurol* 1998;43(1):88- 97.
23. Pack AI, Black JE, Schwartz JRL, Matheson JK; US Modafinil in Obstructive Sleep Apnea Study Group. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. *Am J Resp Crit Care Med* 2001;164:1675-81.
24. Black JE, Doublas NJ, Earl CQ. Efficacy and safety of modafinil as adjunctive therapy for excessive sleepiness associated with obstructive sleep apnea [abstract 030.J]. *Sleep* 2002;25:A22-23.
25. Center for Drug Evaluation and Research. Psychopharmacologic Drugs Advisory Committee, meeting transcript from March 23, 2006. Available at: <http://www.fda.gov/ohrms/dockets/ac/06/transcripts/2006-4212T1-Part1.htm>. Accessed June 26, 2006
26. Chan KM, Strohschein FJ, Rydz D, Allidina A, Shuaib A, Westbury CF. Randomized controlled trial of modafinil for the treatment of fatigue in postpolio patients. *Muscle Nerve*. 2006 Jan;33(1):138-41.

27. Ondo WG, Fayle R, Atassi F, Jankovic J. Modafinil for daytime somnolence in Parkinson's disease: double blind, placebo controlled parallel trial. *J Neurol Neurosurg Psychiatry*. 2005 Dec;76(12):1636-9.
28. Randall DC, Cafferty FH, Shneerson JM, Smith IE, Llewelyn MB, File SE. Chronic treatment with modafinil may not be beneficial in patients with chronic fatigue syndrome. *J Psychopharmacol*. 2005 Nov;19(6):647-60.
29. Sevy S, Rosenthal MH, Alvir J, Meyer S, Visweswaraiiah H, Gunduz-Bruce H, Schooler NR. Double-blind, placebo-controlled study of modafinil for fatigue and cognition in schizophrenia patients treated with psychotropic medications. *J Clin Psychiatry*. 2005 Jul;66(7):839-43.
30. Thase ME, Fava M, DeBattista C, Arora S, Hughes RJ. Modafinil augmentation of SSRI therapy in patients with major depressive disorder and excessive sleepiness and fatigue: a 2-week, open-label, extension study. *CNS Spectr*. 2006 Feb;11(2):93-102.
31. Schwartz JR, Feldman NT, Bogan RK. Dose effects of modafinil in sustaining wakefulness in narcolepsy patients with residual evening sleepiness. *J Neuropsychiatry Clin Neurosci*. 2005 Summer;17(3):405-12. Erratum in: *J Neuropsychiatry Clin Neurosci*. 2005 Fall;17(4):561.
32. Czeizler CA, Dinges, Walsh JK, Roth T, Niebler G. Modafinil for the treatment of excessive sleepiness in chronic shift work sleep disorder. *Sleep* 2003 26:A114.
33. Gill M, Haerich P, Westcott K, Godenick KL, Tucker JA. Cognitive performance following modafinil versus placebo in sleep-deprived emergency physicians: a double-blind randomized crossover study. *Acad Emerg Med*. 2006 Feb;13(2):158-65. Epub 2006 Jan 25. Erratum in: *Acad Emerg Med*. 2006 Apr;13(4):477.
34. Czeisler CA, Walsh JK, Roth T, Hughes RJ, Wright KP, Kingsbury L, et. al.; U.S. Modafinil in Shift Work Sleep Disorder Study Group. Modafinil for excessive sleepiness associated with shift-work sleep disorder. *N Engl J Med*. 2005 Aug 4;353(5):476-86. Erratum in: *N Engl J Med*. 2005 Sep 8;353(10):1078.
35. Biederman J, Swanson JM, Wigal SB, Kratochvil CJ, Boellner SW, Earl CQ, et. al. Efficacy and safety of modafinil film-coated tablets in children and adolescents with attention-deficit/hyperactivity disorder: results of a randomized, double-blind, placebo controlled, flexible-dose study. *Pediatrics*. 2005 Dec;116(6):e777-84.

36. Swanson JM, Greenhill LL, Lopez FA, Sedillo A, Earl CQ, Jiang JG, et. al. Modafinil film-coated tablets in children and adolescents with attention-deficit/hyperactivity disorder: results of a randomized, double-blind, placebo-controlled, fixed-dose study followed by abrupt discontinuation. *J Clin Psychiatry*. 2006 Jan;67(1):137-47.
37. Biederman J, Swanson JM, Wigal SB, Boellner SW, Earl CQ, Lopez FA; et al. Modafinil ADHD Study Group. A comparison of once-daily and divided doses of modafinil in children with attention-deficit/hyperactivity disorder: a randomized, double-blind, and placebo-controlled study. *J Clin Psychiatry*. 2006 May;67(5):727-35.
38. Greenhill LL, Biederman J, Boellner SW, Rugino TA, Sangal RB, Earl CQ, et. al. A randomized, double-blind, placebo-controlled study of modafinil film-coated tablets in children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2006 May;45(5):503-11.
39. Boellner SW, Earl CQ, Arora S. Modafinil in children and adolescents with attention-deficit/hyperactivity disorder: a preliminary 8-week, open-label study. *Curr Med Res Opin*. 2006 Dec;22(12):2457-65.
40. Provigil [package insert]. Fraser, PA: Cephalon Inc; March 2008
41. Vasconcelos OM, Prokhorenko OA, Salajegheh MK, Kelley KF, Livornese K, Olsen et. al. Modafinil for treatment of fatigue in post-polio syndrome: a randomized controlled trial. *Neurology*. 2007 May 15;68(20):1680-6.
42. Pierre JM, Peloian JH, Wirshing DA, Wirshing WC, Marder SR. A randomized, double-blind, placebo-controlled trial of modafinil for negative symptoms in schizophrenia. *J Clin Psychiatry*. 2007 May;68(5):705-10.
43. Vaishnavi S, Gadde K, Alamy S, Zhang W, Connor K, Davidson JR. Modafinil for atypical depression: effects of open-label and double-blind discontinuation treatment. *J Clin Psychopharmacol*. 2006 Aug;26(4):373-8. Erratum in: *J Clin Psychopharmacol*. 2006 Oct;26(5):523.
44. Narcolepsy. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC, American Psychiatric Association, 2000: 609-615
45. *The International Classification of Sleep Disorders; Diagnostic and Coding Manual*.. 2<sup>nd</sup> ed. Westchester, IL: American Academy of Sleep Medicine, 2005.

46. Morgenthaler TI, Lee-Chiong T, Alessi C, et al.; Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine report. *Sleep*. 2007 Nov 1;30(11):1445-59.
47. Czeisler CA, Walsh JK, Roth T, et al.; U.S. Modafinil in Shift Work Sleep Disorder Study Group. Modafinil for excessive sleepiness associated with shift-work sleep disorder. *N Engl J Med*. 2005 Aug 4;353(5):476-86. Erratum in: *N Engl J Med*. 2005 Sep 8;353(10):1078.
48. Kamimori GH, Johnson D, Thorne D, Belenky G. Multiple caffeine doses maintain vigilance during early morning operations. *Aviat Space Environ Med*. 2005 Nov;76(11):1046-50.
49. Wesensten NJ, Killgore WD, Balkin TJ. Performance and alertness effects of caffeine, dextroamphetamine, and modafinil during sleep deprivation. *J Sleep Res*. 2005 Sep;14(3):255-66.
50. Dagan Y, Doljansky JT. Cognitive performance during sustained wakefulness: A low dose of caffeine is equally effective as modafinil in alleviating the nocturnal decline. *Chronobiol Int*. 2006;23(5):973-83.
51. Wesensten NJ, Belenky G, Kautz MA, Thorne DR, Reichardt RM, Balkin TJ. Maintaining alertness and performance during sleep deprivation: modafinil versus caffeine. *Psychopharmacology (Berl)*. 2002 Jan;159(3):238-47.
52. Bastuji H, Jouvet M. Successful treatment of idiopathic hypersomnia and narcolepsy with modafinil. *Prog Neuropsychopharmacol Biol Psychiatry*. 1988;12(5):695-700.
53. Nuvigil [package insert]. Fraser, PA: Cephalon Inc; July 2008

Cross References
Xyrem <sup>®</sup> , sodium oxybate dru093
Nuvigil <sup>®</sup> , armodafinil dru185

Codes	Number	Description
N/A		