Clinical Policy Bulletin:  
Multiple Sleep Latency Test (MSLT)

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Policy

I. Aetna considers the multiple sleep latency test (MSLT) medically necessary for either of the following 2 indications:

   A. For evaluation of symptoms of narcolepsy, to confirm the diagnosis;  
      or  
   B. For evaluation of persons with suspected idiopathic hypersomnia to help differentiate idiopathic hypersomnia from narcolepsy.

Aetna considers MSLT experimental and investigational for all other indications because its effectiveness for indications other than the ones listed above have not been established, including (not an all-inclusive list): chronic fatigue syndrome; circadian rhythm disorders; insomnia, neurologic disorders other than narcolepsy (e.g., dementia (including Alzheimer's disease and dementia with Lewy bodies) and Parkinson's disease); obstructive sleep apnea syndrome; and evaluation of the effectiveness of modafinil therapy in narcolepsy.

II. Aetna considers repeat MSLT tests not medically necessary, unless:

   A. The initial test was invalid or uninterpretable;  
   B. The initial test is affected by extraneous circumstances or when study conditions were not present during initial testing;  
   C. The patient is suspected to have narcolepsy but earlier MSLT evaluation did not provide polygraphic confirmation.

III. Aetna considers single nap studies experimental and investigational because a full MSLT is required for accurate diagnosis of narcolepsy.

IV. Aetna considers home MSLT experimental and investigational because home MSLT has not been proven to be equivalent to formal MSLT performed in a sleep laboratory.
See also CPB 0004 - Obstructive Sleep Apnea in Adults.

**Background**

The multiple sleep latency test (MSLT) involves multiple trials during a day to objectively assess sleep tendency by measuring the number of minutes it takes the patient to fall asleep. The patient may be instructed to lie down in a dark room, with permission or a suggestion given to sleep (MSLT) or to sit up in a dimly lit room and try to stay awake (maintenance of wakefulness test). The MSLT is the better test for demonstration of sleep-onset rapid eye movement (REM) periods, a determination that is important in establishing the diagnosis of narcolepsy.

Parameters necessary for sleep staging (including 1 to 4 channels of EEG, EOG, and chin EMG) are recorded.

According to AASM guidelines (Littner, et al., 2005), the MSLT is indicated as part of the evaluation of patients with suspected narcolepsy to confirm the diagnosis. The MSLT may be indicated as part of the evaluation of patients with suspected idiopathic hypersomnia to help differentiate idiopathic hypersomnia from narcolepsy. The MSLT is not routinely indicated in the initial evaluation and diagnosis of obstructive sleep apnea syndrome or in assessment of change following treatment with nasal CPAP (Littner, et al., 2005). The MSLT is not routinely indicated for evaluation of sleepiness in medical and neurological disorders (other than narcolepsy), insomnia, or circadian rhythm disorders.

According to the AASM (Littner, et al., 2005), repeat MSLT testing may be indicated in the following situations: (a) when the initial test is affected by extraneous circumstances or when appropriate study conditions were not present during initial testing, (b) when ambiguous or uninterpretable findings are present, (c) when the patient is suspected to have narcolepsy but earlier MSLT evaluation(s) did not provide polygraphic confirmation.

Huang et al (2008) noted that the cause and pathogenesis of Kleine-Levin syndrome, a recurrent hypersomnia affecting mainly male adolescents, remain unknown, with only scant information on the sleep characteristics during episodes. These investigators described findings obtained with polysomnography (PSG) and MSLT and correlation obtained between clinical and PSG findings from different episodes. A total of 19 patients (17 males) were investigated with PSG and MSLT; 10 had data during both symptomatic episode and asymptomatic interval. The analyses considered day of onset of symptoms and relationship between this time of onset and day of recording during the symptomatic period. When PSG was performed early (before the end of the first half of the symptomatic period), an important reduction in slow wave sleep (SWS) was always present with progressive return to normal during the second half (with percentages very similar to those monitored during the asymptomatic period) despite persistence of clinical symptoms. Rapid eye movement sleep remained normal in the first half of the episode but decreased in the second half: the differences between first and second half of episodes were significant for SWS (p = 0.014) and REM sleep (p = 0.027). The overall mean sleep latency at MSLT was 9.51 +/- 4.82 mins and 7 of 17 patients had 2 or more sleep onset REM periods during the symptomatic period. The authors concluded that important
changes in sleep occur over time during the symptomatic period, with clear impairment of SWS at symptom onset. However, MSLT is of little help in defining sleep problems and findings from the MSLT do not correlate with symptom onset.

Yeh and Schenck (2010) compared MSLT and Epworth sleepiness scale (ESS) for evaluating the effectiveness of modafinil in treating excessive daytime sleepiness in patients with narcolepsy. A total of 10 consecutive patients with narcolepsy-with-cataplexy who were treated with 200 mg/day modafinil for more than 6 months were included in this study. This comparative study was prompted by the requirement of the Bureau of National Health Insurance in Taiwan that modafinil users need to be followed-up with MSLTs every 6 to 12 months. The mean age at onset of narcolepsy in these 10 patients was 11.8 +/- 3.3 years, and 8 (80 %) were male. These investigators compared the differences in MSLT and ESS between baseline and follow-up at 6 to 12 months after starting modafinil therapy using paired-t tests. Epworth Sleepiness Scale scores (p < 0.001) were considerably more sensitive than MSLT scores (p < 0.05) in documenting the effectiveness of modafinil and that improvements in MSLT scores were minimal and remained in the pathologically sleepy range. These findings suggested that the ESS is a more sensitive and clinically meaningful tool to evaluate the effectiveness of modafinil in narcolepsy.

Mariman et al (2013) evaluated undiagnosed and co-morbid disorders in patients referred to a tertiary care center with a presumed diagnosis of chronic fatigue syndrome (CFS). Patients referred for chronic unexplained fatigue entered an integrated diagnostic pathway, including internal medicine assessment, psychodiagnostic screening, physiotherapeutic assessment and PSG + MSLT. Final diagnosis resulted from a multi-disciplinary team discussion. Fukuda criteria were used for the diagnosis of CFS, DSM-IV-TR criteria for psychiatric disorders, ICSD-2 criteria for sleep disorders. Out of 377 patients referred, 279 (74.0 %) were included in the study [84.9 % female; mean age of 38.8 years (SD 10.3)]. A diagnosis of unequivocal CFS was made in 23.3 %. In 21.1 %, CFS was associated with a sleep disorder and/or psychiatric disorder, not invalidating the diagnosis of CFS. A predominant sleep disorder was found in 9.7 %, 19.0 % had a psychiatric disorder and 20.8 % a combination of both. Only 2.2 % was diagnosed with a classical internal disease. In the total sample, a sleep disorder was found in 49.8 %, especially obstructive sleep apnea syndrome, followed by psychophysiologic insomnia and periodic limb movement disorder. A psychiatric disorder was diagnosed in 45.2 %; mostly mood and anxiety disorder. The authors concluded that a multi-disciplinary approach to presumed CFS yielded unequivocal CFS in only a minority of patients, and revealed a broad spectrum of exclusionary or co-morbid conditions within the domains of sleep medicine and psychiatry.

However, an UpToDate review on “Clinical features and diagnosis of chronic fatigue syndrome” (Gluckman, 2014) does not mention the use of MSLT as a diagnostic tool.

Ferman et al (2014) stated that excessive daytime sleepiness (EDS) is a commonly reported problem in dementia with Lewy bodies (DLB). These researchers examined the relationship between nighttime sleep continuity and the propensity to fall asleep during the day in clinically probable DLB compared to
Alzheimer’s disease (AD) dementia. A full-night polysomnography was carried out in 61 participants with DLB and 26 with AD dementia. Among this group, 32 participants with DLB and 18 with AD dementia underwent a daytime MSLT. Neuropathologic examinations of 20 participants with DLB were carried out. Although nighttime sleep efficiency did not differentiate diagnostic groups, the mean MSLT initial sleep latency was significantly shorter in participants with DLB than in those with AD dementia (mean of 6.4 ± 5 mins versus 11 ± 5 mins, p < 0.01). In the DLB group, 81% fell asleep within 10 mins compared to 39% of the AD dementia group (p < 0.01), and 56% in the DLB group fell asleep within 5 mins compared to 17% in the AD dementia group (p < 0.01). Daytime sleepiness in AD dementia was associated with greater dementia severity, but mean MSLT latency in DLB was not related to dementia severity, sleep efficiency the night before, or to visual hallucinations, fluctuations, parkinsonism or rapid eye movement sleep behavior disorder. These data suggested that EDS is a unique feature of DLB that does not depend on nighttime sleep fragmentation or the presence of the 4 cardinal DLB features. Of the 20 DLB participants who underwent autopsy, those with transitional Lewy body disease (brainstem and limbic) did not differ from those with added cortical pathology (diffuse Lewy body disease) in dementia severity, DLB core features or sleep variables. The authors concluded that daytime sleepiness is more likely to occur in persons with DLB than in those with AD dementia. They stated that daytime sleepiness in DLB may be attributed to disrupted brainstem and limbic sleep-wake physiology, and further work is needed to better understand the underlying mechanisms.

Cochen De Cock and colleagues (2014) stated that EDS is a frequent complaint in Parkinson’s disease (PD); however the frequency and risk factors for objective sleepiness remain mostly unknown. These researchers investigated both the frequency and determinants of self-reported and objective daytime sleepiness in patients with PD using a wide range of potential predictors. A total of 134 consecutive patients with PD, without selection bias for sleep complaint, underwent a semi-structured clinical interview and a 1-night polysomnography followed by a MSLT. Demographic characteristics, medical history, PD course and severity, daytime sleepiness, depressive and insomnia symptoms, treatment intake, pain, restless legs syndrome, REM sleep behavior disorder, and nighttime sleep measures were collected. Self-reported daytime sleepiness was defined by an ESS score above 10. A mean sleep latency on MSLT below 8 mins defined objective daytime sleepiness. Of 134 patients with PD, 46.3% had subjective and only 13.4% had objective sleepiness with a weak negative correlation between ESS and MSLT latency. A high body mass index (BMI) was associated with both ESS and MSLT, a pain complaint with ESS, and a higher apnea/hypopnea index with MSLT. However, no associations were found between both objective and subjective sleepiness, and measures of motor disability, disease onset, medication (type and dose), depression, insomnia, restless legs syndrome, REM sleep behavior disorder and nighttime sleep evaluation. The authors concluded that they found a high frequency of self-reported EDS in PD, a finding which is however not confirmed by the gold standard neurophysiological evaluation.

Bjornara et al (2014) noted that sleep disturbances, such as REM-sleep behavior disorder (RBD) and EDS, are more common in patients with PD than in the general population. Apart from that, their relation to PD seems to diverge considerably. These researchers explored the frequency and associated motor-
and non-motor features of sleep related symptoms in PD. A total of 107 patients with PD, 65 men and 42 women, were included in a cross-sectional study. Excessive daytime sleepiness was examined by the ESS; probable RBD (pRBD) was diagnosed by the validated RBD screening questionnaire. Further sleep symptoms were explored by the PD sleep scale. Motor- and non-motor symptoms were assessed and compared in patients with and without pRBD and EDS, respectively. pRBD was present in 38% and EDS was present in 29% of the patients. As opposed to EDS, pRBD showed no association to disease duration or severity. Parkinson’s disease patients with pRBD reported more cognitive problems. There was a trend towards more autonomic dysfunction in patients with pRBD. Nocturia and sleep fragmentation were the most frequent general sleep problems reported by the patients. The authors concluded that these findings suggested that EDS is related to disease duration, and possibly caused by progressive neurodegeneration. They stated that pRBD seems to be a distinct feature present in only a proportion of PD patients.

Ataide et al (2014) noted that sleep disorders are major non-motor manifestations of patients with PD, and EDS is one of the most common symptoms. These investigators reviewed a current literature concerning major factors that influence EDS in PD patients, using MSLT. A Medline search found 23 studies. The presence of EDS was observed in 12.7% to 47% in patients without complaints of daytime sleepiness and 47% to 66.7% with complaints of daytime sleepiness. Despite being recognized by several authors, major factors that influence EDS, such as severity of motor symptoms, use of dopaminergic medications, and associated sleep disturbances, presented contradictory data. The authors concluded that available data suggested that the variability of the results may be related to the fact that it was conducted with a small sample size, not counting the neuropathological heterogeneity of the disease. Thus, before carrying out longitudinal studies with significant samples, careful analysis should be done by assigning a specific agent on the responsibility of EDS in PD patients.

Schrempf et al (2014) noted that sleep disorders in patients with PD are very common and have an immense negative impact on their quality of life. Insomnia, daytime sleepiness with sleep attacks, restless-legs syndrome (RLS) and RBD are the most frequent sleep disorders in PD. Neurodegenerative processes within sleep regulatory brain circuitries, anti-parkinsonian (e.g., levodopa and dopamine agonists) and concomitant medication (e.g., anti-depressants) as well as co-morbidities or other non-motor symptoms (such as depression) were discussed as causative factors. For the diagnosis of sleep disturbances these researchers recommended regular screening using validated questionnaires such as the Pittsburgh Sleep Quality Index (PSQI) or the Medical Outcomes Study Sleep Scale (MOS), for evaluating daytime sleepiness these investigators suggested to use the ESS, the inappropriate sleep composite score (ISCS) or the Stanford sleepiness scale (SSS). All of these questionnaires should be used in combination with a detailed medical history focusing on common sleep disorders and medication. If necessary, patients should be referred to sleep specialists or sleep laboratories for further investigations. Management of sleep disorders in PD patients usually starts with optimization of (dopaminergic) anti-parkinsonian therapy followed by specific treatment of the sleep disturbances. Aside from these clinical issues of sleep disorders in PD, the concept of RBD as an early sign for emerging neurodegenerative diseases is of pivotal interest for future research on
biomarkers and neuroprotective treatment strategies of neurodegenerative diseases, and particularly PD.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

95805  Multiple sleep latency or maintenance of wakefulness testing, recording, analysis and interpretation of physiological measurements of sleep during multiple trials to assess sleepiness

Other CPT codes related to the CPB:

95782  Polysomnography; younger than 6 years, sleep staging with 4 or more additional parameters of sleep, attended by a technologist

95806 - 95807  Sleep study

95808 - 95811  Polysomnography; sleep staging, attended by a technologist

ICD-9 codes covered if selection criteria are met:

327.11 - 327.12  Idiopathic hypersomnia with long sleep time

347.00 - 347.11  Cataplexy and narcolepsy [after obstructive sleep apnea has been ruled out by polysomnography] [MSLT is not covered for the evaluation of the effectiveness of modafinil therapy in narcolepsy]

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive list):

307.42  Persistent disorder of initiating or maintaining sleep

327.23  Obstructive sleep apnea (adult)(pediatric)

327.30 - 327.39  Circadian rhythm sleep disorders

780.51 - 780.52  Insomnia

780.53  Hypersomnia with sleep apnea, unspecified

780.71  Chronic fatigue syndrome

Other ICD-9 codes related to the CPB:
327.00 € Organic sleep disorders
327.10,
327.13 €
327.22,
327.24 €
327.29,
327.40 €
327.8

478.29 Other diseases of pharynx
780.50 Sleep disturbance, unspecified
780.55 Disruptions of 24-hour sleep-wake cycle, unspecified
780.56 Dysfunctions associated with sleep stages or arousal from sleep
780.57 Unspecified sleep apnea

The above policy is based on the following references:


31. AIM Specialty Health. Multiple sleep latency testing (MSLT) and maintenance of wakefulness testing (MWT). Chicago, IL: AIM Specialty Health; May 20, 2014.