# Drugs Used in Narcolepsy and Other Hypersomnias

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**KEYWORDS**

• Narcolepsy • Idiopathic hypersomnia • Nonpharmacological treatment • Pharmacologic treatment • Stimulants • Sodium oxybate • Pitolisant

**KEY POINTS**

- State-of-the-art treatment of narcolepsy and hypersomnias of central origin consists of a combination of facilitating acceptance of the disorder, lifestyle advice, and pharmacologic treatment.
- The treatment goal of pharmacologic treatment must be improved performance and avoidance of side effects.
- Even when optimally treated, excessive daytime sleepiness will never completely disappear. In contrast, cataplexy, hypnagogic hallucinations, and sleep paralysis may completely disappear.

## INTRODUCTION

Hypersomnolence may have various expressions and lead to a variety of complaints, including a subjective feeling of sleepiness, difficulty in sustaining attention, impaired performance, memory complaints, automatic behavior, unintended naps, irritability, and/or an increased amount of sleep. Regarding sleep, usually 1 of 2 distinctive phenotypes is predominantly present: an inability to stay awake during the day or an increased need for sleep. This distinction may not only guide the underlying diagnosis but may also predict efficacy of certain (pharmacologic) treatment interventions. By definition, the complaint is present each and every day.

Narcolepsy with cataplexy is a typical example of a disorder characterized by an inability to stay awake during the day, usually accompanied by an inability to stay asleep at night but without a significant increase in the hours spent asleep during the 24 hours of the day. The classic form of idiopathic hypersomnia (IH) is the typical example of an increased need for sleep: there is an irresistible need for an increased number of hours spent asleep during the night and, despite this increase, there are complaints of sleepiness during the day. This latter phenotype is more difficult to treat.

It must be kept in mind that by far the most prevalent cause of excessive daytime sleepiness (EDS) is sleep deprivation. Complaints caused by sleep deprivation are neither quantitatively nor qualitatively different from complaints caused by sleep disorders, which may cause diagnostic challenges. In case of doubt, patients must always be first advised to extend sleep to assess whether sleep deprivation is the likely cause of their complaints. It is also important to realize that if a sleep disorder is the cause for EDS, sleep apnea is a much more prevalent cause than narcolepsy or IH because of its much higher prevalence.

## THE COMPLAINTS TO BE TREATED

The key problem of most patients who suffer from narcolepsy or IH is their inability to remain fully alert and/or even awake during longer periods of the day, relentlessly present each and every day of their life.[1,2] In narcolepsy with cataplexy in addition, the strict physiologic boundaries of specific

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components of wake and sleep stages are fluid. This leads to partial expressions, particularly identifiable in rapid eye movement (REM) sleep, explaining such symptoms as cataplexy, hypnagogic hallucinations (HHs), and sleep paralysis (SP).[2] The loss of state boundaries leads to more symptoms that are not always mentioned in textbooks, such as automatic behavior, memory complaints, and dream delusions.

## COMORBIDITY

Patients who suffer from narcolepsy with cataplexy clearly bear a risk to become obese, and those who suffer from narcolepsy and IH have an increased chance to develop complaints of fatigue and psychiatric comorbidities, such as anxiety and depression.[2,3]

It may be important to treat these comorbidities as well; however, that is beyond the scope of this article.

## BURDEN

It is not difficult to imagine that narcolepsy and IH have a severe negative impact on daily functioning and the experienced quality of life. It is even more detrimental when it starts during childhood because of the additional negative impact on social development and achievements at school.[2,4]

## EPIDEMIOLOGY

Narcolepsy with cataplexy has an estimated prevalence of 25 to 50 per 100,000 population. The incidence is estimated to be 0.74 to 1.37 per 100,000 person-years.[5–7] There are no reliable prevalence or incidence estimations of narcolepsy without cataplexy and IH but the prevalence is probably lower than for narcolepsy with cataplexy.

The age of onset is usually between 15 and 35 years but it may start at any age. There is a trend for a diagnosis at younger age and, probably, also for an earlier symptom onset during the last decade.

## CURRENTLY AVAILABLE TREATMENTS

Before starting treatment, it is of paramount importance that patients and their relatives are informed about the consequences of their chronic disease and learn to accept the diagnosis. This greatly facilitates the implementation of the behavioral modifications and decreases the burden of the disease. Accepting the diagnosis implies implementing behavioral or lifestyle modifications. Initiating pharmacologic treatment only after the implementation of lifestyle changes will prevent medication being used to compensate for a lack of lifestyle adjustment and will optimize treatment response. Only when medication is added to lifestyle adjustments can optimal and long-term improvement be established.

In addition, a supportive social environment (eg, family members, friends, employer, colleagues, patient group organizations, and support groups) is highly valuable.

## TREATMENT GOALS

Unfortunately, there is currently only symptomatic treatment of narcolepsy and IH. Although symptomatic, it may lead to profound improvement. There are 2 known effective treatment modalities: behavioral modification and pharmacologic therapy. As a rule, both are needed to achieve sufficient improvement.[2]

Therapy for EDS as expression of narcolepsy or IH should focus on the key problem: improving sustained attention and, therefore, performance, and reducing the chance for involuntary sleep attacks or naps. Because treatment is symptomatic, EDS complaints will never completely disappear. It should be explained to patients that the treatment goal is to improve the quality and duration of wakefulness during the day. They must be warned that there will usually remain a high chance of falling asleep in sedentary situations.

When initiating treatment of cataplexy, HHs, and SP, the intention should be to let them disappear. To reach this, pharmacologic treatment is almost always needed. HHs may sometimes be less prevalent when falling asleep in the supine position is avoided.

### *Behavioral Modification*

Patients should be advised to live a regular life, go to bed at the same hour each night, and get up at the same time each morning as much as possible. Scheduled daytime naps, usually less than 20 minutes, may temporarily alleviate and prevent daytime sleepiness, and a short nap just before certain activities demanding a high degree of attention may facilitate the proper completion. The optimal frequency, duration, and timing of these naps must be established on an individual basis. In most narcoleptic patients, longer naps have no better or longer lasting refreshing properties. Moreover, it is more difficult and inconvenient to wake up after a longer nap because, in most instances, deep sleep will occur. However, some patients only do well with longer naps. Unfortunately, there are few published studies regarding this important topic.[8]

Many particularly narcoleptic patients experience an influence from diet. They feel better when avoiding (large amounts of) carbohydrates during the day. Unfortunately, there also are few scientific data regarding this observation.[9] Alcohol consumption should preferably be avoided.