



IN DIZZINESS# WITH NAUSEA-VOMITING, ANXIETY

# Stemetil MD

Prochlorperazine maleate 5mg Mouth Dissolving tablets

**Faster Relief, Better Control**

Rx



## Vestibular compensation takes up to 7 days for completion<sup>1</sup>

AVAILABLE AS



Mouth dissolving tablet<sup>2</sup>



Inj 12.5 mg (for acute cases)<sup>2</sup>

**Abridged Prescribing Information**

**Stemetil MD** (Prochlorperazine mouth dissolving tablets)

**Composition:** Each tablet contains: Prochlorperazine maleate 5mg I.P.

**Indications:** Symptomatic treatment of vertigo due to Meniere's syndrome, labyrinthitis and other causes; nausea and vomiting of any aetiology, including that associated with migraine; in the treatment of schizophrenia, acute mania and as an adjunct in short term management of anxiety. **Dosage and Administration:** *Prevention of nausea and vomiting:* 5-10 mg twice or thrice daily. *Treatment of nausea and vomiting:* 20 mg stat followed, if necessary, by 10 mg two hours later. *Vertigo and Meniere's syndrome:* 5 mg thrice daily increasing, if necessary, to a total of 30 mg daily. After several weeks dosage may be reduced gradually to 5-10 mg daily. *Prevention of migraine:* 5 mg three or four times daily. *Treatment of migraine:* 20 mg stat, followed by 10 mg two hours later, if required. *Schizophrenia and other psychotic disorders:* Treatment varies depending on the condition. *Adjunct in the short term management of anxiety:* 15-20 mg daily in divided doses initially, but this may be increased, if necessary, to a maximum of 40 mg daily in divided doses. **Contraindications:** Hypersensitivity to phenothiazines or history of narrow angle glaucoma. **Precautions and Warnings:** Keep out of reach of children. Should be used with caution in elderly patients. To avoid in patients with renal and hepatic dysfunction, epilepsy, Parkinson's disease. To be avoided in pregnancy unless the treating Physician considers it essential. Nursing mothers: Breast-feeding should be suspended. **Adverse effects:** Generally well tolerated. Transient drowsiness, mild skin reactions, liver dysfunction, postural hypotension, extrapyramidal symptoms and rarely cardiovascular disorders have been reported. **Presentation:** 5 mg of Mouth Dissolving tablets: Strip of 10 tablets.

1. Curthoys et al. 1998. Vestibular Compensation. Therapy. Adv. Otorhinolaryngol. Basel, Karger, 55-82-110 2. Prochlorperazine. Prescribing Information. 2015 #OfVertiginous Origin

Please read the full prescribing information before usage.

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# A Clinical Insight into the Pharmacological Treatment of Vertigo

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## ABSTRACT

Vertigo and dizziness are common symptoms in everyday clinical practice. The treatment is dependent on the specific etiology. Depending on the cause of the vertigo, drugs with different mechanisms of action may be used to combat this disabling disease. Symptomatic treatment is given special importance in the treatment of vertigo. This article critically reviews the commonly used drugs, single or in combination, in the therapy of patients with vertigo.

**Keywords:** Pharmacotherapy of vertigo, cinnarizine, dimenhydrinate, dizziness, vertigo

Vertigo is one of the most common complaints in everyday clinical practice. Vertigo and dizziness are reflective of the symptoms of a variety of disorders that involve the peripheral and/or the central vestibular systems. In acute cases, vertigo, nausea and vomiting are the symptoms while in case of chronic disease, dizziness and/or disequilibrium may be the manifest symptoms.<sup>1</sup>

## METHODOLOGY

PubMed, Cochrane database and Google Scholar were the databases used for the literature search. The search strategy included a combination of 'key word search' and 'backward chronological search'. The search terms included pharmacotherapy of vertigo, cinnarizine + dimenhydrinate, treatment of vertigo and dizziness, side effects of drug therapy in vertigo, dizziness, vertigo, guidelines. Boolean operators were used for the search. Twenty-five original research articles, systematic reviews and meta-analyses were included for the development of this review (Table 1).

## WHEN IS A PHARMACOLOGICAL TREATMENT GIVEN?

The pharmacological treatment of vertigo and dizziness depends on:<sup>1</sup>

- ⇒ Correct diagnosis
- ⇒ Correct drug

- ⇒ Appropriate dosage
- ⇒ Sufficient duration.

The pharmacological management of vertigo is decided after the underlying causes behind it are correctly evaluated.<sup>2</sup> The most commonly observed reasons for starting vertigo treatment are:<sup>2,3</sup>

- ⇒ Acute vestibular related clinical presentation
- ⇒ Causes of vestibular symptoms such as Meniere's disease and epilepsy (disease-specific treatment)
- ⇒ Any chronic vestibular disorder such as central vestibular symptomatology (non-specific but empirical treatment strategy).

## PHARMACOLOGICAL TREATMENT

Dizziness often represents a wide range of symptoms. For managing dizziness, physicians should consider a comprehensive approach which includes faster resolution of symptoms for restoring normalcy, treating vertigo of any origin to avoid recurrence, managing associated conditions like nausea, vomiting; addressing anxiety, stress which delays recovery and increases recurrence. Such a comprehensive approach will not only facilitate recovery, but also help in improving quality-of-life and thus will increase patient satisfaction.

Common medication classes that are beneficial in the treatment of vertigo include anticholinergics, antihistamines, benzodiazepines, calcium channel antagonists and dopamine receptor antagonists. These medications are endowed with multiple actions and can modify the intensity of symptoms or they may affect

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**Table 1. Literature Search Strategy**

Databases	Search terms	Result	Comments
PubMed, Cochrane, Google Scholar	Pharmacotherapy of vertigo, cinnarizine + dimenhydrinate, treatment of vertigo and dizziness, side effects of drug therapy in vertigo, dizziness, vertigo, guidelines	25 Original research articles + systematic reviews + meta-analyses	Published literature corresponding only to human subjects and in English language were selected

the underlying disease process. Most of these agents, especially the ones with a sedative potential, also have a potential to modulate the rate of compensation for vestibular damage.<sup>4</sup>

Also, medications are highly useful for treating acute vertigo that lasts a few hours to several days. Vertigo which persists for more than a few days points to a permanent vestibular injury, and in these cases, medications should be stopped. A broad range of medications are used to treat vertigo and the frequently concurrent vegetative symptoms of nausea and vomiting.<sup>5</sup>

In the case of patients with benign paroxysmal positional vertigo (BPPV), an early diagnosis and treatment is warranted as it will result in decreased levels of anxiety, decreased number of other related panic disorders as well as less severe depression. An immediate and symptomatic relief is extremely important as it will help in reducing length of hospital stay, number of hospital admissions, costs associated with medical testing and loss of wages.<sup>6</sup> The treatment of vertigo should be organized and methodical to maximize patient satisfaction. The treatment aims at the elimination of vertigo and vestibular suppressants and antiemetic drugs (such as prochlorperazine, meclizine and diazepam) are the mainstay of treatment of vertigo. Prochlorperazine improves vestibular as well as associated vegetative symptoms of vertigo. The most commonly used pharmacological drugs are elucidated in the following paragraphs.<sup>7</sup>

Based on the available literature, the most commonly used therapeutic drugs are presented in Table 2.<sup>2,8,9</sup>

### Cinnarizine

Cinnarizine is a calcium channel blocker which has vestibular suppressant effect. It also has anticholinergic, antihistaminic effects. Cinnarizine is recommended when antihistamines and antiemetics have had no effect. The effect of suppression of the vestibular response is achieved for a longer period of 6-8 weeks. The most common side effect of cinnarizine is drowsiness and also weight gain. Gastric disturbances and depression may also occur, although less commonly. Calcium

channel blockers like cinnarizine are drugs which are not recommended in pregnancy.<sup>9,10</sup>

### Betahistine

Betahistine has been claimed to be one of the most frequently chosen anti-vertigo drug globally. Betahistine is involved in facilitating vestibular compensation. The efficacy of this drug in vertigo management is due to its action on histamine receptors.<sup>2,11</sup>

Betahistine is used in the management of vertigo and vestibular pathologies with different etiologies. Its therapeutic effect is dependent on the dose and the duration of the treatment.<sup>12</sup> However, betahistine is not fully approved by the Food and Drug Administration (FDA) in the US. It is moderately effective in suppressing the symptoms of Meniere's disease.<sup>10</sup>

The optimal therapeutic effects are visible only after a few months; hence, it is recommended to use it for 2-3 months.<sup>2</sup> Comparatively, prochlorperazine is prescribed for short-term (up to 7 days) symptomatic management of vertigo and it also takes care of extrapyramidal symptoms.<sup>7</sup>

### Prochlorperazine

Prochlorperazine has been used in the treatment of vertigo since a long time. It was reported to be superior to be cinnarizine in the treatment of vertigo irrespective of the central or peripheral vertigo, in a study conducted in Indian patients.<sup>13</sup> Another study showed that where cinnarizine caused drowsiness in 8% of the study population, prochlorperazine caused drowsiness in only 3% of the study patients.<sup>13</sup> In a registry of patients, prochlorperazine provided immediate relief in BPPV and long-term benefits in Meniere's disease.<sup>14</sup> According to a review, prochlorperazine has anticholinergic and antidopaminergic effects and thus relieves the patient from the very debilitating rotating/spinning sensation and also from the associated vegetative symptoms.<sup>15</sup> Dizziness is commonly associated with nausea and vomiting in patients with vestibular disorder which can be debilitating. Prochlorperazine has been a safe, effective and appropriate option for the treating

**Table 2.** Commonly Used Therapeutic Drugs in the Treatment of Vertigo<sup>2,8,9</sup>

Drugs	Dose and duration	Mechanism of action	Side effects	Used in
Cinnarizine	75 mg/day for 3 days	Selective calcium channel blocker, acts primarily on the peripheral vestibular labyrinth by affecting local calcium ion flux. Beneficial in vertiginous syndrome caused by over-reactivity or unbalanced activity of labyrinthine apparatus in the inner ear	Sedation Pedal edema Extrapyramidal disorders Weight gain	Vertigo (peripheral cases)
Cinnarizine + dimenhydrinate	Cinnarizine 20 mg + dimenhydrinate 40 mg/day for 3 days	Cinnarizine regulates vestibular calcium influx of the labyrinth and improves cerebral circulation Dimenhydrinate regulates vestibular nuclei and adjacent vegetative nuclei and adjacent vegetative centers in the brainstem Dimenhydrinate augments the actions of cinnarizine	Affect the occupation and cognition extrapyramidal side effects High somnolence	Vertigo Motion sickness
Betahistine	48 mg/day, 3-6 months	Increased cochlear and vestibular blood flow Enhances histamine turnover in the central nervous system Increase in the level of histamine in damaged vestibular nuclei diminishes inhibition by intact vestibular nuclei by H3 hetero-antagonistic action	Mild side effects such as gastrointestinal complaints, fatigue and altered taste	Vertigo
Prochlorperazine	10-15 mg/day	Reduces abnormal excitement in the brain Does not impact any measure of nystagmic or perceptual vestibular function	Drowsiness and dizziness Dry mouth	Acute vertigo and dizziness Nausea, vomiting Anxiety
Diazepam	5 mg/6-8 hours	Causes inhibition throughout the central nervous system, including activity in the vestibular nerve and vestibular nuclei	Drowsiness Dizziness Respiratory depression	Anxiety, vertigo

dizziness associated with nausea and/or vomiting in vertiginous disorders.<sup>16</sup> A study showed that prochlorperazine with supplemental anti-nausea and antiemetic properties significantly reduced recurrence of both these symptoms in the first week of treatment initiation.<sup>14</sup>

### Combination Drug: Cinnarizine + Dimenhydrinate

The combination of cinnarizine and dimenhydrinate is an effective and well-tolerated option for the symptomatic treatment of vertigo.<sup>17</sup> However, in the treatment of vertigo, combination of drugs belonging to the same class is not recommended.<sup>18</sup> It has also been shown that long-term use of vestibular suppressants and/or tranquilizers is counterproductive for vestibular compensation. These agents should only be considered

in case of truly acute vertigo and stopped as soon the symptoms subside.<sup>19</sup>

A double-blind, placebo-controlled, repeated measures design study was conducted with healthy male volunteers in order to investigate the clinical and cognitive side effects of baclofen, meclizine, dimenhydrinate + cinnarizine and promethazine + d-amphetamine. It was shown that dimenhydrinate-cinnarizine combination had a negative influence on the working memory. Other significant side effects of the combination included sleepiness and blurred vision.<sup>20</sup>

Another study also showed that dimenhydrinate adversely affects psychomotor function; however, single dose cinnarizine is not associated with any negative effects on performance.<sup>21</sup> Cinnarizine is

also known to cause drowsiness, in turn hampering the performance of complex motor tasks such as driving a car. It is also not recommended for use in pregnancy.<sup>9,10</sup>

Another important factor which can not be missed in the safety and efficacy studies on combination of cinnarizine and dimenhydrinate is that since the study population comprises of a heterogenous group and there is a lack of control group, the susceptibility of vertigo symptoms to placebo effects must be adequately considered when interpreting the efficacy results.<sup>22</sup>

### CLINICAL PRACTICE UPDATES

The American Academy of Otolaryngology-Head and Neck Surgery Foundation have issued comprehensive clinical practice guidelines to identify and treat patients with BPPV, which is one of the most common vestibular disorder in adults.<sup>23</sup>

The guidelines are intended to improve quality of care and outcomes for BPPV by improving the accurate and efficient diagnosis of the condition; limiting the inappropriate use of ancillary tests such as radiographic imaging and vestibular testing, and to promote the use of effective repositioning maneuvers for treatment.<sup>23</sup>

The guidelines strongly recommend clinicians to diagnose posterior semicircular canal BPPV with an office-based diagnostic test and also test patients for a second type of BPPV affecting the lateral semicircular canal when initial testing is inconclusive.<sup>23</sup> The guidelines strongly recommend that clinicians should treat or refer to a clinician who have expertise in treating patients with posterior canal BPPV with a canalith repositioning procedure (CRP). It also recommends that clinicians should not recommend post-procedural postural restrictions after CRP for posterior canal BPPV. Another recommendation is that the clinician may offer vestibular rehabilitation in the treatment of BPPV.<sup>23</sup>

The guidelines are against the routine use of vestibular suppressant medications such as antihistamines or benzodiazepines to treat BPPV. This is to decrease the use of unnecessary medications with potentially harmful side effects as well as cost of treatment. The guidelines state that the medications may be used for short-term management of autonomic symptoms, such as nausea or vomiting, in a severely symptomatic patient. Antiemetics may also be considered for prophylaxis for patients who have previously had severe nausea and/or vomiting with the Dix-Hallpike

maneuvers and in whom a CRP is planned. It is also advisable for a clinician to provide counseling that the rates of cognitive dysfunction, falls, drug interactions and machinery and driving accidents increase with use of vestibular suppressants.<sup>23</sup> Pharmacologic treatment seems to have no role in the treatment of BPPV. Vestibular suppressant medications should be avoided since they can interfere with central compensation and may increase the risk of falls.<sup>24</sup>

In those cases where vertigo is due to vestibular neuritis, treatment is done with medications and vestibular rehabilitation. Antiemetics and antinausea medications should not be used for more than 3 days. Vertigo and associated nausea or vomiting can be treated with a combination of antihistaminic, antiemetic or benzodiazepine.<sup>24</sup>

In the treatment of vertigo caused in Meniere's disease, vestibular suppressant medications may be used for acute attacks. Prochlorperazine, promethazine and diazepam have been found to be effective.<sup>24</sup>

### PRACTICE CHANGING SUTRA

- A clinician can improve his overall vertigo management practices by giving due importance to associated symptoms being reported by large number of patients, which is important for overall patient satisfaction.
- Pharmacological therapy should only be considered in case of truly acute vertigo and should be stopped as soon as the symptoms subside.
- Symptomatic treatment is of particularly important role, regardless of the etiology of vertigo.
- Vestibular suppressant medications such as benzodiazepines and antihistamines should not be used to treat BPPV.
- If vertigo is due to vestibular neuritis, medications and vestibular rehabilitation are the preferred approach to treatment.
- In case of Meniere's disease, vestibular suppressant medications may be used.

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