



## Therapeutic Class Review<sup>SM</sup>

### GI: Antiemetics – nabilone (Cesamet<sup>TM</sup>)

February 2007

#### New Product for Review:

Nabilone (Cesamet<sup>TM</sup>) [Valeant]

#### Dossier Provided by Manufacturer: No Dossier Evaluation: not applicable

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

#### Executive Summary

- Nabilone (Cesamet) and dronabinol (Marinol) are cannabinoid agonists; cannabinoids are compounds which occur naturally in marijuana plants.
- Both compounds were approved in 1985. Nabilone (Cesamet) was not marketed in the U.S. until 2006.
- Nabilone (Cesamet) is marketed as:
  - A synthetic cannabinoid.
  - More convenient than dronabinol (Marinol) due to its twice-a-day, weight-based dosing.
  - An option that is not detected as THC on urine testing, and can avoid patient issues with drug testing for employment or associated stigmas.
- Conventional therapies for CINV include 5-HT<sub>3</sub> antagonists (ondansetron [Zofran], dolasetron [Anzemet], granisetron [Kytril]), corticosteroids (dexamethasone), and aprepitant (Emend).
- Nabilone (Cesamet) and dronabinol (Marinol) are indicated for patients who have not responded to conventional antiemetic agents.
- Alternatives to cannabinoids include metoclopramide, droperidol, prochlorperazine, and promethazine.
- Nabilone (Cesamet) is a Schedule II Controlled Substance under the Federal Controlled Substance Act. Dronabinol (Marinol) is Schedule III, however, may be considered Schedule II under more stringent state regulations.
- The inability to detect THC in urine after ingestion of nabilone (Cesamet) may have the unintended consequence of increasing the "street value" of this medication.

#### Evidence

- There was no useful evidence for nabilone (Cesamet) versus placebo, or versus active comparator, in the treatment of CINV.
- Study flaws included large numbers lost to follow up, lack of intent-to-treat (ITT) analysis, and small numbers of subjects.

- There are no head-to-head studies comparing nabilone (Cesamet) with dronabinol (Marinol).
- There are no studies that evaluate the efficacy of nabilone (Cesamet) in CINV when first-line antiemetics are not effective or not tolerated.
- Nabilone (Cesamet) studies were not designed or powered for safety.
- The types of adverse reactions reported in nabilone (Cesamet) studies are similar to those reported for dronabinol (Marinol); however, the lack of a head-to-head study does not allow for comparison of tolerability differences between the products.

## Decision

- Nabilone (Cesamet) is a non-formulary/non-preferred product because:
  - There are many preferred/formulary options;
  - There is no evidence of superior efficacy of nabilone (Cesamet) over preferred/formulary alternatives; and
  - There are safety and tolerability concerns with nabilone (Cesamet).

## Products

Drug Products	FDA approval <sup>a</sup>	FDA approved indications	Usual Dose/Route	Potential Off-label Uses <sup>b</sup>
aprepitant (Emend <sup>®</sup> ) <sup>1</sup>	3/2003	<ul style="list-style-type: none"> <li>• In combination with other antiemetics in the prevention of acute and delayed nausea and vomiting (N/V) associated with highly and moderately emetogenic chemotherapy.</li> <li>• Prevention of post-operative nausea and vomiting.</li> </ul>	125 mg orally on day 1, and 80 mg daily on days 2 and 3 (chemo-therapy).	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, hyperemesis gravidarum.
dolasetron (Anzemet <sup>®</sup> ) <sup>2</sup>	9/1997	<ul style="list-style-type: none"> <li>• Prevention of N/V associated with moderately emetogenic chemotherapy.</li> <li>• Prevention of post-operative N/V.</li> </ul>	Adults: 100 mg orally within 1 hour before chemotherapy.  Pediatric: 1.8mg/kg within 1 hour before chemotherapy; maximum of 100 mg per dose (ages 2 to 16 years).	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, radiation-induced nausea and vomiting, hyperemesis gravidarum.
dronabinol (Marinol <sup>®</sup> ) <sup>3</sup>	5/1985	<ul style="list-style-type: none"> <li>• Anorexia associated with weight loss in patients with AIDS.</li> <li>• N/V associated with chemotherapy in patients who have failed to respond to conventional antiemetics.</li> </ul>	5 mg/m <sup>2</sup> orally four to six times per day. May increase in 2.5mg/m <sup>2</sup> increments up to 15 mg/m <sup>2</sup> per dose.	Glaucoma, hiccups, pain, multiple sclerosis.
granisetron (Kytril <sup>®</sup> ) <sup>4</sup>	3/1995	Prevention of N/V associated with: <ul style="list-style-type: none"> <li>• Emetogenic cancer therapy.</li> <li>• Radiation, including total body irradiation (TBI) and fractionated abdominal radiation.</li> </ul>	1 mg orally twice daily or 2 mg once daily.	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, migraines, neuroleptic-induced akathisia, radiation-induced N/V, hyperemesis gravidarum.
metoclopramide (Reglan) <sup>5</sup>	12/1980	Symptomatic relief of: <ul style="list-style-type: none"> <li>• Gastroesophageal reflux.</li> <li>• Diabetic Gastroparesis.</li> </ul>	For CINV: 30 mg orally every 4 to 6 hours for 5 days.	CINV, anorexia nervosa, migraine headaches, postoperative N/V.
nabilone (Cesamet <sup>™</sup> ) <sup>6</sup>	12/1985	<ul style="list-style-type: none"> <li>• Treatment of N/V associated with cancer chemotherapy who have failed to respond to conventional antiemetic Rx.</li> </ul>	1 to 2 mg orally twice daily; maximum of 6 mg per day.	Anorexia associated with weight loss in patients with AIDS, anxiety, glaucoma, dystonia.

ondansetron (Zofran <sup>®</sup> ) <sup>7</sup>	12/1992	Prevention of N/V: <ul style="list-style-type: none"> <li>• Due to moderately and highly emetogenic cancer chemotherapy.</li> <li>• Due to radiotherapy (TBI, single high-dose fraction to the abdomen, or daily fractions to the abdomen).</li> <li>• In postoperative patients.</li> </ul>	Adults: 8 mg orally two to three times per day (12 years of age and older).  Pediatrics: 4 mg orally three times per day (ages 4 to 11 years).	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, psychotic disorder with Parkinson's disease, hyperemesis gravidarum.
prochlorperazine (Compazine <sup>®</sup> ) <sup>8</sup>	10/1956	<ul style="list-style-type: none"> <li>• Severe N/V.</li> <li>• Schizophrenia.</li> <li>• Non-psychotic anxiety.</li> </ul>	<ul style="list-style-type: none"> <li>• 5 to 10 mg three to four times /day.</li> <li>• 25 mg rectally twice daily.</li> </ul>	Dizziness, headache.

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> As listed in ©1974 – 2007 Thomson MICROMEDEX database or as referenced.

## References

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