



Therapeutic Class ReviewSM

GI: Antiemetics – nabilone (CesametTM)

February 2007

New Product for Review:

Nabilone (CesametTM) [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)

Available Therapeutic Alternatives:

Preferred/Formulary	Non-preferred/non-formulary
dolasetron (Anzemet [®]) [Sanofi-Aventis]	aprepitant (Emend [®]) [Merck & Co]
granisetron (Kytril [®]) [Roche]	dronabinol (Marinol [®]) [Unimed]
ondansetron (Zofran [®]) [GlaxoSmithKline]	nabilone (Cesamet TM) [Valeant]
metoclopramide (Reglan [®]) [generics]	
prochlorperazine (Compazine [®]) [generics]	
promethazine (Phenergan [®]) [generics]	

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-HT3 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.

Considerations in subpopulations:

	nabilone (Cesamet)	dronabinol (Marinol)
<i>Pediatrics:</i>	Safety and effectiveness of nabilone in patients under 18 years of age has not been established. Caution is recommended in this population due to the psychoactive effects of this agent.	The pediatric dosage for dronabinol in the treatment of CINV is the same as in adults (based on BSA). Caution is recommended in this population due to the psychoactive effects of this agent.
<i>Geriatrics:</i>	Clinical studies with nabilone did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger adults. Caution is advised in elderly patients due to decreases in renal and hepatic function, and the fact this population is more at risk for psychoactive and cardiac effects of this agent.	In antiemetic studies, no difference in efficacy with dronabinol was apparent in patients over 55 years of age. Caution is advised in elderly patients because they are more sensitive to neurological, psychoactive, and postural hypotensive effects of the agent.
<i>Racial/Ethnicity:</i>	No information available.	
<i>Gender:</i>	No information available.	

Conclusion

- 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 ^a	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
aprepitant (Emend®) ¹	3/2003	<ul style="list-style-type: none"> • In combination with other antiemetics in the prevention of acute and delayed nausea and vomiting (N/V) associated with highly and moderately emetogenic chemotherapy. • Prevention of post-operative nausea and vomiting. 	125 mg orally on day 1, and 80 mg daily on days 2 and 3 (chemotherapy).	\$352 (3-day course) Note: used in addition to other antiemetics	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, hyperemesis gravidarum.
dolasetron (Anzemet®) ²	9/1997	<ul style="list-style-type: none"> • Prevention of N/V associated with moderately emetogenic chemotherapy. • Prevention of post-operative N/V. 	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).	\$382	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, radiation-induced nausea and vomiting, hyperemesis gravidarum.
dronabinol (Marinol®) ³	5/1985	<ul style="list-style-type: none"> • Anorexia associated with weight loss in patients with AIDS. • N/V associated with chemotherapy in patients who have failed to respond to conventional antiemetics. 	5 mg/m ² orally four to six times per day. May increase in 2.5mg/m ² increments up to 15 mg/m ² per dose.	\$460 (Max: \$1,378) [1.8m ² patient]	Glaucoma, hiccups, pain, multiple sclerosis.
granisetron (Kytrel®) ⁴	3/1995	Prevention of N/V associated with: <ul style="list-style-type: none"> • Emetogenic cancer therapy. • Radiation, including total body irradiation (TBI) and fractionated abdominal radiation. 	1 mg orally twice daily or 2 mg once daily.	\$597	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, migraines, neuroleptic-induced akathisia, radiation-induced N/V, hyperemesis gravidarum.
metoclopramide (Reglan) ⁵	12/1980	Symptomatic relief of: <ul style="list-style-type: none"> • Gastroesophageal reflux. • Diabetic Gastroparesis. 	For CINV: 30 mg orally every 4 to 6 hours for 5 days.	\$4	CINV, anorexia nervosa, migraine headaches, postoperative N/V.
nabilone (Cesamet™) ⁶	12/1985	<ul style="list-style-type: none"> • Treatment of N/V associated with cancer chemotherapy who have failed to respond to conventional antiemetic treatments. 	1 to 2 mg orally twice daily; maximum of 6 mg per day.	\$400 (Max: \$600)	Anorexia associated with weight loss in patients with AIDS, anxiety, glaucoma, dystonia.

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of November 2006 for 5 days of therapy, unless otherwise specified.

^c As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

Products (Continued)

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
ondansetron (Zofran [®]) ⁷	12/1992	Prevention of N/V: <ul style="list-style-type: none"> • Due to moderately and highly emetogenic cancer chemotherapy. • Due to radiotherapy (TBI, single high-dose fraction to the abdomen, or daily fractions to the abdomen). • In postoperative patients. 	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).	\$438 to \$656 \$394	Idiopathic nausea and vomiting, treatment of postoperative nausea and vomiting, psychotic disorder with Parkinson's disease, hyperemesis gravidarum.
prochlorperazine (Compazine [®]) ⁸	10/1956	<ul style="list-style-type: none"> • Severe N/V. • Schizophrenia. • Non-psychotic anxiety. 	<ul style="list-style-type: none"> • 5 to 10 mg three to four times /day. • 25 mg rectally twice daily. 	\$3 \$19	Dizziness, headache.

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of November 2006 for 5 days of therapy, unless otherwise specified.

^c As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

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