Drug Use Research & Management Program
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Month/Year of Review: November 2013 **Date of Last Review:** May 2006
PDL Classes: Antiemetics, Newer **Source Document:** DERP

Current Status of PDL Class:
- Preferred Agents: ONDANSETRON TAB RAPDIS/SOLUTION/TABLET
- Non-Preferred Agents: APREPITANT/FOSAPREPITANT (EMEND®), DOXYLAMINE SUCCINATE/PYRIDOXINE HCL (DICLEGIS®), DOLASETRON (ANZEMET®), GRANISETRON HCL, GRANISETRON TRANSDERMAL PATCH (SANCUSO®), ONDANSETRON ORAL FILM (ZUPLENZ®), PALONOSETRON (ALOXI®)

Previous Conclusions and Recommendation:
- In patients with post-operative nausea and vomiting (PONV) and chemotherapy induced nausea and vomiting (CINV):
  - Dolasetron, granisetron and ondansetron are equally effective in preventing nausea or vomiting.
  - Palonsetron may be superior to dolasetron and ondansetron for acute/delayed complete response rates.
  - Aprepitant has been studied as an add-on for standard therapy.
- In patients with radiotherapy-induced nausea and vomiting (RINV):
  - Granisetron and ondansetron showed no difference in efficacy.
- In pregnant patients:
  - Ondansetron was not superior to promethazine for effectiveness, but was less sedating.
  - Long term studies show no difference in number of live births, proportion of infant deformities, and birth weight between ondansetron and the active control groups.
- Heterogeneity of trials precludes accurate assessment of comparative tolerability or safety for the newer antiemetic drugs.
- Ondansetron is superior to granisetron for complete response rates in subpopulations based on a predisposition to nausea/vomiting such as motion sickness or previous treatment with emetogenic chemotherapy.

PA Criteria: Prior authorization is in place to: promote preferred drugs, reserve costly antiemetics for appropriate indications, restrict chronic use (> 3 days per week), and if chemotherapy is more frequent than once weekly, approve a quantity sufficient for three days beyond the duration of chemotherapy (Appendix 1).

Conclusions and Recommendations:
- There is evidence that palonsetron may be superior to other 5HT3 antagonists in the treatment of chemotherapy induced nausea and vomiting for moderately emetogenic chemotherapy and that ondansetron, dolasetron, and granisetron are equally effective.
- There is low quality evidence that the combination of doxylamine/pyridoxine led to significantly greater improvement in nausea vomiting symptoms as compared with placebo (-4.8 PUQE score vs. -3.9; p=0.006) but insufficient comparative evidence compared to other available agents. Maintain as non-preferred.
- Evaluate comparative costs in executive session.

Methods:
A recent DERP scan searched Ovid MEDLINE from January 2009 to April 2013 for included drugs and limits for humans, English, and controlled clinical trials. The Cochrane Collection, Agency for Health Care Research and Quality (AHRQ), National Institute for Clinical Evidence (NICE), Canadian Agency for Drugs and Technology in Health (CADTH), Dynamed and Medline OVID were searched for high quality systematic reviews. The FDA website was searched for new drugs,

indications, and safety alerts. Finally, a search for new or updated guidelines was conducted at the AHRQ National Guideline Clearinghouse (NGC).

New Systematic Reviews:
In 2009, the Oregon evidence-based Practice Center completed an update report for DERP on the newer antiemetics. The objective of the review was to evaluate the comparative effectiveness and harms of newer antiemetic drugs including the type 3 serotonin (5-HT3) and substance P/neurokinin 1 (NK1) antagonists. Adults or children with nausea and vomiting related to chemotherapy, radiation, surgery and pregnancy were included. A total of 34 new studies were included in the update (in addition to the 185 from the original report). Main findings were as follows:

Prevention of chemotherapy-induced nausea and vomiting:
- The numbers of patients with complete response were similar with ondansetron, dolasetron, and granisetron, with no consistent statistically significant differences.
- The evidence does not indicate differences between oral and intravenous or between various oral formulations.

Prevention of postoperative nausea and vomiting:
- There were no consistent statistically significant differences in efficacy between dolasetron, granisetron, or the orally disintegrating tablet formulation of ondansetron with traditional ondansetron or in comparisons between dolasetron and granisetron.

Treatment of established nausea and vomiting:
- One trial showed dolasetron was superior to ondansetron in reducing the need for rescue therapy (40% vs. 70%; p=0.004) but there was no difference in the number of nausea and vomiting related hospital admissions.
- One trial demonstrated no statistically significant differences between granisetron and ondansetron in complete response rates (60% for granisetron 0.1 mg, 68% for granisetron 1 mg, 47% for ondansetron).

Tolerability and Safety:
- In chemotherapy patients, 3 trials showed that ondansetron was associated with higher rates of dizziness and abnormal vision than dolasetron and granisetron.
- Dolasetron was associated with higher rates of constipation and diarrhea than ondansetron in 1 trial.
- For the prevention of postoperative nausea and vomiting, no consistent differences were seen for overall adverse events withdrawals due to adverse events, or any particular adverse event.

Canadian Agency for Drugs and Technologies in Health (CADTH)
In February 2013, CADTH produced a rapid response review evaluating ondansetron for the management of chemotherapy induced nausea and vomiting in pediatric patients.[1] A limited literature search was conducted from January 2008 to January 2013. Key findings were as follows:
- For the management of CINV in pediatrics, the effects of ondansetron plus dexamethasone appeared to be better than ondansetron alone or placebo.
- There was no statistically significant difference in antiemetic effect between ondansetron and tropisetron.
- There were some inconsistencies in the results for antiemetic effects of ondansetron compared with granisetron.
- Numerical values suggested that the antiemetic effects of palonsetron was greater compared to ondansetron, however it was unclear if the differences were statistically significant.
- Headache was the most commonly reported adverse event and appeared to be similar for various drug comparisons; however, adverse events were reported in few studies.

Guidelines:
The American Society of Clinical Oncology released an updated practice guideline for antiemetics in Oncology in November 2011.[2] The guideline is based on a systematic review of the literature funded by AHRQ. Recommendations are grouped based on chemotherapy regimens and are as followed:

- *Highly emetogenic agents:* The three-drug combination of an NK1 receptor antagonist, a 5-HT3 receptor antagonist, and dexamethasone is recommended
- *Moderately emetogenic agents:* The two-drug combination of palonosetron and dexamethasone is recommended. If palonosetron is not available, clinicians may substitute a first-generation 5-HT3 receptor antagonist, preferably granisetron or ondansetron. This was based on evidence that supports the equivalency of granisetron and ondansetron and findings that suggested palonsetron provides superior protection against both nausea and vomiting particularly during the period from 24-120 hours after chemotherapy.
- *Low emetogenic agents:* A single 8-mg dose of dexamethasone is suggested.
- Both dexamethasone and a 5-HT3 antagonist are recommended for patients undergoing high-dose chemotherapy.

New drugs:
In April 2013, the combination of doxylamine and pyridoxine (Diclegis®) was approved for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management. This combination was previously available in a fixed-dose combination (Bendectin) for morning sickness, but was voluntarily withdrawn from the US in 1983 because of claims of teratogenicity that have seen been disproven.[3] Approval was based on the results of a 15-day randomized, double-blind placebo-controlled trial in 259 pregnant women with nausea and vomiting not responding to lifestyle changes.[4] Patients were randomized to receive the combination tablets with 10 mg each of doxylamine and pyridoxine or placebo. The combination of doxylamine/pyridoxine led to significantly greater improvement in nausea vomiting symptoms as compared with placebo (-4.8 PUQE score vs. -3.9; p=0.006). Women receiving active treatment were significantly more likely to request continued therapy than those on placebo (48.9% vs. 32.8%; p=0.009).

New Formulations/Indications:
Granisetron transdermal patch (Sancuso®) was FDA approved in September 2008.

Ondansetron oral film (Zuplenz®) was FDA approved in Jul 2010.

New FDA safety alerts:
In December 2012, the FDA notified health care professionals that the 32 mg, single IV dose of ondansetron will no longer be marketed because of the risk of QT interval prolongation, which can lead to Torsades de Pointes. In June 2012, the FDA issued a drug safety communication recommending against the use of a 32 mg IV dose of ondansetron, due to a dose-dependent QT prolongation demonstrated in a QT study. This was an update of a 2011 ongoing safety review and announcement advising against use in those with congenital long QT study. The FDA notes that the lower IV regimen of 0.15 mg/kg every 4 hours for 3 doses may be used in adults with chemotherapy-induced nausea and vomiting, as long as no single dose exceeds 16 mg. The FDA recommended ECG monitoring in patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmias, or concomitant administration of other QT prolonging medications, while receiving ondansetron.

In September of 2011 the FDA approved a safety labeling change warning for Anzemet (dolasetron mesylate) tablet and injection indicating that it has been shown to cause dose dependent prolongation of the PR and QRS interval and reports

of second or third degree atrioventricular block, cardiac arrest and serious ventricular arrhythmias including fatalities in both adult and pediatric patients for which it should be used with caution certain patients.

In December 2010, FDA notified healthcare professionals that the injection form of dolasetron should no longer be used to prevent nausea and vomiting associated with chemotherapy in pediatric and adult patients, due to risk of developing torsade de pointes.

New Trials (Appendix 2):

Since the 2009 DERP update, 7 head to head trials were identified. Placebo-controlled trials were not included.

Habib 2011[5]	**Ondansetron vs. apereitant**	**PONV in adults**
Boccia 2011[6]	**Granisetron transdermal vs granisetron**	**Chemotherapy in adults**
Metaxari 2011[7]	**Granisetron vs. ondansetron**	**PONV in adults**
Sidique 2011[8]	**Granisetron vs. ondansetron**	**Chemotherapy in adults**
Basu 2011[9]	**Polonsetron vs. ondansetron vs. granisetron**	**PONV in adults**
Moon 2012[10]	**Polonsetron vs. ondansetron**	**PONV in adults**
Park 2011[11]	**Polonsetron vs. ondansetron**	**PONV in adults**

References:

1. Canadian Agency for Drugs and Technologies in Health. Ondansetron for the Management of Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients: A Review of the Clinical Effectiveness, Safety and Guidelines. 2013. Available at: http://www.cadth.ca/media/pdf/htis/apr-2013/RC0424-Ondansetron-Final.pdf.

2. Basch E, Hesketh PJ, Kris MG, Prestrud AA, Temin S, Lyman GH. Antiemetics: american society of clinical oncology clinical practice guideline update. *J Oncol Pract*. 2011;7(6):395–398. doi:10.1200/JOP.2011.000397.

3. Diclegis for nausea and vomiting of pregnancy. *Med Lett Drugs Ther*. 2013;55(1422):61–62.

4. Koren G, Clark S, Hankins GDV, et al. Effectiveness of delayed-release doxylamine and pyridoxine for nausea and vomiting of pregnancy: a randomized placebo controlled trial. *Am J Obstet Gynecol*. 2010;203(6):571.e1–7. doi:10.1016/j.ajog.2010.07.030.

5. Habib AS, Keifer JC, Borel CO, White WD, Gan TJ. A comparison of the combination of aprepitant and dexamethasone versus the combination of ondansetron and dexamethasone for the prevention of postoperative nausea and vomiting in patients undergoing craniotomy. *Anesth Analg*. 2011;112(4):813–818. doi:10.1213/ANE.0b013e3181ff47e2.

6. Boccia RV, Gordan LN, Clark G, Howell JD, Grunberg SM, Sancuso Study Group. Efficacy and tolerability of transdermal granisetron for the control of chemotherapy-induced nausea and vomiting associated with moderately and highly emetogenic multi-day chemotherapy: a randomized, double-blind, phase III study. *Support Care Cancer*. 2011;19(10):1609–1617. doi:10.1007/s00520-010-0990-y.

7. Metaxari M, Papaioannou A, Petrou A, Chatzimichali A, Pharmakalidou E, Askitopoulou H. Antiemetic prophylaxis in thyroid surgery: a randomized, double-blind comparison of three 5-HT3 agents. *J Anesth*. 2011;25(3):356–362. doi:10.1007/s00540-011-1119-2.

8. Siddique R, Hafiz MG, Rokeya B, Jamal CY, Islam A. Ondansetron versus granisetron in the prevention of chemotherapy induced nausea and vomiting in children with acute lymphoblastic leukemia. *Mymensingh Med J*. 2011;20(4):680–688.

9. Basu A, Saha D, Hembrom BP, Roy A, Naaz A. Comparison of palanosetron, granisetron and ondansetron as anti-emetics for prevention of postoperative nausea and vomiting in patients undergoing middle ear surgery. *J Indian Med Assoc*. 2011;109(5):327–329.

10. Moon YE, Joo J, Kim JE, Lee Y. Anti-emetic effect of ondansetron and palonosetron in thyroidectomy: a prospective, randomized, double-blind study. *Br J Anaesth*. 2012;108(3):417–422. doi:10.1093/bja/aer423.

11. Park SK, Cho EJ. A randomized, double-blind trial of palonosetron compared with ondansetron in preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery. *J Int Med Res*. 2011;39(2):399–407.

Appendix 1

Antiemetics, New

Goal(s):

- Promote Preferred drugs.
- Reserve costly antiemetics for appropriate indications.
- Restrict chronic use (> 3 days per week).
- If chemotherapy is more frequent than once weekly, approve a quantity sufficient for three days beyond the duration of chemotherapy.

Length of Authorization: 3 days to 6 months (criteria specific)

Requires PA:

- Non-preferred drugs.

Preferred Alternatives: Preferred alternatives listed at: http://www.orpdl.org/ ~~http://www.oregon.gov/DHS/healthplan/tools_prov/pdl.shtml~~

Check the Reason for PA:

- Non-preferred drugs will deny on itiation
- Preferred drugs will deny only when maximum dose exceeded (www.orpdl.org)

HICL	Generic	Brand	Quantity Limit
025058	Aprepitant	Emend	3 doses/ 7 days
016576	Dolasetron	Anzemet	9 doses/ 7 days
007611	Granisetron	Kytril Tablets Kytril solution	6 doses / 7 days (30 ml liquid)

Approval Criteria		
1. What is the diagnosis?	Record ICD9 code	
2. Is the drug requested preferred?	**Yes:** Go to #4	**No**: Go to #3
3. Will the prescriber consider a change to a preferred product? Message: • Preferred products do not require PA for <4 days/week. • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the ~~Health Resources Commission (HRC).~~Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform provider of covered alternatives in class and dose limits. If dose > limits, continue to #4.	**No:** Go to #4
4. Is client currently diagnosed with cancer AND receiving chemotherapy or radiation therapy more frequently than every 7 days?	**Yes:** Approve for 3 days past length of therapy (Chemo regimen more frequently than weekly)	**No:** Go to #5

<table>
<tr><td>5. Does client have refractory nausea that would require hospitalization or ER visits?</td><td>Yes: Go to #6</td><td>No: go to #8</td></tr>
<tr><td>6. Has client tried and failed two conventional antimetics, listed below?

<table><tr><th>Generic Name</th><th>Brand Name</th></tr><tr><td>Metoclopramide</td><td>Reglan</td></tr><tr><td>Prochlorperazine</td><td>Compazine</td></tr><tr><td>Promethazine</td><td>Phenergan</td></tr></table></td><td>Yes: Approve up to 6 months.</td><td>No: Go to #7</td></tr>
<tr><td>7. Does client have contraindications to conventional antiemetics, e.g. Allergy; or cannot tolerate?</td><td>Yes: Document reason and approve up to 6 months.
(Contraindications to required alternative medications)</td><td>No: Pass to RPH; Go to #8</td></tr>
<tr><td colspan="3">8. RPH only:

All other indications need to be evaluated as to whether they are above the line or below the line.

• Above: Deny, (Medical Appropriateness)
• Below: Deny, (Not Covered by the OHP)</td></tr>
</table>

P&T/DUR Action: 9/24/09 (DO/KK), 2/23/06, 2/24/04, 11/18/03, 9/9/03, 5/13/03, 2/11/03
Revision(s): 1/1/10, 7/1/06, 3/20/06, 6/30/04 (added aprepitant), 3/1/04 (removed injectables), 6/19/03
Initiated: ?

Appendix 2: Head to head randomized controlled trials:

Basu, A., D. Saha, et al. (2011). "Comparison of palanosetron, granisetron and ondansetron as anti-emetics for prevention of postoperative nausea and vomiting in patients undergoing middle ear surgery." Journal of the Indian Medical Association 109(5): 327-329.
The objective of the study was to compare the efficacy of palanosetron (0.25 mg), granisetron (3.0 mg) and ondansetron (8.0 mg) used as anti-emetics for the prevention of postoperative nausea/vomiting in patients undergoing middle ear surgery. The study was done among 75 adult patients (age group 30-45 years) of which 50 were males and rest (25) females, all of ASA I and ASA II. The patients were randomly allocated into 3 equal groups: Group I (n = 25) received injection palanosetron (0.25 mg) IV, group II (n = 25) received injection granisetron (3 mg) IV and group III (n = 25) received injection ondansetron (8.0 mg) IV at the end of the surgical procedure. A standard general anaesthesia technique was employed. Emetic episodes and safety assessments were performed during two periods of 0-6 hours in the postanaesthesia care unit and 6-24 hours in the ward after anaesthesia. The incidence of emesis-free patients during the 0- 6 hours period was 100% for group I; 72% for group II and 56% for group III. During the 6-24 hours period incidence of emesis-free patients were 96% for group I; 56% for group II and 32% for group III. So to conclude, a single dose of palanosetron (0.25 mg) is a superior anti-emetic to granisetron (3.0 mg) or ondansetron (8.0 mg) in complete prevention of postoperative nausea and vomiting after middle ear surgery during the first 24 hours period.

Boccia, R. V., L. N. Gordan, et al. (2011). "Efficacy and tolerability of transdermal granisetron for the control of chemotherapy-induced nausea and vomiting associated with moderately and highly emetogenic multi-day chemotherapy: a randomized, double-blind, phase III study." Supportive Care in Cancer 19(10): 1609-1617.
PURPOSE: A novel transdermal formulation of granisetron (the granisetron transdermal delivery system (GTDS)) has been developed to deliver granisetron continuously over 7 days. This double-blind, phase III, non-inferiority study compared the efficacy and tolerability of the GTDS to daily oral granisetron for the control of chemotherapy-induced nausea and vomiting (CINV).
PATIENTS AND METHODS: Six hundred forty-one patients were randomized to oral (2 mg/day, 3-5 days) or transdermal granisetron (one GTDS patch, 7 days), before receiving multi-day chemotherapy. The primary endpoint was complete control of CINV (no vomiting/retching, no more than mild nausea, no rescue medication) from chemotherapy initiation until 24 h after final administration. The prespecified non-inferiority margin was 15%.
RESULTS: Five hundred eighty-two patients were included in the per protocol analysis. The GTDS displayed non-inferiority to oral granisetron: complete control was achieved by 60% of patients in the GTDS group, and 65% in the oral granisetron group (treatment difference, -5%; 95% confidence interval, -13-3). Both treatments were well tolerated, the most common adverse event being constipation.
CONCLUSIONS: The GTDS provides effective, well-tolerated control of CINV associated with moderately or highly emetogenic multi-day chemotherapy. It offers a convenient alternative route for delivering granisetron for up to 7 days that is as effective as oral granisetron.

Habib, A. S., J. C. Keifer, et al. (2011). "A comparison of the combination of aprepitant and dexamethasone versus the combination of ondansetron and dexamethasone for the prevention of postoperative nausea and vomiting in patients undergoing craniotomy." Anesthesia & Analgesia 112(4): 813-818.
BACKGROUND: Postoperative nausea and vomiting (PONV) occur commonly after craniotomy. In patients receiving prophylaxis with ondansetron and dexamethasone, vomiting occurred in 45% of patients at 48 hours. In addition to causing patient discomfort, the physical act of vomiting may increase intracranial pressure or cerebral intravascular pressure, jeopardizing hemostasis and cerebral perfusion. Aprepitant is a neurokin-1 receptor antagonist with a long duration of action and no sedative side effect. In a large multicenter study in patients undergoing abdominal surgery,

aprepitant was significantly more effective than was ondansetron in preventing vomiting at 24 and 48 hours postoperatively. We hypothesized that the combination of aprepitant with dexamethasone will decrease the incidence of postoperative vomiting when compared with the combination of ondansetron and dexamethasone in patients undergoing craniotomy under general anesthesia.
METHODS: Patients scheduled to undergo craniotomy under general anesthesia were enrolled in this prospective, double-blind, randomized study. Patients were randomized to receive oral aprepitant 40 mg (or matching placebo) 1 to 3 hours before induction of anesthesia or ondansetron 4 mg IV (or placebo) within 30 minutes of the end of surgery. All patients received dexamethasone 10 mg after induction of anesthesia. The anesthetic technique was standardized. Data were collected at regular intervals by blinded personnel for 48 hours after surgery. Statistical analysis was performed using Wilcoxon's ranked sum test and (2) test. $P < 0.05$ was considered statistically significant.
RESULTS: One hundred four patients completed the study. The cumulative incidence of vomiting at 48 hours was 16% in the aprepitant group and 38% in the ondansetron group ($P = 0.0149$). The incidence of vomiting was also decreased in the aprepitant group at 2 hours (6% vs. 21%, $P = 0.0419$) and 24 hours (14% vs. 36%, $P = 0.0124$). From 0 to 48 hours, there was no difference between the aprepitant and ondansetron groups in the incidence of nausea (69% vs. 60%), nausea scores, need for rescue antiemetics (65% vs. 60%), complete response (no PONV and no rescue, 22% vs. 36%), or patient satisfaction with the management of PONV.
CONCLUSION: The combination of aprepitant and dexamethasone was more effective than was the combination of ondansetron and dexamethasone for prophylaxis against postoperative vomiting in adult patients undergoing craniotomy under general anesthesia. However, there was no difference between the groups in the incidence or severity of nausea, need for rescue antiemetics, or in complete response between the groups.

Metaxari, M., A. Papaioannou, et al. (2011). "Antiemetic prophylaxis in thyroid surgery: a randomized, double-blind comparison of three 5-HT3 agents." Journal of Anesthesia 25(3): 356- 362.
PURPOSE: The aim of this double-blind randomized study was to compare the antiemetic efficacy of three 5-hydroxytryptamine type 3 antagonists in terms of the incidence and intensity of postoperative nausea and vomiting (PONV) in a homogenous group of female patients undergoing thyroidectomy.
METHODS: The study cohort consisted of 203 American Society of Anesthesiologists PS I-II female patients randomized into four groups to receive at induction of anesthesia an intravenous (IV) bolus of 5 ml solution of one of the following: normal saline (placebo), granisetron 3 mg, ondansetron 4 mg, or tropisetron 5 mg. Nausea and vomiting were evaluated at five time points: during the first hour in the postanesthesia care unit (PACU) and 6, 12, 18, and 24 h postoperatively. Nausea intensity was measured using a visual analogue scale score (0-10).
RESULTS: Patients in the placebo group displayed a high incidence of nausea in the PACU and at 6, 12, and 18 h postoperatively (44, 60, 50, and 34%, respectively) and of vomiting (26, 42, 30 and 10%). The administration of granisetron reduced significantly the incidence of nausea at 6, 12, and 18 h (26, 18, and 2%, respectively) and vomiting at 6 and 12 h (10 and 6%, respectively). Ondansetron reduced significantly the incidence of nausea and vomiting only at 6 h postoperatively (28 and 12%, respectively). The administration of tropisetron did not affect the incidence of PONV compared to placebo.
CONCLUSION: Among the female patients of this study undergoing thyroid surgery, granisetron 3 mg provided the best prophylaxis from PONV. Ondansetron 4 mg was equally effective, but its action lasted only 6 h, whereas tropisetron 5 mg was found ineffective.

Moon, Y. E., J. Joo, et al. (2012). "Anti-emetic effect of ondansetron and palonosetron in thyroidectomy: a prospective, randomized, double-blind study.[Erratum appears in Br J Anaesth. 2012 Jun;108(6):1047-8]." British Journal of Anaesthesia 108(3): 417-422.
BACKGROUND: Palonosetron is a new potent 5-hydroxytryptamine 3 antagonist. Although this drug is thought to be more effective in patients receiving opioid-based patient-controlled analgesia (PCA), clinical data are lacking.

This study compared the effects of i.v. ondansetron and palonosetron administered at the end of surgery in preventing postoperative nausea and vomiting (PONV) in high-risk patients receiving i.v. PCA after thyroidectomy.
METHODS: A total of 100 female non-smoking subjects were randomly assigned into a palonosetron group or an ondansetron group. Ondansetron was given as an 8 mg bolus and 16 mg was added to the i.v. PCA mixture. In the palonosetron group, 0.075 mg was injected as a bolus only. Fentanyl-based PCA was provided for 24 h after operation. The incidence of nausea and vomiting, severity of nausea, requirement for rescue anti-emetics, and adverse effects were evaluated during 0-2 and 2-24 h.
RESULTS: The incidence of PONV during the 24 h postoperative period was lower in the palonosetron group than in the ondansetron group (42% vs 62%, P=0.045). No differences were observed between the groups during the first 2 h. However, the incidence of nausea and vomiting and nausea severity were significantly lower in the palonosetron group than in the ondansetron group during 2-24 h. The only difference in the use of rescue anti-emetics was at 2-24 h (10% with palonosetron compared with 28% with ondansetron, P=0.02).
CONCLUSIONS: Palonosetron is more effective than ondansetron for high-risk patients receiving fentanyl-based PCA after thyroidectomy, especially 2-24 h after surgery.

Park, S. K. and E. J. Cho (2011). "A randomized, double-blind trial of palonosetron compared with ondansetron in preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery." Journal of International Medical Research 39(2): 399-407.
This randomized, double-blind study evaluated the relative efficacy of palonosetron (a new, selective 5-hydroxytryptamine type 3 [5-HT(3)] receptor antagonist) and ondansetron in preventing postoperative nausea and vomiting (PONV) in patients undergoing gynaecological laparoscopic surgery. Patients received either palonosetron 0.075 mg (n = 45) or ondansetron 8 mg (n = 45), intravenously, immediately before induction of general anaesthesia. The occurrence of nausea and vomiting and the severity of nausea according to a visual analogue scale were monitored immediately after the end of surgery and during the following 24 h. The incidence of PONV was significantly lower in the palonosetron group compared with the ondansetron group (42.2% vs 66.7%, respectively). There were no significant statistical differences in the visual analogue scale for nausea. In conclusion, palonosetron 0.075 mg was more effective than ondansetron 8 mg in preventing PONV.

Siddique, R., M. G. Hafiz, et al. (2011). "Ondansetron versus granisetron in the prevention of chemotherapy induced nausea and vomiting in children with acute lymphoblastic leukemia." Mymensingh Medical Journal: MMJ 20(4): 680-688.
Effect of ondansetron and granisetron were evaluated in sixty (60) children (age 4-11 years) irrespective of sex, diagnosed case of acute lymphoblastic leukemia (ALL) who received high dose methotrexate and did not receive any antiemetic 24 hours prior to HDMTX. This was a prospective, randomized, double-blind, single center study. Of 60 children, 30 received oral ondansetron (4mg) and rest 30 granisetron (1mg) half an hour before therapy. Drugs were randomly allocated with appropriate code. The patients were followed up from day 1 to day 5 of therapy. Episodes of nausea and vomiting were recorded and scorings was done every 24 hours following chemotherapy. No significant difference was found between two groups according to acute emesis (Day-1) (p=0.053). In day two and day three it was significant (p<0.05). In day four it was significant (p=0.002). Early chemotherapy induced nausea and vomiting (CINV) were controlled 90% in children who received granisetron and 70% in children who received ondansetron. Delayed (Day 2-4) CINV were controlled in 80% of children who received granisetron and 43.4% who received ondansetron (p<0.05). Granisetron group required additional doses only 3.3% cases and ondanseton group 30% cases on the second day (p<0.05). Result was significant between two groups. About 36.7% patients had episodes of nausea on day four of chemotherapy in ondansetron group and it was only 3.3% in granisetron group due to adverse effects of antiemetic drug itself (p=0.001). Maximum episodes of vomiting were found on the second day in ondansetron group 33.3% and in granisetron group 3.3% (p=0.003). Though adverse effects like headache, constipation, abdominal pain and loose motion were common in both group

of children but their number was much less in children who received granisetron. On second day of therapy score of nausea and vomiting was maximum in ondansetron and minimum in granisetron treated on day 4 and the result was significant. So, to prevent acute and delayed CINV in children with ALL, oral graniseteron can be considered as more effective and well tolerated with minimum adverse effects compared with ondansetrons.