Evaluating the Oral 5-HT3 Antagonists:
Drugs Used to Treat Nausea and Vomiting
Comparing Effectiveness, Safety, and Price
The 5-HT3 antagonists are a class of drugs often recommended as first-choice options for preventing nausea and vomiting in people undergoing cancer treatments. Both problems are common side effects of chemotherapy and radiation. If not controlled, they can lead to other problems, such as dehydration and weight loss, and even interfere with cancer treatments. The information in this report will help you to decide, along with your doctor, which antinausea drug is right for you based on its effectiveness, safety, and price.

Not all chemotherapy or radiation regimens require treatment with an antinausea/vomiting medication, also called antiemetic. Many chemotherapy drugs pose only a low or minimal risk of nausea and vomiting. In general, your doctor will probably prescribe an antiemetic drug only if you are receiving chemotherapy drugs with a moderate to high risk of those side effects (see the list on page 7). The risk of those side effects with radiation treatments depends on the dose of radiation and the area of the body that’s undergoing treatment.

You may also want to talk with your doctor about nondrug treatments—such as hypnosis, biofeedback, guided imagery, electroacupuncture, and other techniques—that may help control your nausea and vomiting. Modifying your diet may also help. This includes avoiding foods that are unappealing (which can change daily when you’re undergoing cancer treatments), eating and drinking bland items that are easy on your stomach, such as ginger ale, toast and crackers; and eating small meals throughout the day.

The drugs in the 5-HT3 antagonist class that are available in pill form are roughly equivalent in effectiveness and safety, so choosing one may come down to price. Taking the evidence for effectiveness, safety, cost, and other factors into account, we have chosen the following as Consumer Reports Best Buy Drugs if you need medication to control nausea and vomiting due to chemotherapy or radiation treatments:

- Generic ondansetron tablet
- Generic ondansetron dissolvable tablet

Ondansetron, either as a tablet or a dissolvable tablet, has been proven to significantly reduce severe nausea and vomiting associated with radiation treatments or chemotherapy drugs with a moderate or high risk for causing those side effects. It is available as an inexpensive generic tablet that is just as effective and safe as more expensive brand-name medicines. Choosing generic ondansetron tablets could save you $100 or more per chemotherapy course compared with the most expensive brand-name 5-HT3 antagonists. The dissolvable tablet is an option for those who have trouble swallowing pills. It is slightly less expensive than the generic tablets, so this option could save you even more money.

Most people will experience at least one side effect from this class of drugs. The most common include constipation, dizziness, fatigue, headache, muscle cramps, nervousness, and sleepiness.

This report was released in November 2009.
This report compares the effectiveness, safety, and cost of a class of oral antinausea/vomiting medications called 5-HT3 antagonists. Drugs used to control nausea and vomiting are also known as "antiemetics." The 5-HT3 antagonists are very effective, and when used alone or in combination with other antiemetic drugs, are often recommended as first-choice options for preventing nausea and vomiting caused by chemotherapy or radiation treatments for cancer.

This evaluation of 5-HT3 antagonist class of drugs is part of a Consumers Union and Consumer Reports project to help guide you to medicines that are most effective and safe, and give you the best value for your healthcare dollar. To learn more about the project and the other classes of drugs we have examined, go to ConsumerReportsHealth.org/BestBuyDrugs.

Nausea and vomiting, also called emesis, are very common side effects of chemotherapy and radiation. As many as eight people out of 10 treated for cancer experience these problems.

Although bouts of nausea and vomiting are almost never life-threatening, the conditions are unpleasant and, if left untreated, can lead to other problems, such as dehydration, loss of appetite, weight loss, and exhaustion. Nausea and vomiting can also interfere with your daily activities and can negatively affect your overall quality of life. In the most severe cases, uncontrolled nausea and vomiting may even lead to changes in your chemotherapy or radiation treatment plans.

The 5-HT3 antagonists, alone or in combination with other antiemetic drugs, are often recommended as first-choice options for controlling nausea and vomiting due to chemotherapy or radiation treatments, but there are many types of antinausea/vomiting medicines available. Other commonly used antiemetic medications include alprazolam (Xanax), aprepitant (Emend), dexamethasone (Decadron), diphenhydramine (Benadryl), dronabinol (Marinol), haloperidol (Haldol), hydroxyzine (Vistaril), lorazepam (Ativan), metoclopramide (Reglan), nabilone (Cesamet), olanzapine (Zyprexa), prochlorperazine (Compazine), and promethazine (Phenergan). Several of these medications are also available as low-cost generics.
The 5-HT3 antagonists are often used together with one or more other types of antiemetics, especially in cases where there is a high risk of nausea and vomiting or if previous antiemetic medications have failed or stopped working.

You may also want to talk with your doctor about other nondrug treatments that might help control your nausea and vomiting. These include biofeedback, electroacupuncture, guided imagery, hypnosis, progressive muscle relaxation, and systematic desensitization. Most of these techniques involve using your mind and body to help with relaxation.

Also too, there are currently several studies underway to see whether ginger may help relieve nausea and vomiting associated with certain regimens of chemotherapy. At the moment, there is not enough clear evidence to suggest that it works.

Modifying your diet may also help. This includes eating small meals throughout the day, eating and drinking bland items that are easy on your stomach, such as ginger ale, toast and crackers, and avoiding foods that are unappealing (which can change daily when you’re undergoing cancer treatments).

There are four 5-HT3 antagonists available in oral, topical patch, and injectable formulations. The topical and injectable versions may be options to consider if you have trouble swallowing pills. Two of the four 5-HT3 antagonists—granisetron and ondansetron—are now available as generic tablets. Granisetron is also available in a patch (Sancuso) that can be applied to the body to deliver the medication through the skin. This patch
was approved by the Food and Drug Administration in late 2008, too late to be included in the most recent analysis conducted by the Oregon Health & Science University Drug Effectiveness Review Project, which forms the basis of this Best Buy Drugs report. Limited evidence from two unpublished studies suggest that it is about as effective as granisetron pills, although there have been reports of patients having trouble keeping the patch stuck to their skin. A capsule formulation of palonosetron (Aloxi) was approved by the FDA in 2008, but the manufacturer, Eisai, decided not to market it. This drug is currently only available in an injectable form. All four 5-HT3 antagonists are listed in the table below:

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Form¹</th>
<th>Brand Name</th>
<th>Available as a Generic?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dolasetron</td>
<td>Tablet</td>
<td>Anzemet</td>
<td>No</td>
</tr>
<tr>
<td>2. Granisetron</td>
<td>Tablet</td>
<td>Kytril</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Skin Patch</td>
<td>Sancuso</td>
<td>No</td>
</tr>
<tr>
<td>3. Ondansetron</td>
<td>Tablet</td>
<td>Zofran</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Dissolvable Tablet</td>
<td>Zofran ODT</td>
<td>Yes</td>
</tr>
<tr>
<td>4. Palonosetron²</td>
<td>Injection</td>
<td>Aloxi</td>
<td>No</td>
</tr>
</tbody>
</table>

¹ All four drugs are also available as injectable formulations, but we do not evaluate any of them in this report.
² Palonosetron (Aloxi) capsules were approved in 2008, but they are not available because the manufacturer decided not to market it.

The 5-HT3 antagonists are also used to treat nausea and vomiting that can occur after certain surgeries. In those cases, the medicines are typically given intravenously just before the procedure. In this context, the choice of medication is often outside of the patient’s hands, so we haven’t evaluated them for that use in this report. For the same reason, we also haven’t evaluated the injections when used for treating nausea and vomiting due to chemotherapy or radiation therapy.

Although researchers have not studied 5-HT3 antagonists to determine if they can prevent the nausea and vomiting that many women experience during pregnancy, the drugs are sometimes used for this purpose. Given the lack of evidence to support this use, we recommend that you talk with your doctor if you experience nausea and vomiting during pregnancy that other treatments have not helped alleviate.

The 5-HT3 antagonists are also sometimes used to treat serious vomiting due to food poisoning, viral infections, certain diseases or medical conditions, or cases in which the cause is unknown. But because they are not FDA-approved for treating these conditions, we did not evaluate the drugs in this report for these treatments.
It is not known exactly how these drugs control nausea and vomiting. They are widely thought to work by blocking the effects of a chemical called serotonin that can set off parts of the brain and stomach that control vomiting.

If you are undergoing chemotherapy or radiation treatment for cancer, your doctor will take several factors into consideration when deciding among the many medication options that control nausea and vomiting which are most appropriate for you. For chemotherapy, this will include the specific drug you are taking, the dose level and the frequency of treatment. For radiation therapy, the important factors include the part of the body being treated, the amount of radiation, and how often you will be undergoing the therapy. Your doctor will also consider the type of nausea and vomiting you are most likely to develop.

There are also several factors that may put you at higher risk for nausea and vomiting regardless of the type of cancer treatment you receive (See Table 1 below.) Some people with greater risk include women, people younger than 50 and those with a history of previous nausea and vomiting, such as morning sickness or motion sickness. If you have one of these conditions or fall into one of these categories, you should bring it to your doctor’s attention.

<table>
<thead>
<tr>
<th>Table 1. People Who May Have Higher Risk of Nausea and Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Those under the age of 50</td>
</tr>
<tr>
<td>Women who had morning sickness during pregnancy</td>
</tr>
<tr>
<td>Previous history of nausea and vomiting due to chemotherapy</td>
</tr>
<tr>
<td>People with a history of motion sickness</td>
</tr>
<tr>
<td>People with anxiety</td>
</tr>
<tr>
<td>Those who drink little or no alcohol</td>
</tr>
</tbody>
</table>

Source: American Cancer Society

Antiemetic drugs are generally given right before you undergo each course of cancer treatment. In some cases, especially with radiation therapy, your doctor may want you to continue taking them up to one to two days after completing your cancer treatment. Most research on this class of drugs has been done with patients undergoing cancer treatment using chemotherapy drugs that have a moderate to high risk of causing nausea and vomiting. (See pages 7 and 8 for a list of chemotherapy drugs and their potential to cause nausea and vomiting.) And these drugs appear to do best in completely preventing the acute type of nausea and vomiting that occurs within the first 24 hours following cancer treatment.

Chemotherapy-Induced Nausea and Vomiting

Nausea and vomiting caused by chemotherapy come in multiple forms, classified as acute, delayed, anticipatory, breakthrough, and refractory. This section explains these different types.
**Acute nausea and vomiting** - This type occurs within the first 24 hours after receiving chemotherapy.

**Delayed nausea and vomiting** - The problems begin after the first 24 hours following chemotherapy. The worst of the nausea and vomiting for certain types of chemotherapy drugs does not occur until 48 to 72 hours after you have taken them. The discomfort can last for up to seven days. It is more likely to happen with certain types of chemotherapy drugs, including cisplatin, carboplatin, cyclophosphamide, and doxorubicin.

**Anticipatory nausea and vomiting** - For some people who have had nausea and vomiting following chemotherapy, just the process of getting ready for the next treatment can be enough to trigger them again.

**Breakthrough nausea and vomiting** – This occurs when antinausea medication fails to prevent the problems. If it happens to you, your doctor may decide to increase the dose of the antinausea medicine you’re taking or switch to a different drug.

<table>
<thead>
<tr>
<th>Table 2. Level of Nausea and Vomiting Risk from Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal1</td>
</tr>
<tr>
<td>Alemtuzumab (Campath)</td>
</tr>
<tr>
<td>Alpha interferon (Intron A, Roferon-A)</td>
</tr>
<tr>
<td>Asparaginase (Elspar)</td>
</tr>
<tr>
<td>Bevacizumab (Avastin)</td>
</tr>
<tr>
<td>Bleomycin (Blenoxane)</td>
</tr>
<tr>
<td>Bortezomib (Velcade)</td>
</tr>
<tr>
<td>Busulfan</td>
</tr>
<tr>
<td>Chlorambucil (by mouth) (Leukeran)</td>
</tr>
<tr>
<td>Cladribine</td>
</tr>
<tr>
<td>Decitabine (Dacogen)</td>
</tr>
<tr>
<td>Denileukin diftitox (Ontak)</td>
</tr>
<tr>
<td>Desatinib (Sprycel)</td>
</tr>
<tr>
<td>Dexrazoxane (Zinecard)</td>
</tr>
<tr>
<td>Minimal¹</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Erlotinib (Tarceva)</td>
</tr>
<tr>
<td>Fludarabine (Fludara)</td>
</tr>
<tr>
<td>Gefitinib (Iressa)</td>
</tr>
<tr>
<td>Gemtuzumab (Mylotarg)</td>
</tr>
<tr>
<td>Hydroxyurea (by mouth) (Hydrea)</td>
</tr>
<tr>
<td>Lenalidomide (Revlimid)</td>
</tr>
<tr>
<td>Melphalan (low-dose, by mouth) (Alkeran)</td>
</tr>
<tr>
<td>Methotrexate (low-dose)</td>
</tr>
<tr>
<td>Nelarabine</td>
</tr>
<tr>
<td>Pentostatin</td>
</tr>
<tr>
<td>Rituximab (Rituxan)</td>
</tr>
<tr>
<td>Sorafenib (Nexavar)</td>
</tr>
<tr>
<td>Sunitinib (Sutent)</td>
</tr>
<tr>
<td>Thalidomide</td>
</tr>
<tr>
<td>Thioguanine (by mouth)</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin)</td>
</tr>
<tr>
<td>Valrubicin (Valstar)</td>
</tr>
<tr>
<td>Vinblastine (Velban)</td>
</tr>
<tr>
<td>Vincristine (Oncovin)</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine)</td>
</tr>
</tbody>
</table>

Source: American Cancer Society

1. The levels of risk for nausea and vomiting apply to patients who do not take antiemetic medicine. Minimal means the drug causes nausea and vomiting in less than 10 percent of patients who do not take antiemetic medicine.

2. Low means the drug causes nausea and vomiting in 10 percent to 30 percent of patients.

3. Moderate means the drug causes nausea and vomiting in 30 percent to 90 percent of patients.

4. High means the drug causes nausea and vomiting in more than 90 percent of patients.
Refractory nausea and vomiting - In this case, the antiemetic medicine stops working after it had been effective. Your doctor might either increase the dose of your antiemetic medicine or try a different drug.

Chemotherapy drugs differ in their risk of causing nausea and vomiting, also known as emetogenicity, and not all types and doses of chemotherapy cause the conditions. Some chemotherapy drugs, such as low-dose methotrexate, have a minimal risk and evidence suggests cause nausea and vomiting in less than 10 percent of people. Other drugs, such as high-dose cisplatin, have a high risk of nausea and vomiting, causing it in more than 90 percent of the patients who take it.

Radiation-Induced Nausea and Vomiting

Factors that affect your risk of nausea and vomiting while receiving radiation therapy include the dose and frequency of the radiation. For example, standard doses of radiation (180 to 200 centiGray) to the abdomen usually cause nausea and vomiting in around 50 percent of people, but when total body radiation is used, up to 90 percent develop nausea and vomiting. And people who receive one large dose of radiation are more likely to develop nausea and vomiting than those who receive several smaller doses of radiation.

Another factor that affects your risk of nausea and vomiting during radiation therapy is the location of your cancer. For example, your chances of nausea and vomiting are greater if you receive radiation to the abdominal region of your body, such as the intestines.

And people who receive radiation in combination with chemotherapy also face a greater chance of developing nausea and vomiting.
Studies have found that 5-HT3 antagonists are very effective at preventing nausea and vomiting due to chemotherapy or radiation treatments. (We discuss this evidence in more detail starting on page 13.) No one medication has been proven clearly superior to another in terms of efficacy or safety, but there is a big difference in price, so this may become your most important consideration when choosing among these drugs.

As you can see in Table 3, below, studies have found that these drugs prevent the acute nausea and vomiting that occurs within 24 hours after a chemotherapy course with moderate risk of nausea and vomiting in 52 percent to 76 percent of the people. The figures come from different studies, so they do not reflect a direct comparison of the drugs as if they were evaluated against each other in a single trial. So the differences should not be taken to mean that one drug is superior to another. When the available evidence is considered all together, the drugs appear to be about equal in terms of effectiveness and safety.

Taking effectiveness, safety, side effects, and cost into account, we have chosen the following as Consumer Reports Best Buy Drugs to prevent or alleviate nausea and vomiting due to chemotherapy or radiation treatments:

- Generic ondansetron tablets
- Generic ondansetron dissolvable tablets

### Table 3. General Effectiveness of 5-HT3 Antagonist Drugs

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Complete prevention of ‘acute’ vomiting, within 24 hours following chemotherapy that is moderately likely to cause nausea or vomiting</th>
<th>Comments/Special Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolasetron tablet</td>
<td>Anzemet</td>
<td>60% to 76%</td>
<td>None</td>
</tr>
</tbody>
</table>
| Granisetron tablet            | Kytril     | 60% to 84%                                                                                                                      | - Also FDA-approved for use in chemotherapy with a high likelihood of causing nausea and vomiting, and with radiation  
  - Generic form available      |
| Granisetron patch             | Sancuso    | 60%                                                                                                                             | - First and only patch form available 
  - Patch can be worn over consecutive courses of chemotherapy for up to 5 days 
  - Can cause mild skin irritation at application site |
| Ondansetron tablet            | Zofran     | 52% to 72%                                                                                                                      | - Also FDA-approved for use in chemotherapy with a high likelihood of causing nausea and vomiting, and with radiation  
  - Generic form available      |
| Ondansetron orally disintegrating tablet | Zofran ODT | 72%                                                                                                                             | - Quickly dissolves in mouth without water, good for people who have difficulty swallowing pills or who are already nauseated  
  - Generic form available      |
| Palonosetron capsule          | Aloxi      | 76%                                                                                                                             | - Capsule formulation is not available; only injectable form is available.              |
If you and your doctor have decided that an oral 5-HT3 antagonist is appropriate for your situation, choosing generic ondansetron tablets could save you more than $100 compared with a more expensive brand-name antiemetic medicine, such as Kytril (See Table 4). Below, we discuss the reasons for our choice for each indication.

Chemotherapy with a moderate risk of nausea and vomiting

All the drugs in this class have been shown to reduce acute nausea and vomiting when taken with chemotherapy drugs that have a moderate risk of nausea and vomiting. None of the oral 5HT3 antagonists has been shown to be any more effective than the others. So the choice comes down to cost. Generic ondansetron tablets or generic ondansetron dissolvable tablets run between $50 and $85 for one course of chemotherapy, which is significantly less expensive than the other drugs in this class, which start at more than $100.

Your chances of having a complete response might be further improved if you take the drug aprepitant (Emend) in addition to a 5-HT3 antagonist plus dexamethasone. But aprepitant is not yet available in a generic form and costs more than $160 a tablet.

Chemotherapy with a high risk of nausea and vomiting

Of the oral agents, dolasetron, granisetron, and ondansetron have been FDA-approved for use in helping to reduce acute nausea and vomiting following chemotherapy with a high risk of nausea and vomiting. There are no clear differences in effectiveness or safety between them. So again, the choice comes down to cost. We recommend ondansetron as your initial Best Buy option because it is significantly less expensive than the others. You could save $20-$50 or more per chemotherapy course by going with generic ondansetron tablets over generic dolasetron or granisetron pills.

Adding aprepitant may be an option you and your doctor want to consider here, too. But studies of aprepitant following chemotherapy with a high likelihood of nausea and vomiting have only looked at adding the drug to the intravenous forms of ondansetron, not the tablet form.

<table>
<thead>
<tr>
<th>Generic Name and Dose1, 3</th>
<th>Brand Name</th>
<th>Number of doses per course of chemotherapy</th>
<th>Average cost per course of chemotherapy2</th>
<th>Average cost per 5 consecutive courses of chemotherapy2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolasetron 100 mg tablet</td>
<td>Anzemet</td>
<td>One</td>
<td>$106</td>
<td>$530</td>
</tr>
<tr>
<td>Granisetron 1 mg tablet</td>
<td>Generic</td>
<td>Two</td>
<td>$136</td>
<td>$680</td>
</tr>
<tr>
<td>Granisetron 1 mg tablet</td>
<td>Kytril</td>
<td>Two</td>
<td>$178</td>
<td>$890</td>
</tr>
<tr>
<td>Granisetron 3.1 mg patch</td>
<td>Sancuso</td>
<td>One</td>
<td>$484</td>
<td>$484</td>
</tr>
<tr>
<td>Ondansetron 8 mg tablet</td>
<td>Generic</td>
<td>Two – Three</td>
<td>$57 - $85</td>
<td>$285 - $425</td>
</tr>
<tr>
<td>Ondansetron 8 mg tablet</td>
<td>Zofran</td>
<td>Two – Three</td>
<td>$121 - $181</td>
<td>$605 - $905</td>
</tr>
<tr>
<td>Ondansetron 8 mg orally disintegrating tablet</td>
<td>Generic</td>
<td>Two – Three</td>
<td>$50 - $76</td>
<td>$250 - $380</td>
</tr>
<tr>
<td>Ondansetron 8 mg orally disintegrating tablet</td>
<td>Zofran ODT</td>
<td>Two – Three</td>
<td>$111 - $166</td>
<td>$555 - $830</td>
</tr>
</tbody>
</table>

1. As typically prescribed. The dose ranges are derived from the drugs’ labeling.
2. Prices reflect nationwide retail average for July 2009, rounded to the nearest dollar. Information derived by Consumer Reports Best Buy Drugs from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite®. Wolters Kluwer Health is not involved in our analysis or recommendations.
3. Palonosetron (Aloxi) capsules are not available because the manufacturer decided not to market this formulation of the drug.
If you undergo consecutive, daily sessions of chemotherapy, you might want to consider the granisetron (Sancuso) patch. It might be more convenient since you won’t have to take a pill. The granisetron patch is not yet available as a generic, so it is quite expensive. One patch currently costs about $484. But it may be cheaper than taking brand-name tablets. For example, the equivalent number of pills of some of the brand-name 5-HT3 antagonists can run $500 or more.

**Delayed nausea and vomiting due to chemotherapy**

This class of drugs has been less studied for their effectiveness at preventing delayed nausea and vomiting that occurs more than 24 hours after receiving a chemotherapy session. But the evidence that is available indicates that granisetron, ondansetron, and palonosetron help alleviate those conditions in 47 percent to 62 percent of the people. Only granisetron and ondansetron are available as pills, and the evidence does not indicate that one drug in pill form is clearly superior to another in this class. So again, we would recommend generic ondansetron tablets based on cost.

**Radiation-induced nausea and vomiting**

Both granisetron and ondansetron have been shown to be similarly effective in preventing nausea and vomiting following radiation therapy for cancer. Generic ondansetron tablets would save you $50 or more over granisetron, so we recommend it as our Best Buy choice if you’re undergoing radiation therapy and your doctor has decided that an antiemetic is appropriate for your situation.
This section presents more detailed information on the effectiveness and safety of the 5-HT3 antagonists.

This report is based on an analysis of the scientific evidence of the 5-HT3 antagonists. Overall, 919 studies and research articles dealing with these medicines were identified and screened. All were published between 1974 and October 2008. From these, the analysis focused on 185 studies that included 81 head-to-head trials that directly compared drugs with each other, 77 controlled clinical trials, 14 studies that performed an analysis of multiple other studies, and 12 observational studies.

How effective are 5-HT3 antagonists?

Most research on these antiemetic drugs in people with cancer has focused on how well they provide a “complete response.” This is defined as no vomiting and no use of medications for breakthrough nausea and vomiting occurring within the first 24 hours after chemotherapy (acute emesis).

Chemotherapy with a moderate risk of nausea and vomiting

5-HT3 antagonists significantly improve chances of a complete response within the first 24 hours after taking chemotherapy medicines known to have a moderate risk of causing nausea and vomiting. One exception is palonosetron (Aloxi) tablets, for which effectiveness in patients below the age of 18 years has not yet been established.

Studies show that about 52 percent to 76 percent of the adults who take one of these antiemetic tablets along with other drugs used to treat nausea, including dexamethasone and metoclopramide, will have a complete response within the first 24 hours following treatment with chemotherapy medicine that has a moderate risk of causing nausea and vomiting. This includes the dissolvable tablet form of ondansetron, which may be a good alternative for people who have trouble swallowing pills. It is slightly less expensive than the standard ondansetron 8 mg tablet.

There are only a few research trials that have directly compared the effectiveness between different pill forms of 5-HT3 antagonists, but none have found significant differences between medications in their ability to improve the chances of a complete response following chemotherapy. Adding another type of antiemetic medication called aprepitant (Emend) to the regimen may improve the chances of a complete response. In a study of 866 women with breast cancer undergoing chemotherapy with a moderate risk of nausea and vomiting, 51 percent of those who had aprepitant added to a regimen of ondansetron and dexamethasone had a complete response compared with 42 percent of those who did not receive aprepitant.

Although chemotherapy may be given daily, weekly, or monthly, most research trials have focused on the effectiveness of tablet forms of these antiemetic drugs for treatment of a single day of chemotherapy treatment. For people who have to undergo consecutive daily sessions of chemotherapy, though, a new transdermal patch form of granisetron (Sancuso) has become available that is applied to the skin. It can be applied once on the first day of chemotherapy and can be worn for up to seven days to deliver an ongoing source of medication. Unpublished research not included in the analysis that forms the basis of this report has found that about 60 percent of people who use the granisetron patch from the start of chemotherapy to five days into the treatment had no vomiting, mild, if any, nausea, and no need for additional drugs for breakthrough vomiting.

Chemotherapy with a high risk of nausea and vomiting

Among the tablet formulations of 5-HT3 antagonists, granisetron and ondansetron have been FDA-approved for use in helping to reduce nausea and vomiting within 24 hours following chemotherapy with a high risk of these conditions, such as high-dose cisplatin (known to cause it in over 90 percent of the patients). In research trials, about 47 percent to 58 percent of adults had complete responses with granisetron tablets or ondansetron tablets.
For chemotherapy with a high risk of nausea and vomiting, you and your doctor may want to consider your options for taking aprepitant in addition to a 5-HT3 antagonist as a way to increase your chances of avoiding acute episodes.

So far, however, research on using aprepitant capsules to prevent vomiting following chemotherapy with a high risk of nausea and vomiting has only focused on using it in addition to the intravenous forms of ondansetron and palonosetron. When aprepitant tablets were added to a standard regimen of intravenous ondansetron plus dexamethasone tablets, 83 percent to 89 percent of the patients had complete responses; this was the case for only 68 percent to 78 percent of patients who only took intravenous ondansetron plus dexamethasone tablets alone.

Similarly, the proportion of people who had a complete response was higher, 67 percent to 70 percent, when aprepitant tablets were added to intravenous palonosetron and dexamethasone tablets, compared with 56 percent of the people who only used intravenous palonosetron and dexamethasone tablets alone.

Delayed nausea and vomiting following chemotherapy

Most tablet forms of 5-HT3 antagonists are given only on the actual days of chemotherapy, and relatively few research studies have evaluated their effectiveness in preventing or treating delayed nausea and vomiting that starts or continues more than 24 hours after chemotherapy. There is limited, but promising evidence for the use of tablet forms of granisetron, ondansetron, and palonosetron. Studies have found that 47 percent to 62 percent of people had a complete response after 24 hours.

Radiation Therapy

Among the oral forms of 5-HT3 antagonists, only granisetron and ondansetron have been proven to prevent nausea and vomiting following treatment of total body irradiation and fractionated abdominal radiation. Within 24 hours following fractionated dosages of radiation to the abdominal region, up to 91 percent of the people taking granisetron and ondansetron tablets can expect to have complete control of their vomiting. However, in the
case of bone-marrow transplants, when total body
radiation is used, only up to around half of the
people taking granisetron or ondansetron tablets
can expect to have complete control of their vom-
iting within 24 hours.

Safety and Side Effects of Antiemetic Drugs

These drugs to treat nausea and vomiting appear to be
very safe. However, in general, it is likely that the use
of this class will lead to at least one side effect, but the
most common are mild and usually not serious.

Studies have found there is no consistent difference
between the 5-HT3 antagonists and the side effects
they can cause. But in a person with cancer, it is hard
to sort out whether any given side effect is being
cau sed by the cancer itself, the chemotherapy or radi-
ation, other illnesses, or other medications they may
be taking. This probably explains why research stud-
ies show a wide variability in the percentage of
patients who experienced at least one side effect from
taking one of these antiemetic drugs, ranging from
only 4 percent all the way up to 87 percent.

Table 5. lists the most common types of side effects
of these drugs reported in research studies.

You should also be aware that dolasetron
(Anzemet) carries a warning that it can cause
changes in the electrical activity of the heart that
can lead to arrhythmias and other heart problems.
Dolasetron has also been associated with rare cases
of cardiac arrest that led to death and heart attacks
in children and adolescents. For those reasons, the
drug should be administered with caution to people
who have or may be at risk of developing certain
changes in the electrical activity of their heart,
especially prolongation of the QTc interval. This
includes patients with low potassium or low mag-
nesium levels, patients also taking diuretics, those
taking anti-arrhythmic drugs, or those on high
doses of the cancer drug anthracycline.

Age, Gender, and Race Differences

Studies have not found any differences between
men and women or between younger people and
those 65 or older in regard to the effectiveness of
these antiemetic drugs when used for the preven-
tion of nausea and vomiting due to cancer
chemotherapy. Race and ethnicity were not report-
ed in most studies, so no conclusions can be drawn
about whether there are differences between groups
in the effectiveness or safety of 5-HT3 antagonists.
Talking With Your Doctor

It's important for you to know that the information we present here is not meant to substitute for a doctor's judgment. But we hope it will help you and your doctor arrive at a decision about which 5-HT3 medication and dose is best for you, and which will give you the most value for your health-care dollar.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctor and that studies have found that doctors do not routinely take price into account when prescribing medicine. Unless you bring the issue up, your doctors may assume that cost is not a factor for you.

Many people (including physicians) think that newer drugs are better. While that's a natural assumption to make, it's not true. Studies consistently find that many older medicines are as good as—and in some cases better than—newer medicines. Think of them as "tried and true," particularly when it comes to their safety record. Newer drugs have not yet met the test of time, and unexpected problems can and do crop up once they become available to the market.

Of course, some newer prescription drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer vs. older medicine, including generic drugs.

Prescription medicines go "generic" when a company's patents on a drug lapse, usually after about 12 to 15 years. At that point, other companies can make and sell the drug.

Generics are much less expensive than newer brand-name medicines, but they are not lesser-quality drugs. Indeed, most generics remain useful even many years after first being marketed. That is why today more than 60% of all prescriptions in the U.S. are written for generics.

Another important issue to talk with your doctor about is keeping a record of the drugs you are taking. There are several reasons for this:

- First, if you see several doctors, each may not be aware of the medicine the others have prescribed.
- Second, since people differ in their response to medications, it is very common for doctors today to prescribe several medicines before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs and dietary supplements at the same time. They can interact in ways that can either reduce the benefit you get from the drug or be dangerous.
- And fourth, the names of prescription drugs—both generic and brand—are often hard to pronounce and remember.

For all these reasons, it's important to keep a written list of all the drugs and supplements you are taking and periodically review it with your doctors.

Always be sure, too, that you understand the dose of the medicine being prescribed for you and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at a pharmacy, or if you get it by mail, check to see that the dose and the number of pills per day on the pill bottle match the amounts that your doctor told you.
How We Picked the Best Buy Drugs

Our evaluation is based in part on an independent scientific review of the studies and research literature on antiemetic drugs conducted by a team of physicians and researchers at the Oregon Health & Science University Evidence-Based Practice Center. This analysis—which reviewed 919 studies including those conducted by the drugs’ manufacturers—was conducted as part of the Drug Effectiveness Review Project, or DERP. DERP is a first-of-its-kind 11-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP’s analysis of antiemetic drugs forms the basis for this report. A consultant to Consumer Reports Best Buy Drugs is also a member of the Oregon-based research team, which has no financial interest in any pharmaceutical company or product. The full DERP review of the antiemetic (OR 5-HT3 antagonists) drugs is available at http://www.ohsu.edu/ohsuedu/research/policycenter/DERP/about/final-products.cfm. (This is a long and technical document written for physicians.)

Consumers Union and Consumer Reports selected the Best Buy Drugs using the following criteria. The drug had to:

- Be approved by the FDA to treat nausea and vomiting.
- Be as effective as or more effective than other antiemetic medicines when prescribed appropriately according to FDA guidelines.
- Have a safety record equal to or better than other antiemetic medicines when prescribed appropriately.

The monthly costs we cite were obtained from a health-care information company that tracks the sales of prescription drugs in the U.S. Prices for a drug can vary quite widely. All the prices in this report are national averages based on sales in retail outlets. They reflect the cash price paid for a month’s supply of each drug in July 2009.

The Consumers Reports Best Buy Drugs methodology is described in more detail in the Methods section at ConsumerReportsHealth.org/BBD.
About Us

Consumers Union, publisher of Consumer Reports magazine, is an independent and nonprofit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. Its Web site is at www.consumer.org. The magazine’s Web site is at www.consumerreports.org.

Consumer Reports Best Buy Drugs is a public education project administered by Consumers Union. Two outside sources of generous funding made the project possible. They are a major grant from the Engelberg Foundation, a private philanthropy, and a supporting grant from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the project is available at ConsumerReportsHealth.org/BestBuyDrugs.

We followed a rigorous editorial process to ensure that the information in this report and on the Consumer Reports Best Buy Drugs Web site is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error, we will correct it as quickly as possible. However, Consumer Reports and its authors, editors, publishers, licensors, and any suppliers cannot be responsible for medical errors or omissions, or any consequences from the use of the information on this site. Please refer to our user agreement at ConsumerReportsHealth.org/BestBuyDrugs for further information.

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