

WHITE PAPER

How Do Nurses Manage CINV? The Role for SANCUSO® (Granisetron Transdermal System)

Sancuso® (Granisetron Transdermal System) is a serotonin subtype 3 (5-HT₃) receptor antagonist indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to five consecutive days. A thin, translucent, matrix-type transdermal patch, Sancuso has been incorporated into the antiemesis clinical practice guidelines of two important organizations, the National Comprehensive Cancer Network and the American Society of Clinical Oncology. A recent ONS:Edge survey of oncology nurses indicated that more than half of respondents have used Sancuso with their patients; of those, almost all said they would use it again because of continuous delivery of drug, effectiveness, and the transdermal delivery system. However, the survey found that use and awareness of Sancuso are low. This paper reports on that survey and reviews the evidence regarding Sancuso and the product's support programs. For complete product information, see the package insert, www.sancuso.com.

What Are Nurses Doing Now?

In 2013, ONS:Edge (a for-profit division of the Oncology Nursing Society [ONS]) and ProStrakan, the manufacturer of Sancuso, fielded a survey of oncology nurses. The aims of the survey were to:

- Determine how oncology nurses currently help their patients manage chemotherapy-induced nausea and vomiting (CINV)
- Determine nurse preferences in CINV management
- Learn how much nurses know about Sancuso
- Explore whether nurses are using Sancuso with patients
- Evaluate the current impact of Sancuso patient support programs
- Evaluate the current usefulness and educational needs regarding Sancuso's patient support programs

The survey was administered via ONS:Edge's online system. Seven thousand six hundred eight (7,608) oncology nurses were invited to respond. Five hundred sixty (560) completed the survey, for a response rate of 7%.

Survey respondents¹

Most of the respondents, 474 (85%), indicated that they are practicing RNs. Some indicated other or additional credentials: 48 are advanced practice RNs, 44 are nurse practitioners, 18 are nurse navigators, and 14 noted other credentials. The respondents are highly experienced, with 307 (55%) reporting more than 20 years of experience and another 30% (164) reporting more than 15 years. A substantial majority (442, 80%), work in medical oncology. Other specialties included blood and marrow transplantation (36, 7%), surgical oncology (28, 5%), and radiation oncology (20, 4%); additional specialties were listed by relatively few nurses. The nurses reported a wide variety of work settings, with the most common being:

- Outpatient hospital-based clinic (161, 29%)
- Outpatient physician office/infusion center (142, 26%)
- Inpatient medical unit – oncology (118, 22%)

The nurses reported that they worked in multiple types of cancers, most commonly breast cancer, colorectal cancer, lung cancer, lymphoma, multiple myeloma, and leukemia.

How Do Oncology Nurses Manage CINV?

ONS:Edge and ProStrakan wanted to know what nurses do for their patients to manage CINV. One question asked, “What are your preferred agents to prevent and/or manage CINV resulting from *moderately* emetogenic chemotherapy?” The nurses could select all that they preferred.

As Figure 1 shows, the nurses most frequently selected intravenous (IV) ondansetron, oral dexamethasone, oral ondansetron, injected palonosetron, and oral prochlorperazine for the management of CINV due to *moderately* emetogenic chemotherapy.

The nurses were also asked about their preferences in managing CINV caused by *highly* emetogenic chemotherapy, and those results are shown in Figure 2. Again, the nurses most frequently selected IV ondansetron, oral dexamethasone, injected palonosetron, but for highly emetogenic chemotherapy, they added all forms of aprepitant as well as oral ondansetron. Lorazepam was a frequently noted other agent.

The respondents were also asked to rank by preference the various delivery methods for therapies used to prevent or manage CINV. Overall, the nurses ranked oral tablets number one, followed by IV, oral liquids, suppository, and transdermal patch. Factors influencing product selection include awareness, availability, and cost.

Are Nurses Using Sancuso?

As Figures 1 and 2 show, relatively few responding nurses use Sancuso to manage CINV with either moderately or highly emetogenic chemotherapy regimens. Only 39 (7%) reported using it for moderately emetogenic chemotherapy, and only 54 (9%) reported using it for highly emetogenic che-

motherapy. In addition, they reported using all other delivery methods more than the transdermal patch, Sancuso’s method. Why don’t nurses use Sancuso?

One factor may be awareness: 45% of respondents indicated that they had not heard of Sancuso before the survey. Another factor may be availability: 44% indicated that they had never used Sancuso with their patients. The most frequently selected reason for non-use was that the product is not on the approved institutional formulary. In addition, many respondents indicated that physicians are not ordering the drug, perhaps because they do not know about it or because they have encountered payment or reimbursement issues for it which they did not resolve.

Slightly more than half of respondents indicated that they had used Sancuso with their patients, and of those, almost all said they would use it again.

The non-users were asked what factors would be important for them to consider using Sancuso. Eighty-six percent (86%) of non-users said that they would be more likely to use it in appropriate patients if it were available in their e-prescribing systems. Additional factors are shown in Table 1, in ranked order of preference.

Non-users (N = 135) did recognize that Sancuso could be appropriate for certain patients they treat. They indicated that they would consider it for patients who have difficulty swal-

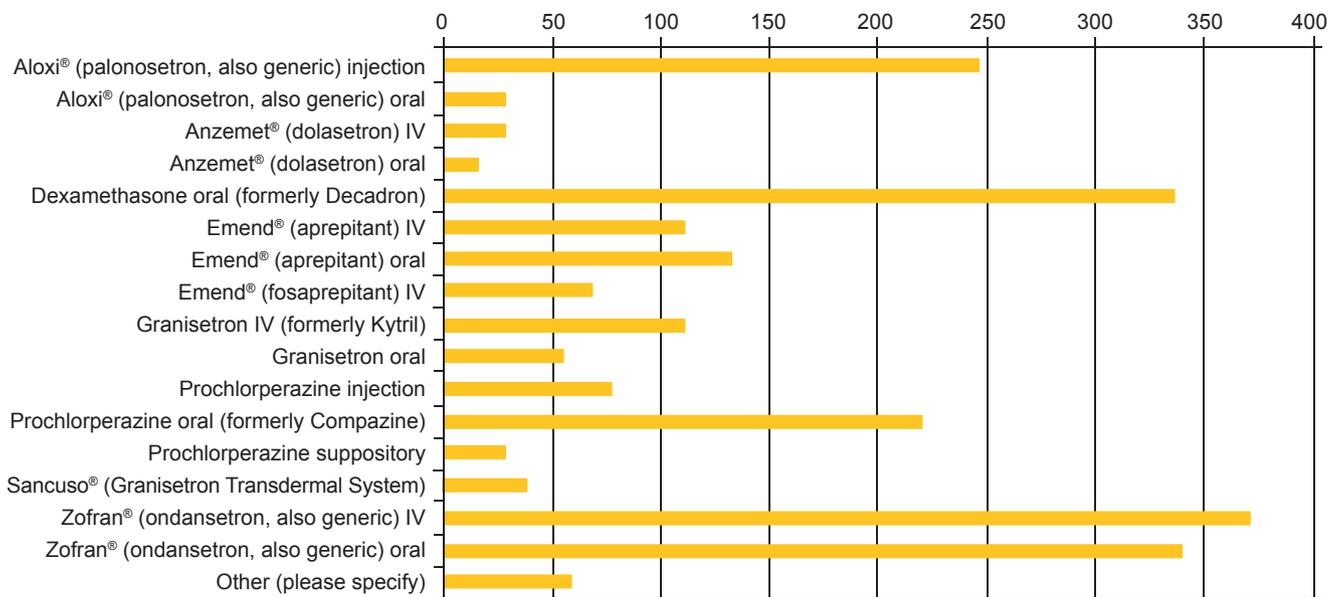


Figure 1. Preferred Agents for Moderately Emetogenic Chemotherapy

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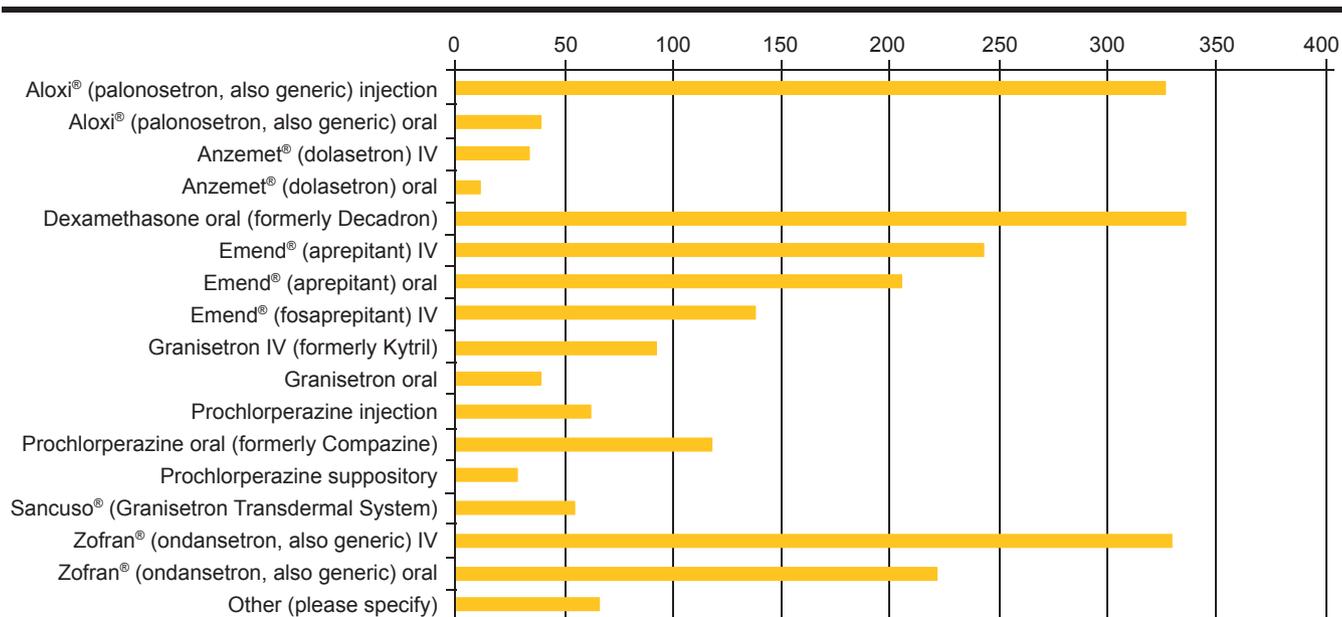


Figure 2. Preferred Agents for Highly Emetogenic Chemotherapy

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lowing (84%), have oral mucositis (75%), have gut motility issues (68%), experience breakthrough CINV (65%), receive multiday chemotherapy (60%), and/or have difficulty with adherence because of cognitive impairment or other problems (60%).

Slightly more than half (56%) of respondents indicated that they had used Sancuso with their patients, and of those, almost all said they would use it again (98%). Only four respondents said they would not because it is not on formulary, it is not effective, its cost is excessive and insurance coverage is not available, or it is not useful in patients with low blood counts. Relatively few (10) user respondents indicated that there would be barriers to using Sancuso again, with the primary barriers being copay amounts and insurance coverage.

Users gave a number of reasons for continuing to use Sancuso, with the most common being continuous delivery of drug (74%), effectiveness (74%), and the transdermal delivery system (66%) (see Figure 3.)

Sancuso users gave similar responses to those of non-users when asked to describe patients for whom they would consider Sancuso.

The most frequently selected characteristics were difficulty swallowing, breakthrough CINV, oral mucositis, difficulties with adherence, multiday chemotherapy, and gut motility issues.

Awareness of Sancuso Patient Support Programs

Only 60% (104) of respondents who were Sancuso users indicated that they were aware of ProStrakan's Patient Rx Solu-

tions programs, including prior authorization, reimbursement, patch replacement, copay assistance, and patient assistance program. They were asked which of the services they or their patients had used. The mostly widely used program is the Patient Assistance Program, closely followed by the copay card and prior authorization programs.

The respondents were also asked how they had learned about these services. The most frequent selection was

Table 1. Ranked Factors for Consideration of Use of Sancuso

Rank	Factor Affecting Use
1	Formulary approval
2*	Information about copay assistance and insurance coverage
2*	Advertising in journals
3	Word of mouth/testimonials
4	Samples
5	Patient assistance programs
6	Patient education tools
7	Nurse education
8	Evidence of effectiveness
9	Availability of information on the Internet

* Ranked scores were identical.

“copay card delivered by sales representative” (61%). The Sancuso.com website and speaker programs were selected by less than 25% of respondents. PatientRxSolutions.com, the Website for the patient assistance programs, provided information to only 14% of respondents.

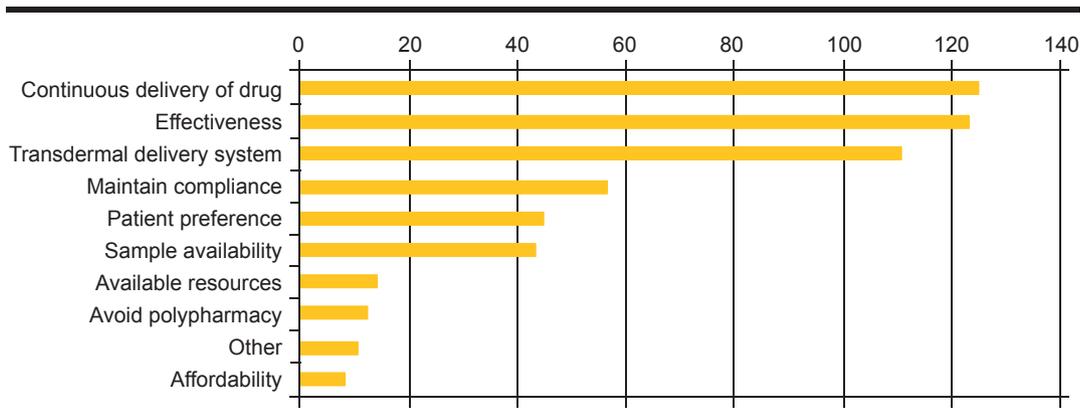


Figure 3. Reasons Nurses Said They Would Use Sancuso Again

Survey Conclusions

The ONS:Edge/ProStrakan survey demonstrated that although slightly more than half of oncology nurse respondents have heard of Sancuso and have used it with their patients, a substantial minority had not heard of it prior to the survey and many had not used it. Even when nurses know about Sancuso, it might be unavailable on their institutions’ formularies or their physicians may not be accustomed to prescribing it.

Those nurses who have used Sancuso noted that it provides transdermal delivery of therapy and is useful in patients who have difficulty with swallowing and other adherence issues.

Nurses also do not seem to be well-acquainted with Sancuso’s patient access programs—Patient Rx Solutions. Very few have used the patch-replacement service, although more have used patient assistance, the copay card, and the prior authorization program. The nurses were largely unfamiliar with web-based resources. It is likely that if nurses were aware of these services, some of the stated objections to Sancuso’s cost or difficulties with insurance coverage and reimbursement could be resolved.

To build upon the survey’s findings and to provide information to oncology nurses about Sancuso, we now discuss Sancuso’s:

- Indication and dosage
- Clinical evidence
- Citation in clinical practice guidelines
- Direction for use
- Patient and healthcare provider support programs.

Sancuso® (Granisetron Transdermal System)

Sancuso is a serotonin subtype 3 (5-HT₃) receptor antagonist indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to five consecutive days. Sancuso is approved for use in adults.

Sancuso is a thin, translucent transdermal patch that is rectangular-shaped with rounded corners, consisting of a backing, the drug matrix, and a release liner. The granisetron in Sancuso crosses intact skin into the systemic circulation by a passive diffusion process.¹ “Passive diffusion” can be defined as the movement of drug across a membrane in a manner driven solely by the concentration gradient. In passive diffusion, drug moves from a region of greater concentration to a region of lesser concentration.²

Clinical Trial Experience

The effectiveness of Sancuso in the prevention of CINV was evaluated in a Phase III, randomized, parallel-group, double-blind, double-dummy study conducted in the United States and abroad. The study compared the efficacy, tolerability, and safety of Sancuso with that of 2 mg oral granisetron once daily in the

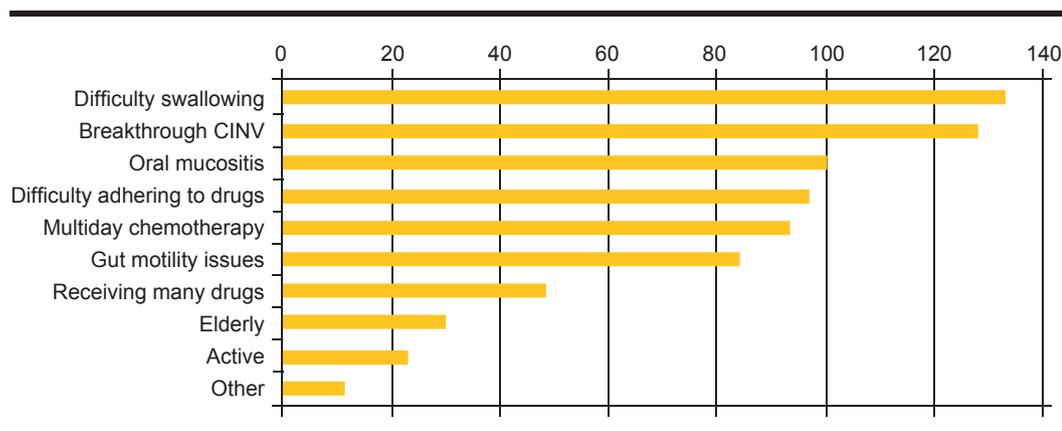


Figure 4. Patients for Whom Nurses Would Consider Sancuso

Use of Sancuso Patch for CINV by Cancer Type

Breast Cancer

Recommended treatments for breast cancer commonly cause CINV.⁴ Highly and moderately emetogenic chemotherapy regimens include doxorubicin, cyclophosphamide, and epirubicin. Females are more susceptible to CINV compared to males.⁵ A history of morning sickness during pregnancy increases risk up to 2.5 times.⁶ Recent surgery, such as a mastectomy, can increase risk almost four times.⁶ Age younger than 40 can increase CINV risk about 2.5 times.⁴

Sancuso has been studied successfully in breast cancer in a phase III trial.⁷ It provides continuous coverage with one application, so adherence to treatment is not an issue.¹ More than 70% of breast cancer patients work full-time during treatment.⁸ These patients need continuous CINV coverage to prevent interruptions in their daily lives.

Sancuso dosage and administration in this trial were the same as in the phase III registration trial.⁷

Gastrointestinal Cancer

Recommended treatments for gastrointestinal cancers commonly cause CINV.⁹ Highly emetogenic chemotherapy and moderately emetogenic chemotherapy regimens include cisplatin, which carries a greater than 90% risk of CINV¹⁰, epirubicin, and 5-fluorouracil. There is a greater than 65% risk of developing delayed CINV with cisplatin.¹⁰ Multiday regimens result in overlapping periods of acute and delayed CINV. Surgery results in comorbid conditions that can interfere with CINV treatments. Furthermore, chemotherapy in combination with radiation therapy can potentiate CINV effects.

Sancuso has been successfully studied in gastrointestinal cancers in a phase III trial.¹¹ It helps to avoid CINV caused by moderately and highly emetogenic regimens;¹ provides continuous coverage with one application, so adherence is not an issue;¹ and avoids doubt about gut motility issues and GI absorption of an oral medication.

Sancuso dosage and administration in this trial were the same as in the phase III registration trial.¹¹

Head and Neck Cancer

Recommended treatments for head and neck cancer commonly cause CINV.¹² Highly emetogenic chemotherapy and moderately emetogenic chemotherapy regimens include agents such as cisplatin, carboplatin, paclitaxel, and 5-fluorouracil. Multiday regimens result in overlapping periods of acute and delayed CINV. Chemotherapy in combination with radiation therapy potentiates CINV effects and also may cause oral mucositis and dysphasia, which can make swallowing an oral antiemetic painful or prohibitive.

Sancuso has been studied successfully in head and neck cancers in a phase III trial.¹³ It helps to prevent CINV caused by highly and moderately emetogenic regimens;¹ provides continuous coverage with one application, so adherence to treatment is not an issue¹; and is an alternative to taking pills to achieve CINV protection.

Sancuso dosage and administration in this trial were the same as in the phase III registration trial.¹³

Gynecological Cancer

Recommended treatments for gynecological cancer commonly cause CINV.¹⁴ Highly and moderately emetogenic chemotherapy regimens include agents such as cisplatin and carboplatin. Chemotherapy is often in combination with abdominal/pelvic radiation, potentiating CINV effects and limiting gut motility. Females are more susceptible to CINV compared to males.⁵ A history of morning sickness during pregnancy can increase CINV risk up to 2.5 times.⁶

Sancuso has been studied successfully in ovarian and cervical cancers in a phase III trial.¹⁵ It helps to avoid the increased risk of CINV due to patient demographic characteristics and platinum-based regimens.¹ Sancuso provides continuous coverage with one application, so adherence to treatment and inability to absorb an oral medication are not issues.¹

Sancuso dosage and administration in this trial were the same as in the phase III registration trial.¹⁵

prevention of nausea and vomiting in a total of 641 patients receiving multiday chemotherapy.¹

The randomized trial population included 48% males and 52% females, aged 16 to 86 years, receiving moderately (ME) or highly emetogenic (HE) multiday chemotherapy. Seventy-eight (78%) of patients were white, 12% Asian, 10% Hispanic/Latino, and 0% black.^{1,3} For the Sancuso arm of the study, the granisetron patch was applied 24–48 hours before the first dose of chemotherapy and kept in place for seven days. For the oral agent arm, oral granisetron was administered daily for the duration of the chemotherapy regimen, one hour before each dose of chemotherapy. Efficacy was assessed from the first administration until 24 hours after the start of the last day's administration of the chemotherapy regimen.^{1,3}

The primary endpoint of the trial was the proportion of patients achieving total control (no vomiting and/or retching, no more than mild nausea, and no rescue medication) from the first administration until 24 hours after the start of the last day's administration of multiday chemotherapy. Using this definition, the effect of Sancuso was established in 60.2% of patients in the Sancuso arm and 64.8% of patients receiving oral granisetron (difference of –4.89%; 95% confidence interval –12.91% to +3.13%). The results of the primary efficacy assessments indicated that the granisetron transdermal system was non-inferior to oral granisetron in the control of CINV in patients receiving multiday chemotherapy.^{1,3}

Fewer than 1% of patches became detached over the seven-day application period.¹



Figure 5. Sancuso (Granisetron Transdermal System)

The safety of Sancuso was evaluated in a total of 404 patients undergoing chemotherapy who participated in two double-blind, comparator studies with patch treatment durations of up to seven days. The control groups included a total of 406 patients who received a daily dose of 2 mg oral granisetron, for one to five days.¹

Adverse reactions considered by the investigators as drug-related occurred in 8.7% of patients (35 of 404) receiving Sancuso and 7.1% (29/406) of patients receiving oral granisetron. The most common adverse reaction was constipation, that occurred in 5.4% of patients in the Sancuso group and 3.0% of patients in the oral granisetron group.¹ In the pivotal clinical trial, skin tolerability of the patch was good; only one application-site reaction was reported, and no patient withdrew due to skin toxicity.³

Granisetron does not induce or inhibit the cytochrome p450 drug-metabolizing enzyme system *in vitro*, and no clinically relevant drug interactions have been reported in clinical studies with Sancuso.¹ The effect of granisetron on QTc prolongation was evaluated in a randomized, single-blind, positive (moxifloxacin 400 mg)—and a placebo-controlled parallel study in healthy subjects. A total of 240 subjects were administered Sancuso patch, intravenous granisetron (10 mcg/kg over 30 seconds). In a study with demonstrated ability to detect small effects, the upper bound of the 90% confidence interval for the largest placebo-adjusted, baseline-corrected QTc based on Fridericia correction method (QTcF) for Sancuso was below 10 ms, the threshold for regulatory concern.¹

No adequate and well-controlled studies of Sancuso have been conducted in pregnant women; it should be used in pregnancy only if clearly needed. It is also not known whether granisetron is excreted in human milk, and caution should be exercised in administration to nursing women. The safety and effectiveness of Sancuso in patients younger than 18 have not

been established. Sancuso should be used with caution in older patients to account for comorbidities or other drug therapies.¹

Sancuso in Antiemesis Clinical Practice Guidelines

Sancuso has been incorporated into the antiemesis clinical practice guidelines of two important organizations, the National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO). These inclusions recognize evidence of Sancuso's utility and effectiveness.

National Comprehensive Cancer Network

High emetic risk. NCCN guidelines suggest the use of serotonin (5-HT₃) antagonists before the start of highly emetogenic chemotherapy. Granisetron, a serotonin antagonist, can be administered orally or *via transdermal patch* applied 24–48 hours prior to first dose of highly emetogenic chemotherapy, with duration of patch to be seven days. In addition, NCCN recommends the use of both dexamethasone and neurokinin-1 antagonists or lorazepam or an H2 blocker.¹⁷

Moderate emetic risk. Serotonin (5-HT₃) antagonists should be administered on day 1 before the start of moderately emetogenic chemotherapy. Granisetron can be administered orally or *via transdermal patch* applied 24–48 hours prior to first dose of moderately emetogenic chemotherapy, with duration of patch to be seven days. In addition, NCCN recommends the use of dexamethasone with or without neurokinin-1 antagonists or lorazepam or a H2 blocker. If needed, additional therapy may be provided on days 2 and 3: 5-HT₃ antagonist monotherapy; or steroid monotherapy; or an NK-1 antagonist with or without a steroid, lorazepam, and/or H2 blocker.¹⁷

American Society of Clinical Oncology

High emetic risk. The three-drug combination of an NK1 receptor, a 5-HT₃ receptor antagonist (day 1 only), and dexamethasone (days 1 through 3 or 1 through 4) is recommended for patients receiving highly emetogenic chemotherapy. Patients receiving multiday chemotherapy can also be offered the granisetron transdermal patch that delivers therapy over multiple days rather than taking a serotonin antagonist daily.¹⁸

How Is Sancuso Used?

Sancuso (Granisetron Transdermal System) is supplied as a 52 cm² patch containing 34.3 mg of granisetron. Each patch is printed on one side with the words “Granisetron 3.1 mg/24 hours.” Each patch is packaged in a separate, sealed, foil-lined plastic pouch. Sancuso is available in packages of 1 (NDC 42747-726-01) patch.

Patches should be stored at 20°–25°C (68°–77°F); excursions are permitted at 15°–30°C (59°–86°F). Sancuso should be stored in the original packaging.

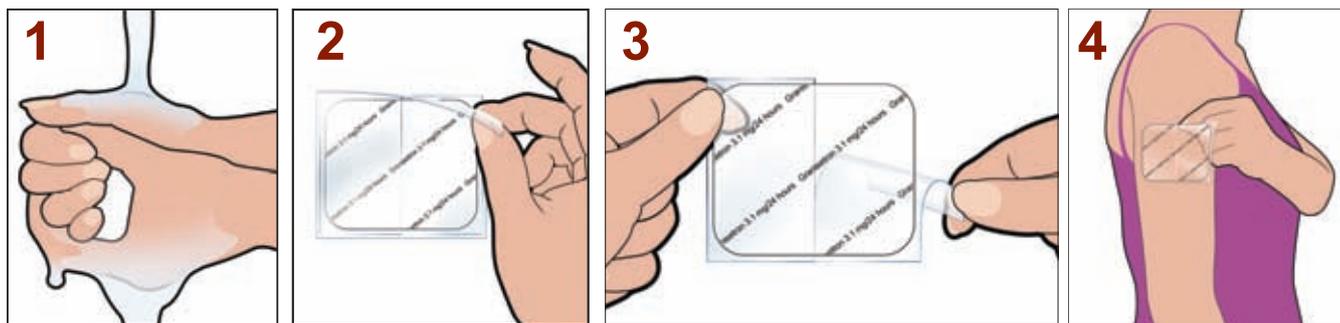


Figure 6. How to Apply Sancuso

Application Instructions and Advice to Patients¹

The transdermal system (patch) should be applied to clean, dry, intact healthy skin on the upper outer arm. Sancuso should not be placed on skin that is red, irritated, or damaged. Each patch is packed in a pouch and should be applied directly after the pouch has been opened.

Because the use of granisetron may mask a progressive ileus and/or gastric distention caused by the underlying condition, patients should be instructed to tell their physician if they have pain or swelling in their abdomen. Patients should be instructed to remove the patch if they have a severe skin reaction or a generalized skin reaction (e.g., allergic rash, including erythematous, macular, or papular rash, or pruritus). When patients remove the patch, they should be instructed to peel it off gently.

Granisetron may be degraded by direct sunlight or exposure to sunlamps. In addition, an *in vitro* study using Chinese hamster ovary cells suggests that granisetron has the potential for photogenotoxicity. Patients must be advised to cover the patch application site (e.g. with clothing) if there is a risk of exposure to sunlight or sunlamps throughout the period of wear and for 10 days after its removal.

Sancuso Patient Rx Solutions Support Programs

An important element of expanding the use of Sancuso for patients receiving moderately or highly emetogenic chemotherapy is increasing awareness and use of the Patient Rx Solutions programs. Patient Rx Solutions include the following support programs: the Patient Assistance Program, the Prior Authorization Assistance Program, the Copay Assistance Card, and the Patch Replacement Program. It is critical that healthcare providers and their patients know that they can be supported in managing the cost of the agent, navigating insurance and reimbursement, and receiving answers to clinical questions. Information about all these programs is available at PatientRxSolutions.com.

Patient Assistance Program

Designed for uninsured patients with no public or private prescription coverage, the Patient Assistance Program seeks

to assist such patients in obtaining Sancuso. In order to be eligible for assistance, patients must meet certain criteria.

- Legal resident of United States or its territories
- Not be eligible for or have prescription drug coverage through any private or public prescription coverage program, including Medicaid and Medicare
- Annual household income must be at or below 300% of the current federal poverty level
- Must submit recent federal tax return or alternate proof of income

The application form may be obtained at www.patientrxsolutions.com.

Prior Authorization Assistance Program

When patients have prescription insurance coverage, the program's experienced staff will make it easier for them to gain access to Sancuso by working directly with them on coverage-related questions. The program:

- Uses all available discounts and assistance programs to make Sancuso more accessible
- Works with retail pharmacies and physician dispensing pharmacies to provide Sancuso
- Connects patients to mail-order services to ship directly to their homes

The prior authorization process takes 24–72 hours, but the average response/status update duration is less than 24 hours. For the quickest service, fill out the Prior Authorization Assistance Program form and fax it with the prescription for Sancuso. The application form is available at www.patientrxsolutions.com. Alternatively, healthcare providers may call 1-800-SANCUSO. Be sure to have the following available when calling:

- Patient information
- Prescription
- Patient's prescription drug insurance card information
- Physician information.

Copay Assistance Card

Each Copay Assistance Card can save a patient as much as \$2,200 over 11 Sancuso prescription fills; in no case will the monthly benefit exceed \$200. Patients can save up to \$200 on each prescription after paying the first \$30. Each Sancuso card is good for 11 fills, up to four patches per fill to a maximum

of 44 patches, subject to prescription coverage.

For an example of costs under the Copay Card Program, see Table 2. Copay cards can be downloaded free at www.sancuso.com.

Patch Replacement Program

If chemotherapy is delayed or canceled, the Sancuso Patch Replacement Program may be able to help a patient get a replacement patch. Patients should work with their physicians to complete the application, which must be signed by the physician prior to submission. A receipt for proof of purchase and the completed, signed application must be provided. The application form can be obtained at www.patientrxsolutions.com.

Sancuso.com

Finally, patients and healthcare providers can obtain information and support from SANCUSO.com. There, patients can learn about CINV, Sancuso, and all of the programs under Patient Rx Solutions, including the copay card. They can watch a video about CINV and Sancuso's continuous protection. Healthcare providers can access the same information as well as more detailed clinical information, such as sustained bioavailability and the use of Sancuso with particular cancers.

Importantly, resources have been created "just for nurses." At www.sancuso.com, they can watch a video illustrating application of the patch, request a conversation with a sales representative or a medical science liaison, or request more information.

Potential Benefits of Sancuso

Due to its route of administration, Sancuso may be an option for patients who are unable to take or retain oral antiemetics.^{17,22} As Boccia et al. pointed out, "this may be especially valuable in patients for whom swallowing is difficult or absorption of oral medications is uncertain, such as patients with previous head, neck, or gastrointestinal surgery or radiotherapy, or comorbid conditions such as xerostomia."^{23,19} Sancuso provides an additional choice for patients receiving oral chemotherapy, helping them avoid intravenous antiemetic administration. Sancuso's convenience may also

Table 2. Example of Costs with the Copay Card Program

Out-of-Pocket Cost	Patient Pays	Copay Card Pays
\$75	\$30	\$45
\$230	\$30	\$200
\$300	\$100	\$200

help improve adherence to antiemetic therapy, with possible benefits to quality of life, overall treatment satisfaction, and compliance with future anticancer treatments.^{3,20}

Sancuso provides continuous protection from CINV and avoids the peaks and troughs of daily oral antiemetics.¹⁹ It reduces CINV even in the toughest-to-treat patients.^{1,3,6} The easy-to-apply patch supplies continuous granisetron regardless of a patient's weight, body mass index, gender, age, or renal function.^{1,21} It can be worn for seven days, which gives five days of continuous CINV prevention.^{1,20} Furthermore, it is recommended in the NCCN and ASCO CINV clinical guidelines.^{17,18}

For more information or to request contact from a sales representative or medical science liaison, please call 1-800-SANCUSO or e-mail sancuso@prostrakan.com.

Indication and Important Safety Information

SANCUSO® (Granisetron Transdermal System) is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration. Do not use SANCUSO if you are allergic to granisetron or any of the other ingredients in SANCUSO. Tell your healthcare professional if you are pregnant, if you plan to become pregnant, or you are breastfeeding. Tell your healthcare professional if you have pain or swelling in stomach area (abdomen), or if you are allergic to medical adhesive tape, adhesive dressings, or other skin patches. Tell your healthcare professional about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Other medicines may affect how SANCUSO works. SANCUSO may also affect how your other medicines work. The medicine in SANCUSO (granisetron) may not work well and/or may affect your skin if exposed to direct sunlight and the light from sunlamps or tanning beds. While wearing the patch keep it covered with clothing if you will be in sunlight or near a sunlamp, including tanning beds. Keep the skin where SANCUSO was applied covered for another 10 days after the patch is taken off to protect from exposure to direct sunlight. You may see mild redness on the skin where the patch is removed. This redness should go away within three days. If redness continues, tell your healthcare professional. The most common side effect of SANCUSO is constipation. Tell your healthcare professional if you have any side effect that bothers you or that does not go away. This is not the only possible side effect of SANCUSO. For more information, ask your healthcare professional or pharmacist. To report suspected adverse reactions, contact ProStrakan, Inc. at 1-800-SANCUSO and www.sancuso.com, or FDA at 1-800-FDA-1088 or www.fda.gov/med-watch.

ONS:Edge thanks Vanna M. Dest, MSN, APRN, BC, AOCN®, for review of this paper. She is manager, Oncology Advanced Practice Providers, and oncology nurse practitioner in thoracic oncology at Smilow Cancer Hospital at Yale in New Haven, CT.

References

- 1 Sancuso (Granisetron Transdermal System) full prescribing information. ProStrakan, 2012.
- 2 Pharmacokinetics and Biopharmaceutics (46:138). Lecture Tutorial. Passage of Xenobiotics across Biological Membranes. University of Iowa. Retrieved March 8, 2013. Available at: <http://www.uiowa.edu/~c046138/tut-mem.htm>
- 3 Boccia RV, Gordan LN, Clark G, et al. 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; 19:1609–1617.
- 4 National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology™: Breast cancer*. V.3.2013. http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf. Accessed May 15, 2013.
- 5 Lohr L. Chemotherapy-induced nausea and vomiting. *Cancer J*. 2008;14(2):85-93.
- 6 Booth CM, Clemons M, Dranitsaris G, et al. Chemotherapy-induced nausea and vomiting in breast cancer patients: a prospective observational study. *J Support Oncol*. 2007;5(8):374-380.
- 7 Data on file. ProStrakan, Inc.
- 8 Hassett MJ, O'Malley AJ, Pakes JR, Newhouse JP, Earle CC. Frequency and cost of chemotherapy-related serious adverse effects in a population sample of women with breast cancer. *J Natl Cancer Inst*. 2006;98(16):1108-1117.
- 9 National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology™: Colon cancer*. V.3.2013. http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf. Accessed May 15, 2013. (See also: National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology™: Gastric cancer*. V.2.2013. http://www.nccn.org/professionals/physician_gls/PDF/gastric.pdf. Accessed May 15, 2013.)
- 10 Hesketh PJ. Defining the emetogenicity of cancer chemotherapy regimens: relevance to clinical practice. *Oncologist*. 1999;4(3):191-196.
- 11 Data on file. ProStrakan, Inc.
- 12 National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology™: Head and neck cancers*. V.1.2013. http://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf. Accessed May 15, 2013.
- 13 Data on file. ProStrakan, Inc.
- 14 National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology™: Ovarian cancer, including fallopian tube cancer and primary peritoneal cancer*. V.1.2013. http://www.nccn.org/professionals/physician_gls/PDF/ovarian.pdf. Accessed May 15, 2013.
- 15 Data on file. ProStrakan, Inc.
- 16 Data on file. ProStrakan, Inc.
- 17 National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology™ (NCCN Guidelines®). Antiemesis*. V.1.2013. <http://www.nccn.org>. Accessed March 6, 2013.
- 18 Basch E, Prestrud A, Hesketh PJ, et al. Antiemetics: *American Society of Clinical Oncology Clinical Practice Guideline Update*. <http://www.asco.org/guidelines/antiemetics>. Accessed March 8, 2013.
- 19 Kraut L, Fauser AA. Anti-emetics for cancer chemotherapy induced emesis: potential of alternative delivery systems. *Drugs*. 2001;61:1553–1562.
- 20 Schnell FM. Chemotherapy-induced nausea and vomiting: the importance of acute antiemetic control. *Oncologist*. 2003;8:187–198.
- 21 Howell J, Smeets J, Drenth HJ, Gill D. Pharmacokinetics of a granisetron transdermal system for the treatment of chemotherapy-induced nausea and vomiting. *J Oncol Pharm Pract*. 2009;15:223–231.
- 22 Schulmeister L. Granisetron transdermal system: a new option to help prevent chemotherapy-induced nausea and vomiting. *Clin J Oncol Nurs*. 2009;13:711-714

Highly and Moderately Emetogenic Chemotherapy Agents

Moderately to Highly Emetogenic Oral Antineoplastic Agents¹

Altretamine
 Busulfan > 4 mg/day
 Crizotinib
 Cyclophosphamide ≥ 100 mg/m²/day
 Estramustine
 Etoposide
 Lomustine (single day)
 Mitotane
 Procarbazine
 Temozolomide > 75 mg/m²/day
 Vismegodegib

Highly Emetogenic IV Antineoplastic Agents

(90% frequency of emesis²)

- AC combo: doxorubicin or epirubicin + cyclophosphamide
- Carmustine > 250 mg/m²

- Cisplatin ≥ 50 mg/m²
- Cyclophosphamide > 1,500 mg/m²
- Dacarbazine
- Doxorubicin > 60 mg/m²
- Epirubicin > 90 mg/m²
- Ifosfamide > 2 g/m² per dose
- Mechlorethamine
- Streptozocin

Moderately Emetogenic IV Antineoplastic Regimens

(30%-90% frequency of emesis²)

- Aldesleukin > 12-15 million IU/m²
- Amifostine > 300 mg/m²
- Arsenic trioxide
- Azacitadine
- Bendamustine
- Busulfan > 4 mg/d
- Carboplatin
- Carmustine ≤ 250 mg/m²
- Cisplatin < 50 mg/m²
- Clofarabine
- Cyclophosphamide ≤ 1,500 mg/m²
- Cytarabine > 200 mg/m²

- Dactinomycin
- Daunorubicin
- Doxorubicin < 60 mg/m²
- Epirubicin ≤ 90 mg/m²
- Idarubicin
- Ifosfamide < 2 g/m²
- Interferon alfa ≥ 10 million IU/m²
- Irinotecan
- Melphalan > 50 mg/m²
- Methotrexate ≥ 250 mg/m²
- Oxaliplatin > 75 mg/m²
- Temozolomide

References

1. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis*. V.1.2013. Page AE-9. http://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed Aug. 7, 2013.
2. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis*. V.1.2013. Page AE-7. http://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed Aug. 7, 2013.



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www.onsedge.com

Sancuso[®]

(Granisetron Transdermal System)

ProStrakan, Inc.
1-800-SANCUSO
<http://www.sancuso.com/>

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Sancuso (Granisetron Transdermal System) safely and effectively. See full prescribing information for Sancuso.

Sancuso (Granisetron Transdermal System) Initial U.S. Approval: 2008

-----RECENT MAJOR CHANGES-----
Warnings and Precautions, Serotonin Syndrome (5.4) 09/2014

-----INDICATIONS AND USAGE-----

Sancuso is a serotonin subtype 3 (5-HT₃) receptor antagonist indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days. (1)

---DOSAGE AND ADMINISTRATION---

Apply a single transdermal system (patch) to the upper outer arm a minimum of 24 hours before chemotherapy. The patch may be applied up to a maximum of 48 hours before chemotherapy as appropriate. Remove the patch a minimum of 24 hours after completion of chemotherapy. The patch can be worn for up to 7 days depending on the duration of the chemotherapy regimen. (2)

---DOSAGE FORMS AND STRENGTHS---

52 cm² patch containing 34.3 mg of granisetron delivering 3.1 mg per 24 hours. (3)

-----CONTRAINDICATIONS-----

Known hypersensitivity to granisetron or to any of the components of the patch. (4)

----WARNINGS AND PRECAUTIONS----

- Granisetron may mask a progressive ileus and/or gastric distention caused by the underlying condition. (5.1)
- Mild application site reactions have occurred; remove patch if severe reactions or a generalized skin reaction occur. (5.2)
- Avoid direct exposure of application site to natural or artificial sunlight by covering with clothing while wearing the patch and for 10 days after removing it. (5.3)
- Serotonin syndrome has been reported with 5-HT₃ receptor antagonists alone but particularly with concomitant use of serotonergic drugs. (5.4)

-----ADVERSE REACTIONS-----

The most common adverse reaction is constipation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact ProStrakan Inc. at 1-800-SANCUSO and www.sancuso.com, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----DRUG INTERACTIONS-----

- No clinically relevant drug interactions have been reported in clinical studies with Sancuso. (7)
- Use during pregnancy only if clearly needed. (8.1)
- Use caution when administering to nursing women. (8.3)

Safety and effectiveness in pediatric patients have not been established. (8.4)

- Clinical studies of Sancuso did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger patients. (8.5)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 09/2014

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Sancuso® (Granisetron Transdermal System) is indicated for the prevention of nausea and vomiting in patients receiving moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration.

2 DOSAGE AND ADMINISTRATION

The transdermal system (patch) should be applied to clean, dry, intact healthy skin on the upper outer arm. Sancuso should not be placed on skin that is red, irritated or damaged.

Each patch is packed in a pouch and should be applied directly after the pouch has been opened. The patch should not be cut into pieces.

2.1 Adults

Apply a single patch to the upper outer arm a minimum of 24 hours before chemotherapy. The patch may be applied up to a maximum of 48 hours before chemotherapy as appropriate. Remove the patch a minimum of 24 hours after completion of chemotherapy. The patch can be worn for up to 7 days depending on the duration of the chemotherapy regimen.

3 DOSAGE FORMS AND STRENGTHS

Sancuso is a 52 cm² patch containing 34.3 mg of granisetron. The patch releases 3.1 mg of granisetron per 24 hours for up to 7 days.

4 CONTRAINDICATIONS

Sancuso is contraindicated in patients with known hypersensitivity to granisetron or to any of the components of the patch.

5 WARNINGS AND PRECAUTIONS

5.1 Gastrointestinal

The use of granisetron in patients may mask a progressive ileus and/or gastric distention caused by the underlying condition.

5.2 Skin Reactions

In clinical trials with Sancuso, application site reactions were reported which were generally mild in intensity and did not lead to discontinuation of use. The incidence of reactions was comparable with placebo.

If severe reactions, or a generalized skin reaction occur (e.g. allergic rash, including erythematous, macular, papular rash or pruritus), the patch must be removed.

5.3 Exposure to Sunlight

Granisetron may be affected by direct natural or artificial sunlight. Patients must be advised to cover the patch application site, e.g. with clothing, if there is a risk of exposure to sunlight throughout the period of wear and for 10 days following its removal because of a potential skin reaction (see Section 13.2).

5.4 Serotonin Syndrome

The development of serotonin syndrome has been reported with 5-HT₃ receptor antagonists. Most reports have been associated with concomitant use of serotonergic drugs

(e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors, mirtazapine, fentanyl, lithium, tramadol, and intravenous methylene blue). Some of the reported cases were fatal. Serotonin syndrome occurring with overdose of another 5-HT₃ receptor antagonist alone has also been reported. The majority of reports of serotonin syndrome related to 5-HT₃ receptor antagonist use occurred in a post-anesthesia care unit or an infusion center.

Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes

(e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, with or without gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome, especially with concomitant use of Sancuso and other serotonergic drugs. If symptoms of serotonin syndrome occur, discontinue Sancuso and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if Sancuso is used concomitantly with other serotonergic drugs. [see Drug Interactions (7), Patient Counseling Information (17.4)].

Other:

fever; events often associated with chemotherapy have also been reported: leucopenia, decreased appetite, anemia, alopecia, thrombocytopenia.

7 DRUG INTERACTIONS

Granisetron does not induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system *in vitro*. There have been no definitive drug-drug interaction studies to examine pharmacokinetic or pharmacodynamic interaction with other drugs. However, in humans, granisetron hydrochloride injection has been safely administered with drugs representing benzodiazepines, neuroleptics and anti-ulcer medications commonly prescribed with antiemetic treatments. Granisetron hydrochloride injection also does not appear to interact with emetogenic cancer therapies. In agreement with these data, no clinically relevant drug interactions have been reported in clinical studies with Sancuso.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

The safety of Sancuso was evaluated in a total of 404 patients undergoing chemotherapy who participated in two double-blind, comparator studies with patch treatment durations of up to 7 days. The control groups included a total of 406 patients who received a daily dose of 2 mg oral granisetron, for 1 to 5 days.

Adverse reactions considered by the investigators as drug-related occurred in 8.7% (35/404) of patients receiving Sancuso and 7.1% (29/406) of patients receiving oral granisetron. The most common adverse reaction was constipation that occurred in 5.4% of patients in the Sancuso group and 3.0% of patients in the oral granisetron group.

Table 1 lists the treatment emergent adverse reactions that occurred in at least 3% of patients treated with Sancuso or oral granisetron.

Table 1: Incidence of Adverse Reactions in Double-Blind, Active Comparator Controlled Studies in Cancer Patients Receiving Chemotherapy (Events ≥ 3% in either group)

Body System Preferred Term	Sancuso TDS N=404 (%)	Oral granisetron N=406 (%)
Gastrointestinal disorders		
Constipation	5.4	3.0
Nervous system disorders		
Headache	0.7	3.0

5-HT₃ receptor antagonists, such as granisetron, may be associated with arrhythmias or ECG abnormalities. Three ECGs were performed on 588 randomized patients in the Phase 3 study: at baseline before treatment, the first day of chemotherapy, and 5 to 7 days after starting chemotherapy. QTcF prolongation greater than 450 milliseconds was seen in a total of 11 (1.9%) patients after receiving granisetron, 8 (2.7%) on oral granisetron and 3 (1.1%) on the patch. No new QTcF prolongation greater than 480 milliseconds was observed in any patient in this study. No arrhythmias were detected in this study.

6.2 Granisetron Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse events reported in clinical trials with other formulations of granisetron include the following: **Gastrointestinal:** abdominal pain, diarrhea, constipation, elevation of ALT and AST levels, nausea and vomiting

Cardiovascular: hypertension, hypotension, angina pectoris, atrial fibrillation and syncope have been observed rarely

Central Nervous System: dizziness, insomnia, headache, anxiety, somnolence and asthenia

Hypersensitivity: rare cases of hypersensitivity reactions, sometimes severe (e.g. anaphylaxis, shortness of breath, hypotension, urticaria) have been reported

7 DRUG INTERACTIONS

Granisetron does not induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system *in vitro*. There have been no definitive drug-drug interaction studies to examine pharmacokinetic or pharmacodynamic interaction with other drugs. However, in humans, granisetron hydrochloride injection has been safely administered with drugs representing benzodiazepines, neuroleptics and anti-ulcer medications commonly prescribed with antiemetic treatments. Granisetron hydrochloride injection also does not appear to interact with emetogenic cancer therapies. In agreement with these data, no clinically relevant drug interactions have been reported in clinical studies with Sancuso.

Because granisetron is metabolized by hepatic cytochrome P-450 drug-metabolizing enzymes (CYP1A1 and CYP3A4), inducers or inhibitors of these enzymes may change the clearance and hence, the half-life of granisetron. In addition, the activity of the cytochrome P-450 subfamily 3A4 (involved in the metabolism of some of the main narcotic analgesic agents) is not modified by granisetron hydrochloride *in vitro*. In *in vitro* human microsomal studies, ketoconazole inhibited ring oxidation of granisetron hydrochloride. However, the clinical significance of *in vivo* pharmacokinetic interactions with ketoconazole is not known. In a human pharmacokinetic study, hepatic enzyme induction with phenobarbital resulted in a 25% increase in total plasma clearance of intravenous granisetron hydrochloride. The clinical significance of this change is not known.

Serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular symptoms) has been described following the concomitant use of 5-HT₃ receptor antagonists and other serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) [see Warnings and Precautions (5.4)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

Reproduction studies with granisetron hydrochloride have been performed in pregnant rats at intravenous doses up to 9 mg/kg/day (54 mg/m²/day, about 24 times the recommended human dose delivered by the Sancuso patch, based on body surface area) and oral doses up to 125 mg/kg/day (750 mg/m²/day, about 326 times the recommended human dose with Sancuso based on body surface area).

Reproduction studies have been performed in pregnant rabbits at intravenous doses up to 3 mg/kg/day (36 mg/m²/day, about 16 times the human dose with Sancuso based on body surface area) and at oral doses up to

32 mg/kg/day (384 mg/m²/day, about 167 times the human dose with Sancuso based on body surface area). These studies did not reveal any evidence of impaired fertility or harm to the fetus due to granisetron. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Sancuso should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

It is not known whether granisetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Sancuso is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness of Sancuso in pediatric patients under 18 years of age have not been established.

8.5 Geriatric Use

Clinical studies of Sancuso did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, cautious treatment selection for an elderly patient is prudent because of the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Renal Failure or Hepatically-Impaired Patients

Although no studies have been performed to investigate the pharmacokinetics of Sancuso in elderly subjects, and in patients with renal or hepatic impairment, pharmacokinetic information is available for intravenous granisetron (see CLINICAL PHARMACOLOGY: Pharmacokinetics 12.3).

No evidence of an effect on plasma prolactin or aldosterone concentrations has been found in studies using granisetron.

The effect on oro-cecal transit time following application of Sancuso has not been studied. Granisetron hydrochloride injection exhibited no effect on oro-cecal transit time in healthy subjects given a single intravenous infusion of 50 mcg/kg or 200 mcg/kg. Single and multiple oral doses of granisetron hydrochloride slowed colonic transit in healthy subjects.

In clinical trials there were no reported cases of overdose with Sancuso.

11 DESCRIPTION

Sancuso contains granisetron, which is an anti-nauseant and antiemetic agent. Chemically it is 1-methyl-N-[(1R,3r,5S)-9-methyl-9-azabicyclo[3.3.1]non-3-yl]-1H-indazole-3-carboxamide with a molecular weight of 312.4. Its empirical formula is C₁₈H₂₄N₄O, while its chemical structure is:

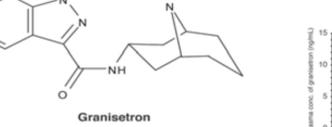
Granisetron crosses intact skin into the systemic circulation by a passive diffusion process.

Following a 7-day application of Sancuso in 24 healthy subjects, high inter-subject variability in systemic exposure was observed. Maximal concentration was reached at approximately 48 hours (range: 24-168 hours) following patch application. Mean C_{max} was 5.0 ng/mL (CV: 170%) and mean AUC_{0-168h} was 527 ng-hr/mL (CV:173%).

Total clearance of granisetron was not affected in patients with severe renal failure who received a single 40 mcg/kg intravenous dose of granisetron hydrochloride.

In patients with hepatic impairment due to neoplastic liver involvement, total plasma clearance following a single 40 mcg/kg intravenous dose of granisetron hydrochloride was approximately halved compared to patients without hepatic impairment. Given the wide variability in pharmacokinetic parameters of granisetron and the good tolerance of doses well above the recommended dose, dose adjustment in patients with hepatic functional impairment is not necessary.

Based on the measure of residual content of the patch after removal, approximately 66% (SD: ± 10.9) of granisetron is delivered following patch application for 7 days.



Granisetron is a white to off-white solid that is insoluble in water. Sancuso is a thin, translucent, matrix-type transdermal patch that is rectangular-shaped with rounded corners, consisting of a backing, the drug matrix and a release liner.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Granisetron is a selective 5-hydroxytryptamine₃ (5-HT₃) receptor antagonist with little or no affinity for other serotonin receptors, including 5-HT₁, 5-HT_{1A}, 5-HT_{1B/C}, 5-HT₂, for alpha₁-, alpha₂-, or beta-adrenoreceptors; for dopamine-D₂; or for histamine-H₁; benzodiazepine; pirototoxin or opioid receptors.

Serotonin receptors of the 5-HT₃ type are located peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. During chemotherapy that induces vomiting, mucosal enterochromaffin cells release serotonin, which stimulates 5-HT₃ receptors. This evokes vagal afferent discharge, inducing vomiting. Animal studies demonstrate that, in binding to 5-HT₃ receptors, granisetron blocks serotonin stimulation and subsequent vomiting after emetogenic stimuli such as cisplatin. In the ferret animal model, a single granisetron injection prevented vomiting due to high-dose cisplatin or arrested vomiting within 5 to 30 seconds.

12.2 Pharmacodynamics

The effect of granisetron on QTc prolongation was evaluated in a randomized, single-blind, positive (moxifloxacin 400 mg) - and placebo controlled parallel study in healthy subjects. A total of 240 subjects were administered Sancuso patch, intravenous granisetron (10 mcg/kg over 30 seconds). In a study with demonstrated ability to detect small effects, the upper bound of the 90% confidence interval for the largest placebo adjusted, baseline corrected QTc based on Fridericia correction method (QTcF) for Sancuso was below 10 ms, the threshold for regulatory concern.

No studies have been performed to investigate the pharmacokinetics of Sancuso in elderly subjects, and in patients with renal or hepatic impairment, the following pharmacokinetic information is available for intravenous granisetron.

In the elderly, and in patients with renal failure or hepatic impairment, the pharmacokinetics of granisetron were determined following a single 40 mcg/kg intravenous dose of granisetron hydrochloride.

In elderly volunteers (mean age 71 years) pharmacokinetic parameters following a single 40 mcg/kg intravenous dose of granisetron hydrochloride, lower clearance and longer half-life were observed compared to younger healthy volunteers.

In patients with severe renal failure who received a single 40 mcg/kg intravenous dose of granisetron hydrochloride, lower clearance and longer half-life were observed compared to younger healthy volunteers.

12.3 Pharmacokinetics

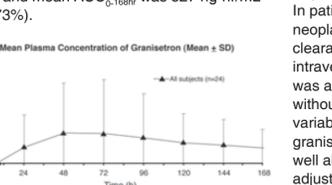
Granisetron crosses intact skin into the systemic circulation by a passive diffusion process.

Following a 7-day application of Sancuso in 24 healthy subjects, high inter-subject variability in systemic exposure was observed. Maximal concentration was reached at approximately 48 hours (range: 24-168 hours) following patch application. Mean C_{max} was 5.0 ng/mL (CV: 170%) and mean AUC_{0-168h} was 527 ng-hr/mL (CV:173%).

Total clearance of granisetron was not affected in patients with severe renal failure who received a single 40 mcg/kg intravenous dose of granisetron hydrochloride.

In patients with hepatic impairment due to neoplastic liver involvement, total plasma clearance following a single 40 mcg/kg intravenous dose of granisetron hydrochloride was approximately halved compared to patients without hepatic impairment. Given the wide variability in pharmacokinetic parameters of granisetron and the good tolerance of doses well above the recommended dose, dose adjustment in patients with hepatic functional impairment is not necessary.

Based on the measure of residual content of the patch after removal, approximately 66% (SD: ± 10.9) of granisetron is delivered following patch application for 7 days.



Based on the measure of residual content of the patch after removal, approximately 66% (SD: ± 10.9) of granisetron is delivered following patch application for 7 days.

Distribution

Plasma protein binding is approximately 65%. Granisetron distributes freely between plasma and red blood cells.

Metabolism

Granisetron metabolism involves N-demethylation and aromatic ring oxidation followed by conjugation. *In vitro* liver microsomal studies show that granisetron's major route of metabolism is inhibited by ketoconazole, suggestive of metabolism mediated by the cytochrome P-450 3A subfamily. Animal studies suggest that some of the metabolites may also have 5-HT₃ receptor antagonist activity.

Elimination

Clearance is predominantly by hepatic metabolism. Based on a study with intravenous injection, approximately 12% of the dose is excreted unchanged in the urine of healthy subjects in 48 hours. The remainder of the dose is excreted as metabolites, 49% in the urine, and 34% in the feces.

Subpopulations

Gender

There is evidence to suggest that female subjects had higher granisetron concentrations than males following patch application. However, no statistically significant difference in clinical efficacy outcome was observed between genders.

Pediatrics

No studies have been performed to investigate the pharmacokinetics of Sancuso in pediatrics.

Elderly, and Renal or Hepatic Impairment

Although no studies have been performed to investigate the pharmacokinetics of Sancuso in elderly subjects, and in patients with renal or hepatic impairment, the following pharmacokinetic information is available for intravenous granisetron.

In the elderly, and in patients with renal failure or hepatic impairment, the pharmacokinetics of granisetron were determined following a single 40 mcg/kg intravenous dose of granisetron hydrochloride.

In elderly volunteers (mean age 71 years) pharmacokinetic parameters following a single 40 mcg/kg intravenous dose of granisetron hydrochloride, lower clearance and longer half-life were observed compared to younger healthy volunteers.

In patients with severe renal failure who received a single 40 mcg/kg intravenous dose of granisetron hydrochloride, lower clearance and longer half-life were observed compared to younger healthy volunteers.

Renal Failure Patients

Total clearance of granisetron was not affected in patients with severe renal failure who received a single 40 mcg/kg intravenous dose of granisetron hydrochloride.

Hepatically-Impaired Patients

In patients with hepatic impairment due to neoplastic liver involvement, total plasma clearance following a single 40 mcg/kg intravenous dose of granisetron hydrochloride was approximately halved compared to patients without hepatic impairment. Given the wide variability in pharmacokinetic parameters of granisetron and the good tolerance of doses well above the recommended dose, dose adjustment in patients with hepatic functional impairment is not necessary.

While you wear the patch, keep it covered with clothing if you will be in sunlight or near a sunlamp, including tanning beds.

Keep the skin where Sancuso was applied covered for another 10 days after the patch is taken off to protect from exposure to direct sunlight.

The area you choose should not be oily, recently shaved or have any skin problems such as being damaged (cut or scraped) or irritated (redness or a rash).

Do not apply Sancuso to areas that have been treated with creams, oils, lotions, powders or other skin products that could keep the patch from sticking well to your skin.

Patient Information

Sancuso® [san-KOO-so] (Granisetron Transdermal System)

IMPORTANT: For skin use only

Read the Patient Information that comes with Sancuso before you start using it and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. If you have any questions about Sancuso, ask your healthcare provider.

What is Sancuso?

Sancuso is a prescription medicine used to prevent nausea and vomiting in people receiving some types of chemotherapy treatment. Sancuso is a skin patch that slowly releases the medicine contained in the adhesive (glue), through clean and intact skin areas into your bloodstream while you wear the patch.

Important: Sancuso contains granisetron, the same medicine in Kytril. Do not take Kytril at the same time you use Sancuso unless your healthcare provider tells you it is alright.

How do I apply the Sancuso patch?

The Sancuso patch comes inside a pouch which is inside the carton.

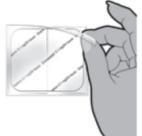
- Do not remove the patch from the pouch until you are ready to use it.
- Do not cut the Sancuso patch into pieces.**
- Remove the pouch from the carton.



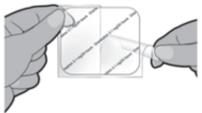
- Tear the pouch open using the slit provided, and remove the patch. Each pouch contains one Sancuso patch stuck onto a rigid plastic film, and a separate thin, clear protective liner.



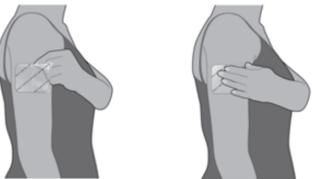
- Remove the thin, clear protective liner to expose the printed side of the patch. Throw away the liner. The protective liner is only included in the pouch to separate the patch from the inside of the pouch, and is not part of the patch.



- The unprinted, sticky side of the patch is covered by a two-piece rigid plastic film. Bend the patch in the middle and remove one half of the rigid plastic film. Be careful not to stick the patch to itself and avoid touching the sticky side of the patch.



- While holding the remaining half of the rigid plastic film, apply the patch to your skin. Remove the second half of the rigid plastic film and press the whole patch firmly in place with your fingers and smooth down. Press firmly making sure it sticks well to the skin, especially around the edges.



- Wash your hands right away after applying the patch to remove any medicine that may have stuck to your fingers.
- Keep the patch in place for the whole time you are having chemotherapy. Remove the patch at least 1 day (24 hours) after your chemotherapy is finished. The patch can be worn for up to 7 days, depending on the number of days your chemotherapy treatment lasts.
- Do not re-use the patch after you remove it. See below for instructions on the right way to remove and throw away the patch.

What to do if the Sancuso patch does not stick well?

If the patch does not stick well, you may use surgical bandages or medical adhesive tape to keep the patch in place. Place tape or bandages on the edges of the patch. Do not completely cover the patch with bandages or tape and do not wrap completely around your arm. If the patch comes more than half off or it becomes damaged see your healthcare provider.

Can I bathe or shower while wearing Sancuso?

You can continue to shower and wash normally while wearing the Sancuso patch. It is not known how other activities, for example swimming, strenuous exercise or using a sauna or whirlpool, may affect Sancuso. Avoid these activities while wearing Sancuso.

How do I remove and dispose of Sancuso?

- When you remove the patch, peel it off gently.
- The used patch will still contain some of the medicine. After removing the used Sancuso patch, fold it in half so that the sticky side sticks to itself. Throw away the Sancuso patch in the garbage, out of the reach of children and pets. Do not re-use the patch.
- After removing the patch you may find some adhesive is left on your skin. Gently wash the area with soap and water to remove it. Do not use alcohol or other dissolving liquids, such as nail polish remover. These may cause skin irritation.
- Wash your hands after handling the patch.
- You may see mild redness on the skin where the patch is removed. This redness should go away within three days. If redness continues, tell your healthcare provider.

What are the ingredients in Sancuso?

Active ingredient: granisetron. Inactive ingredients: acrylate-vinylacetate copolymer, polyester, titanium dioxide, polyamide resin and polyethylene wax.

Manufactured by:

3M Drug Delivery Systems, St. Paul, MN 55107

Manufactured for:

ProStrakan Inc., Bridgewater, NJ 08807

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13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility

In a 24-month carcinogenicity study, rats were treated orally with granisetron 1, 5 or 50 mg/kg/day (6, 30 or 300 mg/m²/day). The 50 mg/kg/day dose was reduced to 25 mg/kg/day (150 mg/m²/day) during week 59 due to toxicity. For a 50 kg person of average height (1.46 m² body surface area), these doses represent about 2.6, 13 and 65 times the recommended clinical dose (3.1 mg/day, 2.3 mg/m²/day, delivered by the Sancuso patch, on a body surface area basis). There was a statistically significant increase in the incidence of hepatocellular carcinomas and adenomas in males treated with 5 mg/kg/day (30 mg/m²/day, about 13 times the recommended human dose with Sancuso, on a body surface area basis) and above, and in females treated with 25 mg/kg/day (150 mg/m²/day, about 65 times the recommended human dose with Sancuso, on a body surface area basis). No increase in liver tumors was observed at a dose of 1 mg/kg/day (6 mg/m²/day, about 2.6 times the recommended human dose with Sancuso, on a body surface area basis) in males and 5 mg/kg/day (30 mg/m²/day, about 13 times the recommended human dose with Sancuso, on a body surface area basis) in females.

In a 12-month oral toxicity study, treatment with granisetron 100 mg/kg/day (600 mg/m²/day), about 261 times the recommended human dose with Sancuso, on a body surface area basis) produced hepatocellular adenomas in male and female rats while no such tumors were found in the control rats. A 24-month mouse carcinogenicity study of granisetron did not show a statistically significant increase in tumor incidence, but the study was not conclusive.

Because of the tumor findings in rat studies, Sancuso should be prescribed only at the dose and for the indication recommended (see INDICATIONS AND USAGE, and DOSAGE AND ADMINISTRATION).

Granisetron was not mutagenic in an *in vitro* Ames test and mouse lymphoma cell forward mutation assay, and *in vivo* mouse micronucleus test and *in vitro* and *ex vivo* rat hepatocyte UDS assays. It, however, produced a significant increase in UDS in HeLa cells *in vitro* and a significant increased incidence of cells with polyploidy in an *in vitro* human lymphocyte chromosomal aberration test.

Granisetron at subcutaneous doses up to 6 mg/kg/day (36 mg/m²/day, about 16 times the recommended human dose of Sancuso, on a body surface area basis), and oral doses up to 100 mg/kg/day (600 mg/m²/day, about 261 times the recommended human dose of Sancuso, on a body surface area basis) was found to have no effect on fertility and reproductive performance of male and female rats.

Granisetron was not phototoxic when tested *in vitro* in a Chinese hamster ovary (CHO) cell line, at 200 and 300 mcg/ml, granisetron increased the percentage of cells with chromosomal aberration following photoirradiation.

Granisetron was not phototoxic when tested *in vitro* in a mouse fibroblast cell line. When tested *in vivo* in guinea-pigs, Sancuso patches did not show any potential for photirritation or photosensitivity. No phototoxicity studies have been performed in humans.

14. CLINICAL STUDIES

The effectiveness of Sancuso in the prevention of chemotherapy-induced nausea and vomiting (CINV) was evaluated in a Phase 3 randomized, parallel group, double-blind, double-dummy study conducted in the U.S. and abroad. The study compared the efficacy, tolerability and safety of Sancuso with that of 2 mg oral granisetron once daily in the prevention of nausea and vomiting in a total of 641 patients receiving multi-day chemotherapy.

The population randomized into the trial included 48% males and 52% females aged 16 to 86 years receiving moderately (ME) or highly emetogenic (HE) multi-day chemotherapy. Seventy-eight (78%) of patients were White, 12% Asian, 10% Hispanic/Latino and 0% Black.

The granisetron patch was applied 24 to 48 hours before the first dose of chemotherapy, and kept in place for 7 days. Oral granisetron was administered daily for the duration of the chemotherapy regimen, one hour before each dose of chemotherapy. Efficacy was assessed from the first administration until 24 hours after the start of the last day's administration of the chemotherapy regimen.

The primary endpoint of the trial was the proportion of patients achieving no vomiting and/or retching, no more than mild nausea and no rescue medication from the first administration until 24 hours after the start of the last day's administration of multi-day chemotherapy. Using this definition, the effect of Sancuso was established in 60.2% of patients in the Sancuso arm and 64.8% of patients receiving oral granisetron (difference -4.89%; 95% confidence interval -12.91% to +3.13%).

An assessment of patch adhesion in 621 patients receiving either active or placebo patches showed that less than 1% of patches became detached over the course of the 7 day period of patch application.

16. HOW SUPPLIED/STORAGE AND HANDLING

Sancuso (Granisetron Transdermal System) is supplied as a 52 cm² patch containing 34.3 mg of granisetron. Each patch is printed on one side with the words "Granisetron 3.1 mg/24 hours". Each patch is packaged in a separate sealed foil-lined plastic pouch.

Sancuso is available in packages of 1 (NDC 42747-726-01) patch.

Store at 20°-25°C (68°-77°F); excursions permitted between 15°-30°C (59°-86°F). [see USP Controlled Room Temperature].

Sancuso should be stored in the original packaging.

17. PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (17.5)

17.1 Gastrointestinal

Because the use of granisetron may mask a progressive ileus and/or gastric distention caused by the underlying condition, patients should be instructed to tell their physician if they have pain or swelling in their abdomen.

17.2 Skin Reactions

Patients should be instructed to remove the patch if they have a severe skin reaction, or a generalized skin reaction (e.g. allergic rash, including erythematous, macular, papular rash or pruritus).

When patients remove the patch, they should be instructed to peel it off gently.

17.3 Exposure to Sunlight

Granisetron may be degraded by direct sunlight or exposure to sunlamps. In addition, an *in vitro* study using Chinese hamster ovary cells suggests that granisetron has the potential for photogenotoxicity (see Section 13.2).

Patients must be advised to cover the patch application site, e.g. with clothing, if there is a risk of exposure to sunlight or sunlamps throughout the period of wear and for 10 days following its removal.

17.4 Serotonin Syndrome

Advise patients of the possibility of serotonin syndrome with concomitant use of Sancuso and another serotonergic agent such as medications to treat depression and migraines. Advise patients to seek immediate medical attention if the following symptoms occur: changes in mental status, autonomic instability, neuromuscular symptoms, with or without gastrointestinal symptoms.

Rx only

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Rev. 09/14

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17.5 FDA-Approved Patient Labeling Patient Information

Sancuso® [san-KOO-so] (Granisetron Transdermal System)

IMPORTANT: For skin use only

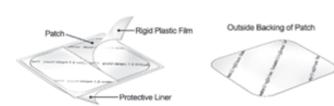
Read the Patient Information that comes with Sancuso before you start using it and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment. If you have any questions about Sancuso, ask your healthcare provider.

What is Sancuso?

Sancuso is a prescription medicine used to prevent nausea and vomiting in people receiving some types of chemotherapy treatment.

Sancuso is a skin patch that slowly releases the medicine contained in the adhesive (glue), through clean and intact skin areas into your bloodstream while you wear the patch.

Important: Sancuso contains granisetron, the same medicine in Kytril. Do not take Kytril at the same time you use Sancuso unless your healthcare provider tells you it is alright.



Who should not use Sancuso?

Do not use Sancuso if you are allergic to any of the ingredients in Sancuso. See the end of this leaflet for a list of ingredients in Sancuso.

What should I tell my healthcare provider before using Sancuso?

Tell your healthcare provider about all your medical conditions, including if you:

- are allergic to medical adhesive tape, adhesive dressings or other skin patches.
- have pain or swelling in your stomach area (abdomen).
- are pregnant. It is not known if Sancuso will harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant.
- are breast-feeding or plan to breast-feed. It is not known if Sancuso passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements. Other medicines may affect how Sancuso works. Sancuso may also affect how other medicines work.

How should Sancuso be used?

Use Sancuso exactly as prescribed.

See the detailed Patient Instructions for Applying Sancuso at the end of this Patient Information leaflet.

What should I avoid while using Sancuso?

Avoid sunlight. The medicine in Sancuso (granisetron) may not work as well and/or may affect your skin if exposed to direct sunlight or the light from sunlamps or tanning beds. It is important to do the following:

- While you wear the patch, keep it covered with clothing if you will be in sunlight or near a sunlamp, including tanning beds.
- Keep the skin where Sancuso was applied covered for another 10 days after the patch is taken off to protect from exposure to direct sunlight.

What are the possible side effects of Sancuso?

Sancuso can cause serious side effects:

- Using Sancuso may make it harder to identify certain stomach and bowel problems that are from other causes.** Tell your healthcare provider if you have any stomach area (abdominal) pain or swelling while using Sancuso.
- Skin reactions.** Skin reactions can happen just at the patch application site or outside the patch application site. Tell your healthcare provider if you get any redness, rashes, bumps, blisters or itching at the patch application site, and especially if they spread outside the place where the patch was or if they appear outside the patch application site. You may need to stop using Sancuso.

Common side effects of Sancuso are:

- constipation
- headache.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Sancuso. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Sancuso?

- Keep Sancuso in the package it comes in.
 - Store Sancuso at 20-25°C (68-77°F).
- Keep Sancuso out of the reach of children.**

General information about Sancuso

Medicines are sometimes prescribed for conditions that are not mentioned in Patient Information leaflets. Do not use Sancuso for a condition for which it is not prescribed. Do not give Sancuso to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about Sancuso. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about Sancuso that is written for health professionals.

For more information, go to www.sancuso.com or call 1-800-SANCUSO.

Patient Instructions for Applying Sancuso

When do I apply the Sancuso patch?

- Apply Sancuso at least 1 day (24 hours) before your scheduled chemotherapy treatment.
- You may apply Sancuso up to 2 days (48 hours) before your scheduled chemotherapy.
- Wear the patch all the time during your chemotherapy.
- Sancuso may be worn for up to 7 days, depending on how long your chemotherapy treatment lasts (up to 5 days).
- Remove the patch at least 1 day (24 hours) after your chemotherapy is finished.
- Keep the patch covered, such as under clothing, while you are wearing it to avoid a skin reaction to sunlight or sunlamps. Keep the skin where Sancuso was applied (application site) covered up for another 10 days after the patch is taken off to prevent a skin reaction. See "What should I avoid while using Sancuso?"

Where do I apply the Sancuso patch?

- Apply Sancuso to a clean, dry, healthy area of skin on the outside part of your upper arm.



- The area you choose should not be oily, recently shaved or have any skin problems such as being damaged (cut or scraped) or irritated (redness or a rash).
- Do not apply Sancuso to areas that have been treated with creams, oils, lotions, powders or other skin products that could keep the patch from sticking well to your skin.**

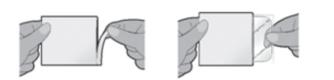
How do I apply the Sancuso patch?

The Sancuso patch comes inside a pouch which is inside the carton.

- Do not remove the patch from the pouch until you are ready to use it.
- Do not cut the Sancuso patch into pieces.**
- Remove the pouch from the carton.



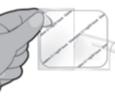
- Tear the pouch open using the slit provided, and remove the patch. Each pouch contains one Sancuso patch stuck onto a rigid plastic film, and a separate thin, clear protective liner.



- Remove the thin, clear protective liner to expose the printed side of the patch. Throw away the liner. The protective liner is only included in the pouch to separate the patch from the inside of the pouch, and is not part of the patch.



- The unprinted, sticky side of the patch is covered by a two-piece rigid plastic film. Bend the patch in the middle and remove one half of the rigid plastic film. Be careful not to stick the patch to itself and avoid touching the sticky side of the patch.



- While holding the remaining half of the rigid plastic film, apply the patch to your skin. Remove the second half of the rigid plastic film and press the whole patch firmly in place with your fingers and smooth down. Press firmly making sure it sticks well to the skin, especially around the edges.



- Wash your hands right away after applying the patch to remove any medicine that may have stuck to your fingers.
- Keep the patch in place for the whole time you are having chemotherapy. Remove the patch at least 1 day (24 hours) after your chemotherapy is finished. The patch can be worn for up to 7 days, depending on the number of days your chemotherapy treatment lasts.
- Do not re-use the patch after you remove it. See below for instructions on the right way to remove and throw away the patch.

What to do if the Sancuso patch does not stick well?

If the patch does not stick well, you may use surgical bandages or medical adhesive tape to keep the patch in place. Place tape or bandages on the edges of the patch. Do not completely cover the patch with bandages or tape and do not wrap completely around your arm. If the patch comes more than half off or it becomes damaged see your healthcare provider.

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You can continue to shower and wash normally while wearing the Sancuso patch. It is not known how other activities, for example swimming, strenuous exercise or using a sauna or whirlpool, may affect Sancuso. Avoid these activities while wearing Sancuso.

How do I remove and dispose of Sancuso?

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- Wash your hands after handling the patch.
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What are the ingredients in Sancuso?

Active ingredient: granisetron. Inactive ingredients: acrylate-vinylacetate copolymer, polyester, titanium dioxide, polyamide resin and polyethylene wax.