

Medication Guide

SUBSYS™ (sub sis) CII
(fentanyl)

sublingual spray

100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg

IMPORTANT:

Do not use SUBSYS unless you are regularly using another opioid pain medicine around-the-clock for your cancer pain and your body is used to these medicines (this means that you are opioid tolerant). You can ask your healthcare provider if you are opioid tolerant.

Keep SUBSYS in a safe place away from children.

Get emergency medical help right away if:

- **a child uses SUBSYS. SUBSYS can cause an overdose and death in any child who uses it.**
- **an adult who has not been prescribed SUBSYS uses it**
- **an adult who is not already taking opioids around-the-clock, uses SUBSYS**

These are medical emergencies that can cause death.

Read this Medication Guide completely before you start using SUBSYS, and each time you get a new prescription. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or your treatment. Be sure to share this important information with members of your household and other caregivers.

What is the most important information I should know about SUBSYS?

SUBSYS can cause life-threatening breathing problems which can lead to death.

- 1. Do not take SUBSYS if you are not opioid tolerant.**
- 2. If you stop taking your around-the-clock opioid pain medicine for your cancer pain, you must stop using SUBSYS.** You may no longer be opioid tolerant. Talk to your healthcare provider about how to treat your pain.
- 3. Use SUBSYS exactly as prescribed by your healthcare provider.**
 - o You must not use more than **2** doses of SUBSYS for each episode of breakthrough cancer pain.
 - o You must wait four hours before treating a new episode of breakthrough pain with SUBSYS. **See the Medication Guide section "How should I**

use SUBSYS?" and the "Instructions for Use" section at the end of this Medication Guide for detailed information about how to use SUBSYS the right way.

4. **Do not switch from SUBSYS to other medicines that contain fentanyl without talking with your healthcare provider.** The amount of fentanyl in a dose of SUBSYS is not the same as the amount of fentanyl in other medicines that contain fentanyl. Your healthcare provider will prescribe a starting dose of SUBSYS that may be different than other fentanyl containing medicines you may have been taking.
5. **Do not** use SUBSYS for short-term pain that you would expect to go away in a few days, such as:
 - pain after surgery
 - headache or migraine
 - dental pain
6. **Never give SUBSYS to anyone else**, even if they have the same symptoms you have. It may harm them or even cause death.

SUBSYS is a federally controlled substance (CII) because it is a strong opioid (narcotic) pain medicine that can be misused by people who abuse prescription medicines or street drugs.

- **Prevent theft, misuse or abuse. Keep SUBSYS in a safe place** to protect it from being stolen. SUBSYS can be a target for people who abuse opioid (narcotic) medicines or street drugs.
- **Selling or giving away this medicine is against the law.**

SUBSYS is available only through a program called the TIRF REMS ACCESS program. To receive SUBSYS, you must:

- talk to your healthcare provider
- understand the benefits and risks of SUBSYS
- agree to all of the instructions
- sign the Patient-Prescriber Agreement form

What is SUBSYS?

- SUBSYS is a prescription medicine that contains the medicine fentanyl.
- SUBSYS is used to manage breakthrough pain in adults with cancer, who are already routinely taking other opioid pain medicines around-the-clock for cancer pain.
- SUBSYS is started only after you have been taking other opioid pain medicines and your body has become used to them (you are opioid tolerant). Do not use SUBSYS if you are not opioid tolerant.
- You must stay under your healthcare provider's care while taking SUBSYS.

- SUBSYS is a liquid medicine that is sprayed underneath your tongue (sublingual) and allowed to absorb.
- SUBSYS is only:
 - o available through the TIRF REMS ACCESS program
 - o given to people who are opioid tolerant

It is not known if SUBSYS is safe and effective in children under 16 years of age.

Who should not use SUBSYS?

Do not use SUBSYS:

- **if you are not opioid tolerant. Opioid tolerant means that you are already taking other opioid pain medicines around-the-clock for your cancer pain, and your body is used to these medicines.**
- for short-term pain that you would expect to go away in a few days, such as:
 - o pain after surgery
 - o headache or migraine
 - o dental pain
- if you are allergic to any of the ingredients in SUBSYS. See the end of this Medication Guide for a complete list of other ingredients in SUBSYS.

What should I tell my healthcare provider before using SUBSYS?

Before using SUBSYS, tell your healthcare provider if you:

- have sores or ulcers in your mouth
- have trouble breathing or lung problems such as asthma, wheezing, or shortness of breath
- have or had a head injury or brain problem
- have liver or kidney problems
- have seizures
- have a slow heart rate or other heart problems
- have low blood pressure
- have mental health problems including major depression, schizophrenia or hallucinations (seeing or hearing things that are not there)
- have a past or present drinking problem (alcoholism), or a family history of drinking problems
- have a past or present drug abuse problem or addiction problem, or a family history of a drug abuse problem or addiction problem
- have any other medical conditions

- are pregnant or plan to become pregnant. SUBSYS may cause serious harm to your unborn baby.
- are breastfeeding or plan to breastfeed. SUBSYS can pass into your breast milk. It can cause serious harm to your baby. You should not use SUBSYS while breastfeeding.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Some medicines may cause serious or life-threatening side effects when taken with SUBSYS. Sometimes, the doses of certain medicines and SUBSYS may need to be changed if used together.

- **Do not take any medicine while using SUBSYS until you have talked to your healthcare provider.** Your healthcare provider will tell you if it is safe to take other medicines while you are using SUBSYS.
- Be very careful about taking other medicines that may make you sleepy, such as other pain medicines, anti-depressants, sleeping pills, anti-anxiety medicines, antihistamines, muscle relaxants or tranquilizers.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use SUBSYS?

Before you can begin to use SUBSYS:

- Your healthcare provider will explain the TIRF REMS ACCESS program to you.
- You will sign the TIRF REMS ACCESS program Patient-Prescriber Agreement form.
- SUBSYS is only available at pharmacies that are part of the TIRF REMS ACCESS program. Your healthcare provider will let you know the pharmacy closest to your home where you can have your SUBSYS prescription filled.

Using SUBSYS:

- **Use SUBSYS exactly as prescribed.** Do not use SUBSYS more often than prescribed.
- See the “Instructions for Use” section at the end of this Medication Guide for detailed information about the right way to use and throw away (dispose of) SUBSYS.
- SUBSYS comes in several strengths. When you are first prescribed SUBSYS, your healthcare provider will start you with the lowest strength medicine, and will change the dose until you and your healthcare provider find the right dose for you. **Do not change your dose of SUBSYS unless your healthcare provider tells you to. Each SUBSYS unit contains enough medicine for 1 spray.**

- **As your dose is adjusted, your healthcare provider will tell you whether your dose of SUBSYS is 1 or 2 sprays given underneath the tongue.**
 - **If your dose of SUBSYS is 1 spray, then you will use 1 SUBSYS unit for each dose.**
 - **If your dose of SUBSYS is 2 sprays, then you will use 2 SUBSYS units for each dose.**
- **Take 1 dose** of SUBSYS when you get an episode of breakthrough cancer pain.
- If you are still in pain after 30 minutes, **take 1 more dose** of SUBSYS as instructed by your healthcare provider.
- **Do not** take more than 2 doses of SUBSYS for an episode of breakthrough cancer pain. If your breakthrough pain does not get better after the second dose of SUBSYS, call your healthcare provider for instructions. **Do not use another dose of SUBSYS at this time.**
- **Wait at least 4 hours** before treating a new episode of breakthrough cancer pain with SUBSYS.
- Keep taking your around-the-clock opioid pain medicine while taking SUBSYS.
- If you have **more than 4 episodes of breakthrough cancer pain in a day**, talk to your healthcare provider. The dose of your around-the-clock opioid pain medicine may need to be adjusted.
- **If you use too much SUBSYS or overdose**, you or your caregiver should call for emergency medical help or have someone take you to the nearest hospital emergency room right away.

What should I avoid while using SUBSYS?

- **Do not drive, operate heavy machinery, or do other dangerous** activities until you know how SUBSYS affects you. SUBSYS can make you sleepy. Ask your healthcare provider when it is okay to do these activities.
- **Do not drink alcohol while using SUBSYS.** It can increase your chance of getting dangerous side effects.

What are the possible side effects of SUBSYS?

SUBSYS can cause serious side effects, including:

1. **Breathing problems that can become life-threatening.** See "What is the most important information I should know about SUBSYS?"
 - **Call your healthcare provider or get emergency medical help right away if you:**

- have trouble breathing
- have drowsiness with slowed breathing
- have shallow breathing (little chest movement with breathing)
- feel faint, very dizzy, confused, or have other unusual symptoms

These symptoms can be a sign that you have used too much SUBSYS or the dose is too high for you. These symptoms may lead to serious problems or death if not treated right away. If you have any of these symptoms, do not use any more SUBSYS until you have talked to your healthcare provider.

2. **Decreased blood pressure.** This can make you feel dizzy or lightheaded if you get up too fast from sitting or lying down.
3. **Physical dependence. Do not stop using SUBSYS or any other opioid, without talking to your healthcare provider.** You could become sick with withdrawal symptoms because your body has become used to these medicines. Physical dependency is not the same as drug addiction.
4. **A chance of abuse or addiction.** This chance is higher if you are or have ever been addicted to or abused other medicines, street drugs, or alcohol, or if you have a history of mental health problems.

The most common side effects of SUBSYS are:

- nausea
- vomiting
- shortness of breath
- sleepiness
- dizziness
- headache

Constipation (not often enough or hard bowel movements) is a very common side effect of pain medicines (opioids) including SUBSYS and is unlikely to go away without treatment. Talk to your healthcare provider about dietary changes, and the use of laxatives (medicines to treat constipation) and stool softeners to prevent or treat constipation while using SUBSYS.

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 SUBSYS. 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 SUBSYS?

- **Always keep SUBSYS in a safe place away from children and from anyone for whom it has not been prescribed.** Protect SUBSYS from theft.
- Store SUBSYS at room temperature, 59°F to 86°F (15°C to 30°C) until ready to use.
- Keep SUBSYS in the original blister package. Do not remove SUBSYS units from the blister packages for storage in a temporary container.
- See the “Instructions for Use” section at the end of this Medication Guide for information about the right way to dispose of SUBSYS when no longer needed.
- Use the SUBSYS Child Safety Kit to help you store SUBSYS and your other medicines out of the reach of children. It is very important that you use the items in the SUBSYS Child Safety Kit to help protect the children in your home or visiting your home.
- Call Insys Therapeutics, Inc. at 1-877-978-2797 for a SUBSYS Child Safety Kit.

The SUBSYS Child Safety Kit contains important information on the storage and handling of SUBSYS.

The SUBSYS Child Safety Kit includes:

- a **portable pouch (Figure A) and lock (Figure B)** for you to keep a small supply of SUBSYS. Keep the rest of your SUBSYS in the locked storage space.

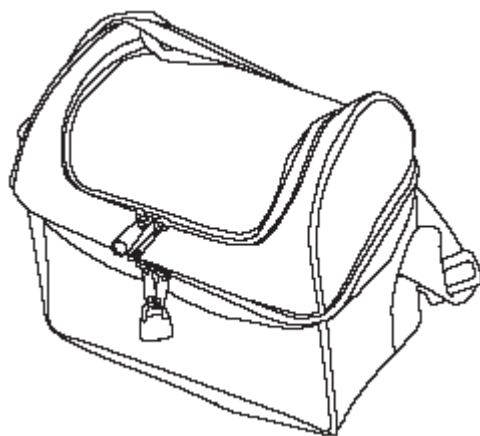


Figure A

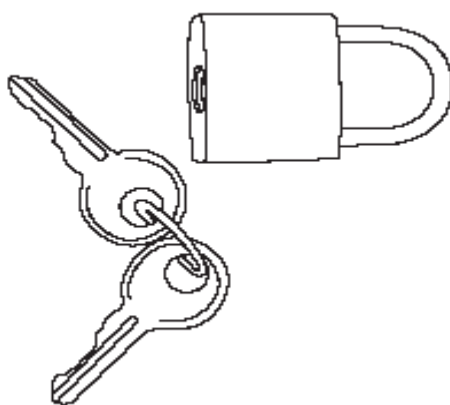


Figure B

- a **package of cabinet and drawer child safety latches (Figure C)** to secure the storage space where SUBSYS is kept at home.

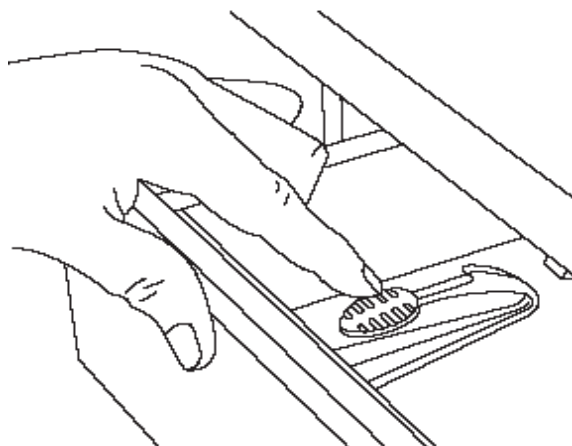


Figure C

- Keep the pouch locked and away from children. **(See Figure C.)**

General information about SUBSYS

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. **Use SUBSYS only for the purpose for which it was prescribed. Do not give SUBSYS to other people, even if they have the same symptoms you have.** SUBSYS can harm other people and even cause death. Sharing SUBSYS is against the law.

This Medication Guide summarizes the most important information about SUBSYS. If you would like more information, talk with your healthcare provider or pharmacist. You can ask your pharmacist or healthcare provider for information about SUBSYS that is written for healthcare professionals.

For more information about the TIRF REMS ACCESS program, go to www.TIRFREMSaccess.com or call 1-866-822-1483.

What are the ingredients in SUBSYS?

Active ingredient: fentanyl

Inactive ingredients: dehydrated alcohol 63.6%, purified water, propylene glycol, xylitol, and L-menthol.

Instructions for Use

Before you use SUBSYS, it is important that you read the Medication Guide and these Instructions for Use. Be sure that you read, understand, and follow these Instructions for Use so that you use SUBSYS the right way. Ask your healthcare provider or pharmacist if you have questions about the right way to use SUBSYS.

What will I find in the SUBSYS package?

Each SUBSYS Carton contains **(See Figure D)**:

- individual blister packages containing single spray units of SUBSYS
- a supply of small white disposal bags for use when disposing of used SUBSYS units
- a Medication Guide (not shown)
- a Package Insert (not shown)

In addition to your supply of SUBSYS spray units, you will be given a separate carton containing:

- a disposal bottle
- a large disposal bag
- a Medication Guide (not shown)

- When you get an episode of breakthrough cancer pain, take the dose prescribed by your healthcare provider as follows: SUBSYS comes in individual blister packages. Do not open the blister package until you are ready to use it.



Figure D

- Remove the SUBSYS spray unit from the blister package by cutting the dashed line with a pair of scissors. **(See Figure E.)**



Figure E

- To correctly use SUBSYS:
 - o Swallow any saliva in your mouth.
 - o Hold the SUBSYS spray unit **upright** using your index and middle fingers and thumb. (See Figure F.)



Figure F

- o Point the nozzle **into** your mouth and **under** your tongue. (See Figures G and H.)



Figure G



Figure H

- o Squeeze your fingers and thumb together to spray SUBSYS under your tongue. **(See Figure I.)**
- o Hold the medicine under your tongue for **30-60 seconds**. Do not spit out any medicine. Do not rinse your mouth.



Figure I

- o The SUBSYS spray unit will remain locked after use. **(See Figure J.)**



Figure J

Disposing of SUBSYS:

After using SUBSYS, dispose of the spray unit as follows:

- Place the used SUBSYS spray unit into one of the disposal bags provided in the carton containing the spray units. **(See Figure K.)**

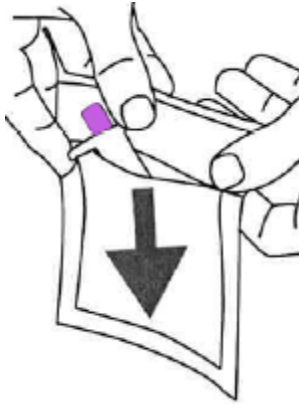


Figure K

- Remove the backing from the adhesive strip.
- Fold the flap to seal the bag. **(See Figure L.)**

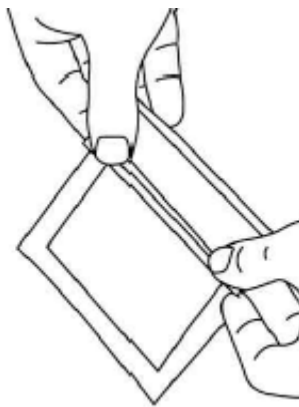


Figure L

- Discard in the trash out of the reach of children. **(See Figure M.)**



Figure M

Do not ingest the contents of the bag.

Disposal of any unused SUBSYS when no longer needed:

Before you throw away the SUBSYS spray units, you must empty all of the medicine into the disposal bottle. This protects others, especially children from harm.

- Remove the SUBSYS spray unit from the blister package by cutting the dashed line with a pair of scissors. **(See Figure N.)**



Figure N

- Squeeze the ribbed areas at the top of the disposal bottle and flip the lid up. **(See Figures O and P.)**

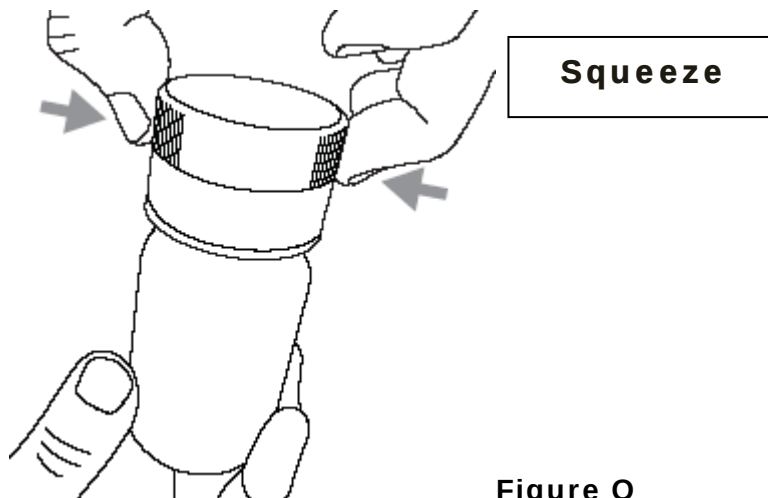


Figure O

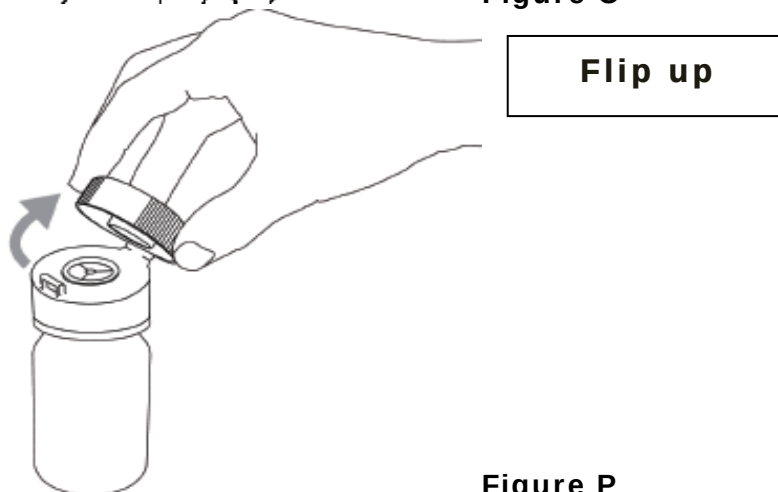


Figure P

- Put the nozzle of the SUBSYS spray unit upside-down into the opening of the bottle. **(See Figure Q.)**

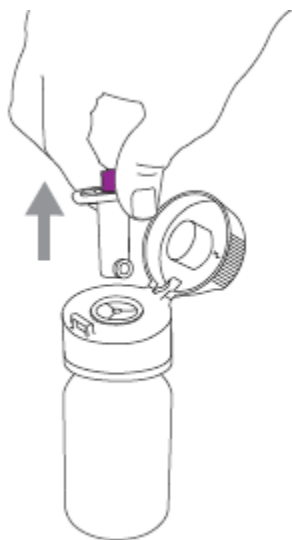


Figure Q

- Press down on the light purple vial holder with your thumb to push the medicine from the nozzle into the bottle. **(See Figure R.)**

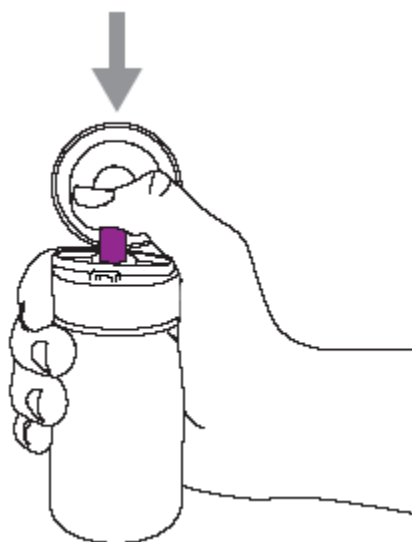
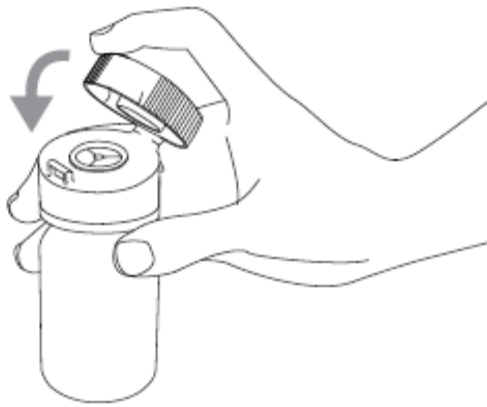


Figure R

- Remove the **entire** spray unit and dispose of it in the small disposal bag. **(See Figures K and L.)**
- **Repeat steps N through R for each unused SUBSYS spray unit.**
- Make sure all unused spray units have been sprayed into the disposal bottle, then removed from the bottle and put in disposal bags. **(See Figures K and L above.)**
- Flip the lid down to close the disposal bottle tightly. **Shake from side to side.** **(See Figures S and T.)**



Flip down lid.

Figure S

Shake side to side.

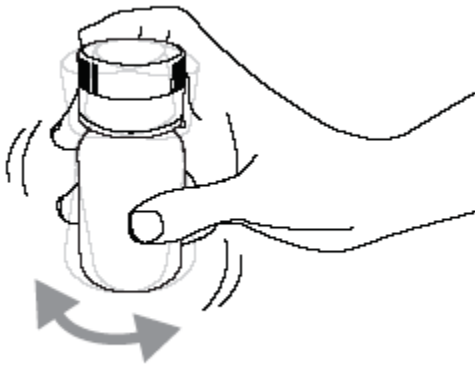


Figure T

- Place the used disposal bottle into the large disposal bag. **(See Figure U.)**

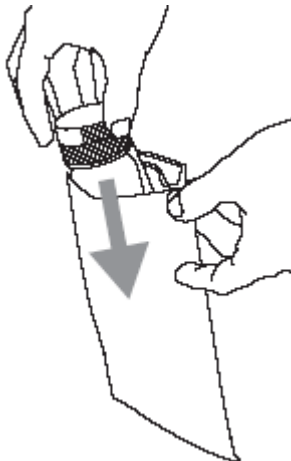


Figure U

- Remove the backing from the adhesive strip. **(See Figure V.)**

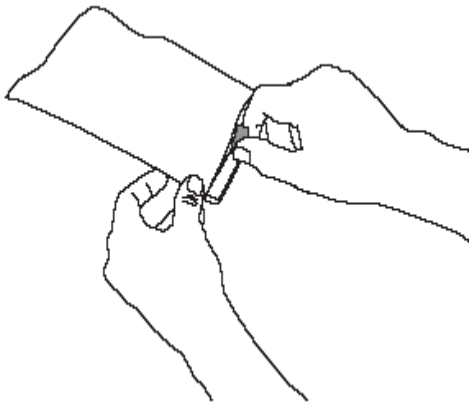


Figure V

- Fold the flap to seal the bag. **(See Figure W.)**

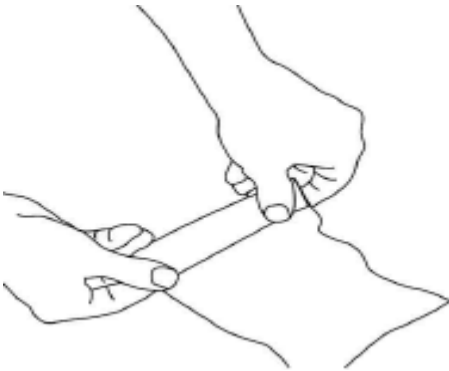


Figure W

- Discard in the trash out of the reach of children. **(See Figure X.)**

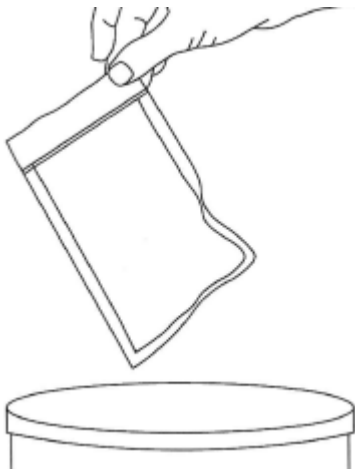


Figure X

Do not ingest the contents of the bag.

If you need help with disposal of SUBSYS, call Insys Therapeutics, Inc. at 1-877-978-2797 or call your local Drug Enforcement Agency (DEA) office.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:
DPT Laboratories, Ltd., Lakewood, NJ 08701

for:
Insys Therapeutics, Inc., Phoenix, AZ 85044

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