

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

NITISINONE TABLETS

Read this carefully before you start taking NITISINONE TABLETS and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about NITISINONE TABLETS.

What are NITISINONE TABLETS used for?

NITISINONE TABLETS are used for the treatment of hereditary tyrosinemia type 1 (HT-1), in addition to limiting the amount of tyrosine and phenylalanine in the diet.

How do NITISINONE TABLETS work?

NITISINONE TABLETS stop the build-up of toxic substances which cause the severe liver and kidney problems in patients with HT-1. By doing that, they also prevent the porphyric crises associated with HT-1.

What are the ingredients in NITISINONE TABLETS?

Medicinal ingredients: Nitisinone.

Non-medicinal ingredients: glyceryl dibehenate, lactose monohydrate.

NITISINONE TABLETS come in the following dosage forms:

Tablets: 2 mg, 5 mg, or 10 mg.

Do not use NITISINONE TABLETS if you:

- Are allergic (hypersensitive) to nitisinone or any of the other ingredients in NITISINONE TABLETS.
- Are breast-feeding. Do not breast feed while taking NITISINONE TABLETS.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take NITISINONE TABLETS. Talk about any health conditions or problems you may have, including if you:

- Are pregnant or planning to become pregnant.

Other warnings you should know about:

Dietary Changes

Taking NITISINONE TABLETS can cause high levels of tyrosine in your blood which can be toxic. As a result, while you are taking NITISINONE TABLETS you must limit the amount of tyrosine and phenylalanine in your diet. Talk to your healthcare professional about which foods are safe to eat and which foods should be avoided.

Eye Problems

Your healthcare professional will check your eyes before starting treatment with NITISINONE TABLETS. If you develop eye problems while taking NITISINONE TABLETS, including sensitivity to light, eye pain, redness, swelling or burning, talk to your healthcare professional immediately.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take NITISINONE TABLETS:

- Take NITISINONE TABLETS exactly as your healthcare professional has told you. Talk to your healthcare professional or pharmacist if you have questions.
- There are a couple of ways to take this medication. Your healthcare professional will discuss these with you and tell you how you should take it.
- NITISINONE TABLETS are usually taken twice a day.
- Your healthcare professional will tell you how many tablets to take.
- Do not change your dose or stop taking this medication without first talking to your doctor.

Preparing and taking the dose:

For patients swallowing the tablets whole

Swallow the tablets whole with a drink of water. NITISINONE TABLETS can be taken with or without food.

For infants and patients who have a problem swallowing the tablets whole

NITISINONE TABLETS may be crushed between two spoons and then mixed with applesauce. As well, NITISINONE TABLETS can be broken down in water in an oral syringe to form a suspension.

Preparing and taking NITISINONE TABLETS by crushing and mixing with applesauce:

1. Wash your hands well before crushing NITISINONE TABLETS.
2. Crush only 1 NITISINONE TABLET at a time.
3. Measure about 1 teaspoon of applesauce and put it into a clean container, such as a glass or bowl.
4. Place 1 NITISINONE TABLET onto a metal teaspoon.
5. Place a second teaspoon on top of the teaspoon holding the tablet.
6. Apply light pressure with the second teaspoon. Press and rotate the two teaspoons against each other until the tablet is crushed to a fine powder.
7. Place all of the NITISINONE TABLET powder from the metal teaspoon into the clean container of applesauce. Be sure that no tablet powder remains on the teaspoon.
8. If the prescribed dose is more than 1 tablet, repeat Steps 4 to 6. Place all of the NITISINONE TABLET powder in the container with the applesauce. You do not need to add more applesauce at this time if you take more than 1 tablet.
9. Stir the NITISINONE TABLET powder and the applesauce. Do this until all the tablet powder is mixed well.

10. Remove the mixture from the container using a teaspoon and swallow. Repeat this step until no mixture is left in the container.
11. Measure another teaspoon of applesauce and place it in the container used before.
12. Stir the fresh applesauce with the mixture that is left in the container.
13. Remove the mixture from the container using a teaspoon and swallow. Repeat this step until no mixture or powder is left in the container.

Take the NITISINONE TABLETS and applesauce mixture within 2 hours.

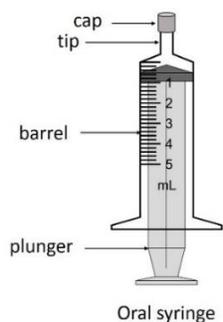
Store the NITISINONE TABLETS and applesauce mixture at room temperature (15 - 30°C).

Keep the NITISINONE TABLETS and applesauce mixture out of direct sunlight until ready for use. The mixture does not need to be refrigerated.

Throw away any mixture that is not used within 2 hours after mixing into a trash can.

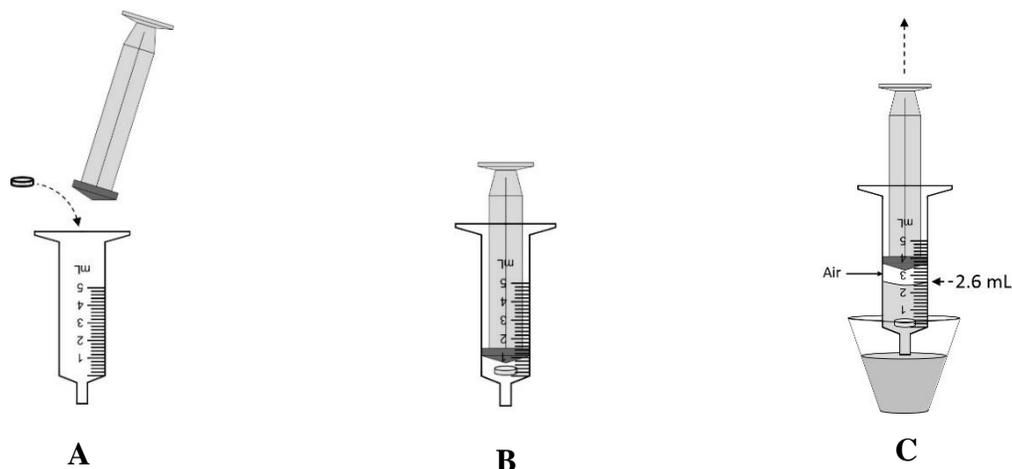
Preparing and taking NITISINONE TABLETS using an oral syringe

- **Prepare only 1 or 2 NITISINONE TABLETS** in an oral syringe at one time.
- Use a 5 mL oral syringe **with a cap** (see below) to prepare NITISINONE TABLETS in an oral syringe. Ask your pharmacist for your oral syringe. You will need more than one 5 mL oral syringe if you take more than 2 NITISINONE TABLETS for your prescribed dose. In this case, use multiple oral syringes to prepare and take your dose as needed.
- The contents of the syringe will appear cloudy and small pieces of tablet will be present.
- Use only **room temperature water** to prepare NITISINONE TABLETS in an oral syringe.
- Wash your hands well before preparing NITISINONE TABLETS using an oral syringe.
- For infants, do NOT give the suspension using a baby bottle.



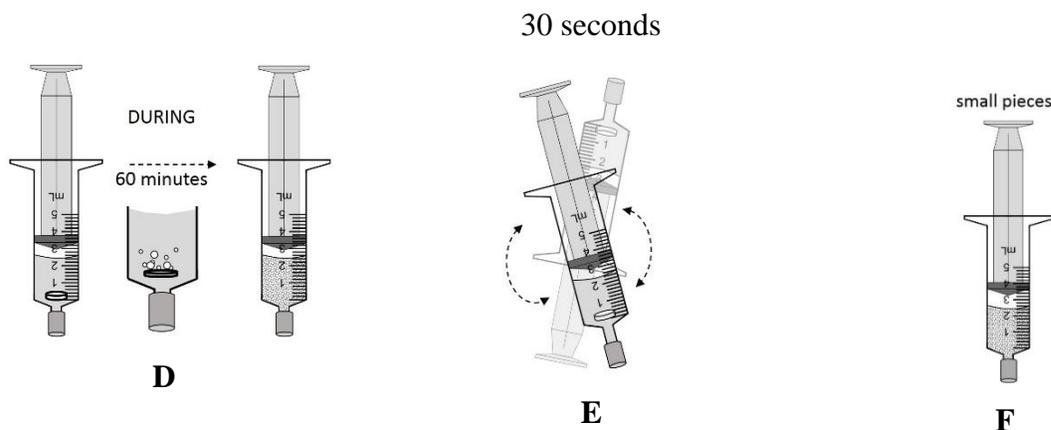
How to prepare and take 1 NITISINONE TABLET using a 5 mL oral syringe:

1. Remove the cap from the 5 mL oral syringe.
2. Remove the plunger from the oral syringe and place 1 whole NITISINONE TABLET inside the oral syringe (See Figure A).
3. Replace the plunger (See Figure B).
4. Draw up **2.6 mL** of **room temperature** water into the oral syringe. There may be some air in the oral syringe. Leave the air in the oral syringe (See Figure C).



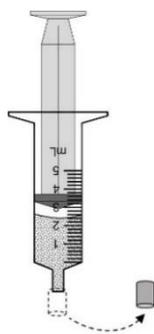
5. Replace the cap on the oral syringe. Let the oral syringe sit for at least **60 minutes** (See Figure D).
6. Turn the oral syringe up and down for at least **30 seconds** (See Figure E).
7. Check the oral syringe to see if the NITISINONE TABLET has broken apart into very small pieces. The pieces should be evenly spread through the water (suspension) (See Figure F). Do NOT take the suspension if you see any large pieces of the NITISINONE TABLET or if they are not evenly spread through the water. In this case, let the oral syringe sit for another 10 minutes.

Before giving the suspension, turn the oral syringe up and down for 30 seconds one more time. Do this to ensure that the pieces of NITISINONE TABLET in the suspension remain evenly spread.

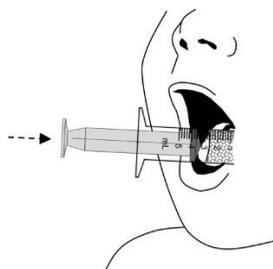


8. **Remove the cap from the oral syringe** (See Figure G).
9. Place the tip of the oral syringe in the mouth right away. If giving to a child, place the tip of the oral syringe along the inner cheek of the child's mouth (See Figure H).

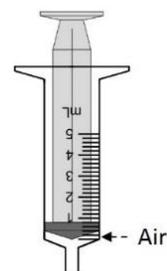
10. While keeping the oral syringe in the mouth, slowly push down on the plunger. Do this **until a small amount of air is left** between the plunger and the tip of the oral syringe (See Figure I). Do NOT press all the way down to the end of the syringe.



G

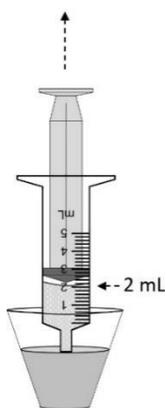


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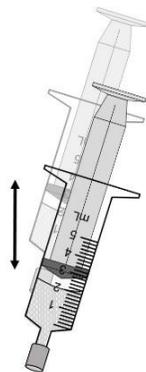


I

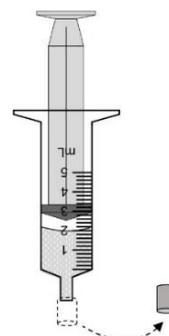
11. Draw up an additional **2 mL** of water into the oral syringe (See Figure J).
12. Replace the cap on the oral syringe. **Shake the oral syringe well for 10 seconds**. Do this to spread the remaining tablet pieces evenly through the water (See Figure K).
13. **Remove the cap from the oral syringe** (See Figure L).



J



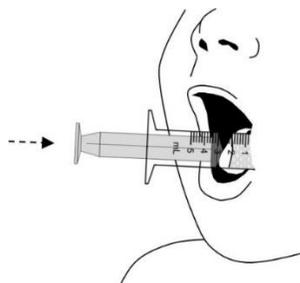
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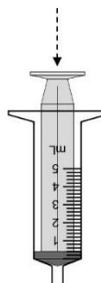
L

14. Place the tip of the oral syringe in the mouth right away. If giving to a child, place the tip of the oral syringe along the inner cheek of the child's mouth (See Figure M).
15. While keeping the oral syringe in the mouth, slowly push down on the plunger. Do this until the oral syringe is empty (See Figure N). In case any pieces of the tablet are still present in the oral syringe, repeat steps 11 through 15.

16. After use, remove the plunger from the syringe barrel. Rinse the syringe and the plunger with water after each use and let it dry. Do NOT put the plunger back into the barrel of the oral syringe until ready to use again. This will allow it to dry. Do NOT throw away the oral syringe or plunger.



M



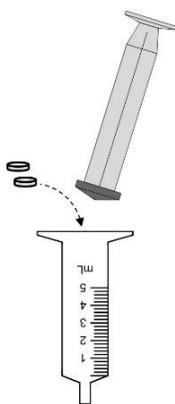
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If you are not taking the water and NITISINONE TABLET suspension as soon as it is prepared, complete steps 1 through 5. When you are ready to take the suspension, complete steps 6 through 16.

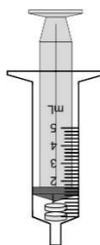
After adding water to the tablet in the oral syringe you can keep the NITISINONE TABLET suspension for 24 hours. Store the NITISINONE TABLET suspension in the oral syringe with the cap on at room temperature (15 - 30°C). Keep the oral syringe out of direct sunlight until ready for use. The suspension does not need to be refrigerated. Throw away any suspension that is not used within 24 hours by emptying the syringe in the drain.

How to prepare and take 2 NITISINONE TABLETS using a 5 mL oral syringe:

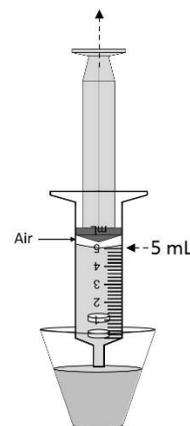
1. Remove the cap from the 5 mL oral syringe.
2. Remove the plunger from the oral syringe and place 2 whole NITISINONE TABLETS inside the oral syringe (See Figure A).
3. Replace the plunger (See Figure B).
4. Draw up 5 mL of **room temperature** water into the oral syringe. There may be some air in the oral syringe. Leave the air in the oral syringe (See Figure C).



A

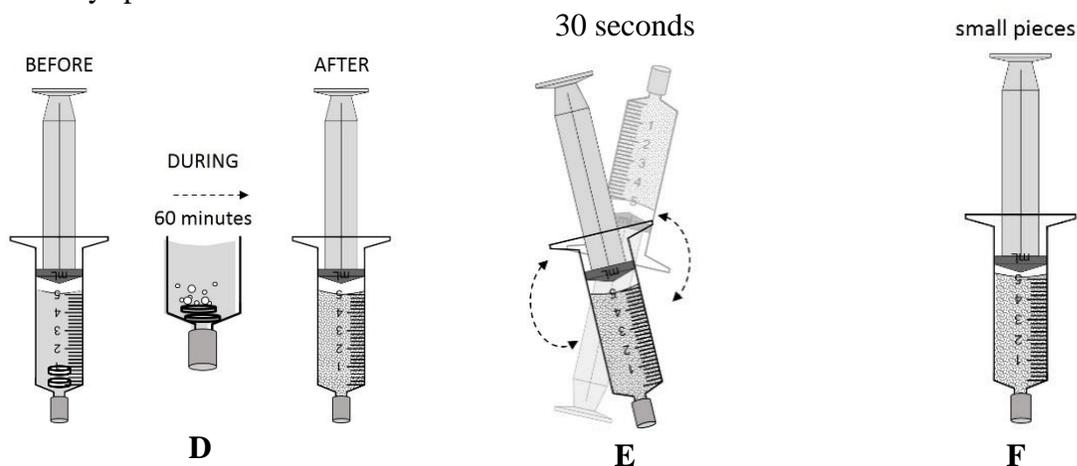


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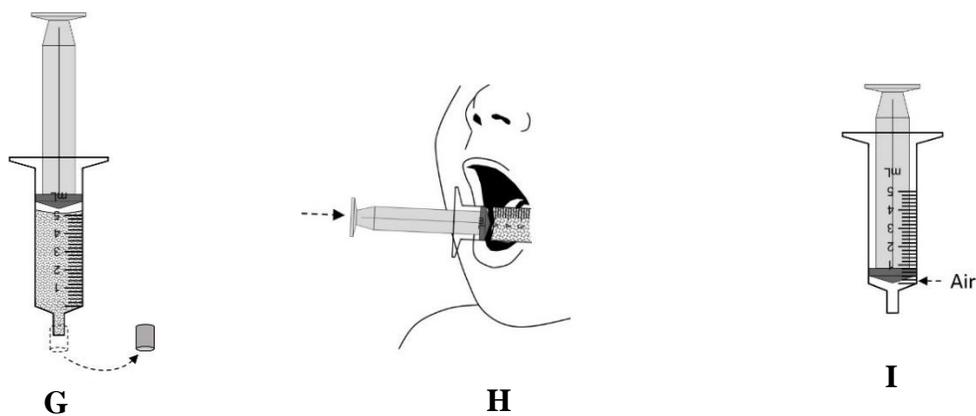


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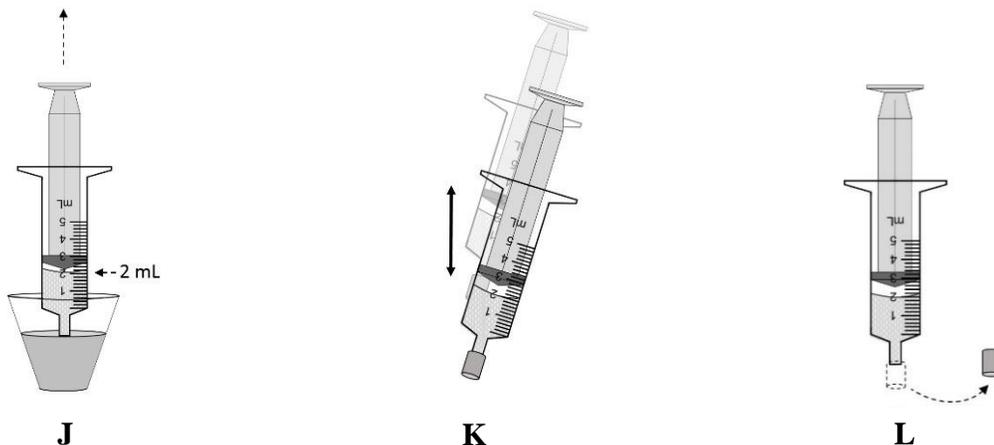
5. Replace the cap on the oral syringe. Let the oral syringe sit for at least **60 minutes** (See Figure D).
6. Turn the oral syringe up and down for at least **30 seconds** (See Figure E).
7. Check the oral syringe to see if the NITISINONE TABLETS have broken apart into very small pieces. The pieces should be evenly spread through the water (suspension) (See Figure F). Do **NOT** take the suspension if you see any large pieces of the NITISINONE TABLETS or if they are not evenly spread through the water. In this case, let the oral syringe sit for another 10 minutes.
Before giving the suspension, turn the oral syringe up and down for 30 seconds one more time. Do this to ensure that the pieces of NITISINONE TABLETS in the suspension remain evenly spread.



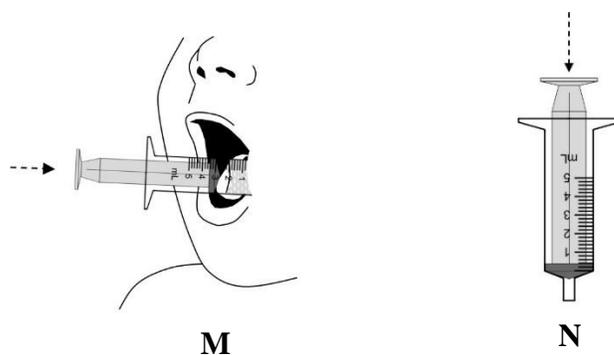
8. **Remove the cap from the oral syringe** (See Figure G).
9. Place the tip of the oral syringe in the mouth right away. If giving to a child, place the tip of the oral syringe along the inner cheek of the child's mouth (See Figure H).
10. While keeping the oral syringe in the mouth, slowly push down on the plunger. Do this **until a small amount of air is left** between the plunger and the tip of the oral syringe (See Figure I). Do **NOT** press all the way down to the end of the syringe.



11. Draw up an additional **2 mL** of water into the oral syringe (See Figure J).
12. Replace the cap on the oral syringe. **Shake the oral syringe** well for **10 seconds**. Do this to spread the remaining tablet pieces evenly through the water (See Figure K).
13. **Remove the cap from the oral syringe** (See Figure L).



14. Place the tip of the oral syringe in the mouth right away. If giving to a child, place the tip of the oral syringe along the inner cheek of the child's mouth (See Figure M).
15. While keeping the oral syringe in the mouth, slowly push down on the plunger. Do this until the oral syringe is empty (See Figure N). In case any pieces of the tablets are still present in the oral syringe, repeat steps 11 through 15.
16. After use, remove the plunger from the oral syringe barrel. Rinse the syringe with water after each use and let it dry. Do NOT put the plunger back into the barrel of the oral syringe until ready to use again. This will allow it to dry. Do NOT throw away the oral syringe or plunger.



If you are not taking the water and NITISINONE TABLETS suspension as soon as it is prepared, complete steps 1 through 5. When you are ready to take the suspension, complete steps 6 through 16.

After adding water to the tablets in the oral syringe you can keep the NITISINONE TABLETS suspension for 24 hours. Store the NITISINONE TABLETS suspension in the oral syringe with the cap on at room temperature (15 - 30°C). Keep the oral syringe out of direct sunlight until ready for use. The suspension does not need to be refrigerated. Throw away any suspension that is not used within 24 hours by emptying the syringe in the drain.

Usual dose:

Your healthcare professional will tell you how many NITISINONE TABLETS to take and when to take them.

Your healthcare professional may need to adjust your dose after blood tests have been done. This may happen based on how you are responding to treatment.

Overdose:

If you think you have taken too many NITISINONE TABLETS, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms. If you go to a healthcare professional or to the hospital, take the NITISINONE TABLETS container with you.

Missed Dose:

If you forget a dose, take the next dose as planned. Do not take a double dose to make up for a forgotten dose. If you forget to take a dose, contact your healthcare professional or pharmacist.

What are the possible side effects from using NITISINONE TABLETS?

These are not all the possible side effects you may feel when taking NITISINONE TABLETS. If you experience any side effects not listed here, contact your healthcare professional.

NITISINONE TABLETS can cause abnormal blood test results. While you are taking NITISINONE TABLETS your healthcare professional will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Liver problems: nausea, vomiting, loss of appetite combined with itching, yellowing of the skin or eyes, dark urine or stools, unexplained weight loss.		√	
Low Platelets: easy or unusual bruising. Bleeding into the skin		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
causing a rash of pinpoint-sized reddish-purple spots, usually in the lower legs, prolonged bleeding from cuts, bleeding from your gums or nose, blood in urine or stools.			
Low White Blood Cells: infections, fatigue, weakness, fever, aches and pains, flu-like symptoms.		√	
Eye Problems: redness, eye discharge, itchy eyes, burning eyes, blurred vision, sensitivity to light, milky or cloudy area on the eye, eye pain, a feeling that there is something in your eye.		√	
RARE			
Skin Problems: dry/cracked/scaly skin, rashes, small flat red bumps, itching that can be severe, blisters, draining fluid and crusting, swelling, burning, tenderness, loss of hair in patches.		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

<p>Reporting Side Effects</p> <p>You can report any suspected side effects associated with the use of health products to Health Canada by:</p> <ul style="list-style-type: none"> • Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or by • Calling toll-free at 1-866-234-2345. <p><i>NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.</i></p>

Storage:

- Store your tablets at room temperature (15 - 30°C), in a dry place.
- Keep the container tightly closed.
- There is an expiry date on the label. Do not use the medicine after this date.
- **Keep out of reach and sight of children.**

If you want more information about NITISINONE TABLETS:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](http://www.healthcanada.gc.ca) (www.healthcanada.gc.ca); the manufacturer's website <http://www.cyclepharma.com> or by calling 1-855-831-5413 (toll-free).

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Full Product Monograph is available at: www.nitisinonetablets.com



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