

Package leaflet: Information for the user

Cynril 200 micrograms compressed lozenges with integral oromucosal applicator
Cynril 400 micrograms compressed lozenges with integral oromucosal applicator
Cynril 600 micrograms compressed lozenges with integral oromucosal applicator
Cynril 800 micrograms compressed lozenges with integral oromucosal applicator
Cynril 1200 micrograms compressed lozenges with integral oromucosal applicator
Cynril 1600 micrograms compressed lozenges with integral oromucosal applicator

fentanyl

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cynril is and what it is used for.
2. What you need to know before you take Cynril
3. How to take Cynril.
4. Possible side effects
5. How to store Cynril
6. Contents of the pack and other information

1. What Cynril is and what it is used for

Cynril contains the active substance fentanyl which is a strong pain-relieving medicine known as an opioid.

The Cynril unit comes as a lozenge on a stick.

- It is used to treat breakthrough pain in adults and adolescents aged 16 years and above with cancer who are already taking other opioid pain medicines for their persistent (around-the-clock) cancer pain. Breakthrough pain is additional sudden pain that occurs suddenly in spite of your having taken your usual opioid pain-relieving medicines.

2. What you need to know before you take Cynril

Do not use Cynril:

- If you are not regularly using a prescribed opioid medicine (e.g. codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine), every day on a regular schedule, for at least a week, to control your persistent pain. If you have not been using these medicines you must not use Cynril, because it may increase the risk of your breathing becoming dangerously slow and/or shallow, or even stop.
- If you are allergic to fentanyl or any of the other ingredients of this medicine (listed in Section 6).
- If you are currently taking monoamine-oxidase (inhibitor (MAOI) (medicines for severe depression) or have taken them in the past 2 weeks (see section 2 under Serotonin syndrome).
- If you have severe breathing problems or severe lung problems where you have an obstruction.
 - If you suffer from short-term pain (e.g. pain from injuries, surgery, headaches or migraines) other than breakthrough pain.

Do not use Cynril if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before using Cynril.

Warnings and precautions:

Keep using the opioid pain medicine you take for your persistent (around-the-clock) cancer pain during your Cynril treatment.

Talk to your doctor or pharmacist before taking Cynril if:

- Your other opioid pain medicine for your persistent (around-the-clock) cancer pain is not stabilised yet.
- You have any illness that affects your breathing (such as asthma, wheezing, or shortness of breath).
- You have a head injury or have had any loss of consciousness.
- You have problems with your heart especially slow heart rate.
- You have liver or kidney problems - this will affect how your system breaks down the medicine.
- You have low blood pressure due to a low amount of fluid in your circulation.
- You have diabetes.
- You are over 65 years old - you may need a lower dose and any dose increase will be reviewed very carefully by your doctor.
- You have a history of alcoholism or any drug abuse or dependence.
- You have ever developed adrenal insufficiency with opioid use, a condition in which the adrenal glands do not produce enough hormones (see section 4 under serious side effects).
- You drink alcohol; please refer to section Cynril with food and drink and alcohol.
- You experience pain or increased sensitivity to pain (hyperalgesia) which does not respond to a higher dosage of your medicine as prescribed by your doctor.
You experience a combination of the following symptoms: nausea, vomiting, anorexia, fatigue, weakness, dizziness and low blood pressure. Together these symptoms may be a sign of a potentially life-threatening condition called adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones.
- You have ever developed adrenal insufficiency or lack of sex hormones (androgen deficiency) with opioid use.

Serotonin syndrome

Talk to your doctor before using Cynril if you use antidepressants or antipsychotics (selective serotonin reuptake inhibitors [SSRIs], serotonin norepinephrine reuptake inhibitors [SNRIs], monoamine oxidase (MAO) inhibitors; see section 2 under Do not use Cynril and Other medicines and Cynril).

The use of these medicines with Cynril can lead to serotonin syndrome a potentially life-threatening condition (see section 2 under Other medicines and Cynril).

Serious allergic reactions

(anaphylaxis, hypersensitivity)

Serious allergic reactions have been reported with fentanyl (see section 4 under Serious side effects), early symptoms can be difficulty in breathing or dizziness, swelling of the tongue, lip or throat.

Dental decay

Cynril contains approximately 2 grams of sugar and a frequent consumption exposes you to an increased risk of dental decay that may be serious. Thus, it is important to continue to take good care of your mouth and teeth during treatment with Cynril. If you present such serious local effects consult your doctor.

Children and adolescents

This medicine is not recommended for children and adolescents below 16 years of age

Other medicines and Cynril

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines:

- Other fentanyl treatments that have been prescribed for your breakthrough pain in the past. If you still have some of these fentanyl treatments at home, do not take more than on short acting fentanyl product for breakthrough at the same time and check with your pharmacist how to dispose of them.
- - if you are using monoamine oxidase (MAO) inhibitors (medicines for severe depression) or have taken them in the past 2 weeks (see section 2 under Warnings and precautions – Serotonin syndrome).

Tell your doctor or pharmacist before using Cynril if you are taking or have recently taken or might take any other medicines:

This includes medicines obtained without a prescription, including herbal medicines. In particular, tell your doctor or pharmacist if you are taking any of the following medicines:

- Any medicines which might make you sleepy such as sleeping pills, medicines to treat anxiety, some medicines for allergic reaction (antihistamines), or tranquillisers.
- Some muscle relaxants (such as baclofen or diazepam).
- Any medicines or other substances that might have an effect on the way in which your body breaks down Cynril, such as: grapefruit juice, drugs used to treat fungal infections, ritonavir or other medications that help control the HIV virus (AIDS) or other medicines called “CYP3A4 inhibitors” such as ketoconazole, itraconazole or fluconazole (used for fungal infections) and troleandomycin, clarithromycin or erythromycin (medicines for bacterial infections) and so-called “CYP3A4 inducers” as rifampin or rifabutin for bacterial infections), carbamazepine, phenobarbital or phenytoin (medicines used to treat convulsions/fits).
- Certain types of strong painkillers, called partial agonist/antagonists e.g. buprenorphine, nelbuphine and pentazocine (medicines for treatment of pain). You could experience symptoms of withdrawal syndrome (nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating) while using these medicines.
- Serotonergic medicinal products used to treat depression (antidepressants: such as selective serotonin reuptake inhibitors [SSRIs] and serotonin norepinephrine reuptake inhibitors [SNRIs]) or antipsychotics. The use of these medicines with Cynril can lead to serotonin syndrome a potentially life-threatening condition (see section 2 under Serotonin syndrome). The symptoms of serotonin syndrome may include mental status changes (e.g. agitation, hallucinations, coma), and other effects such as body temperature above 38 °C, increase in heart rate, unstable blood pressure, and exaggeration of reflexes, muscular rigidity, lack of coordination and/ or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea). Your doctor will tell you whether Cynril is suitable for you.
- Concomitant use of Cynril and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However, if your doctor does prescribe Cynril together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedative medicines you are taking, and follow your doctor’s dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

If you are due to have surgery requiring a general anaesthetic speak with your doctor or nurse

Cynril with food and drink and alcohol

Cynril can be used before or after meals. However, do not use during a meal.

- You may drink some water before using Cynril to moisten the mouth. However, you should not drink or eat anything while using Cynril.
- Do not drink grapefruit juice while using Cynril. This is because it may affect the way your body breaks down Cynril.
- Do not drink alcohol while on treatment with Cynril. It can increase the chance of getting serious side effects.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, you think you may be pregnant or planning to have a baby, ask your doctor or pharmacist before using this medicine.

Pregnancy

Cynril should not be used during pregnancy unless you have discussed this with your doctor. If Cynril is used for a long-time during pregnancy, there is also a risk of the new-born child having withdrawal symptoms which might be life-threatening if not recognized and treated by a doctor. You should not use Cynril during childbirth because fentanyl may cause respiratory depression in the new-born child.

Breast-feeding

Fentanyl can get into breast milk and may cause side effects in the breast-fed infant. Do not use Cynril if you are breast-feeding. You should not start breast-feeding until at least 5 days after the last dose of Cynril.

Driving and using machines

This medicine may affect you being able to drive or use any tools or machines. Talk to your doctor about whether it is safe for you to drive or use any tools or machines in the first few hours after using Cynril.

Do not drive or use any tools or machines if you: feel sleepy or dizzy; have blurred or double vision; have difficulty in concentrating. It is important you know how you react to Cynril before driving or using any tools or machines.

Cynril contains glucose

This medicine contains glucose (as hydrated dextrates). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Glucose containing lozenge of Cynril may be harmful to your teeth. This medicine contains less than 1 mmol (23 mg) per lozenge, that is to say essentially 'sodium-free'

3. How to use Cynril

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

When you first start using Cynril, your doctor will work with you to find the dose that will relieve your breakthrough pain. It is very important that you use Cynril exactly as the doctor tells you

Do not change doses of Cynril or your other pain medicines on your own. Change in dose must be prescribed and checked by your doctor. If you are not sure about the right dose or if you have questions about using this medicine, talk to your doctor

How the medicine is administered

When you place Cynril in your mouth:

- The lozenge dissolves and the active substance is released. It takes around 15 minutes for this to happen.
- The active substance is absorbed through the lining of your mouth, into the blood system. Using the medicine like this allows it to be absorbed quickly. This means that it relieves your breakthrough pain quickly.

While the right dose is being found

You should start to feel some relief quickly while you are using Cynril. However, while you and the doctor are finding out the dose that controls your breakthrough pain, you may not get enough pain relief up to 30 minutes after starting to use one Cynril unit (15 minutes from when you finish using the Cynril unit). If this happens, your doctor may allow you to use a second Cynril unit of the same strength for that

same episode of breakthrough pain. Do not use a second unit unless your doctor tells you to. Never use more than two units to treat a single episode of breakthrough pain.

While the right dose is being found, you may need to have more than one strength of Cynril units at home. However, keep only the strengths of Cynril you need in the house. This is to stop possible confusion or overdose. Talk to your pharmacist about how to dispose of any Cynril units you do not need.

How many units should be used

Once the right dose has been found with your doctor, use 1 unit for an episode of breakthrough pain. Talk to your doctor if your right dose of Cynril does not relieve your breakthrough pain for several episodes of breakthrough pain in a row.

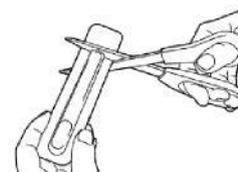
Your doctor will decide if your dose needs to be changed.

You must tell your doctor straight away if you are using Cynril more than four times per day. This is because he may wish to change your medicine for your persistent (around-the-clock) pain. When he has done this, when your persistent pain has been controlled, he may need to change your dose of Cynril. For the most effective relief, tell your doctor about your pain and how Cynril is working for you. This is so that the dose can be changed if needed.

How to take Cynril

Opening the package

- Each Cynril unit is sealed in its own blister package. Do not open the package until you are ready to use Cynril
- Hold the blister package with the printed side away from you.
- Hold the short tab end of the blister package.
- Put the scissors close to the end of the Cynril unit and cut the long tab end completely off (as shown).
- Separate the printed backing from the blister package and pull the printed backing completely off from the blister package.



Remove the Cynril unit from the blister pack and put the lozenge in your mouth straight away

Using the Cynril unit

- Put the lozenge between your cheeks and gum.
- Using the handle, keep moving Cynril around in your mouth especially along your cheeks. Twirl the handle often.
- You may drink some water before using Cynril, to help with taking the product but you should not drink or eat anything while using Cynril.
- To get the most effective relief, finish the Cynril completely in 15 minutes. If you finish too quickly, you will swallow more of the medicine and get less relief from your breakthrough pain.
- Do not bite or chew the lozenge. This would mean lower levels of Fentanyl in your blood and less pain relief than when used as directed.
- If for some reason you are not finishing the whole lozenge each time you have breakthrough pain, talk to your doctor.

How often you should use Cynril Once a dose is found that effectively controls your pain, do not use more than four units of Cynril per day. If you think you might need to use more than four Cynril units per day, talk to your doctor straight away

How many Cynril units you should use

Do not use more than two units to treat any single episode of breakthrough pain.

If you use more Cynril than you should

The most common side effects of using too much Cynril are feeling sleepy, sick or dizzy.

- If you begin to feel dizzy, sick, or very sleepy before the lozenge is completely dissolved, take it out of your mouth and call another person in your house to help you.

A serious side effect of Cynril is slow and/or shallow breathing. This can occur if your dose of Cynril is too high or if you take too much Cynril. Other serious side effects associated with overdose include altered mental status, loss of consciousness, coma and cardiorespiratory arrest (sudden heart attack).

- If this happens, get medical help straight away.

What to do if a child or adult accidentally takes Cynril

If you think someone has accidentally taken Cynril, get medical help straight away. Try to keep the person awake (by calling their name and shaking their arm or shoulder) until emergency help arrives.

If you forget to use Cynril

If you still have breakthrough pain, you may use Cynril as your doctor has told you. If the breakthrough pain disappears, do not use Cynril until the next breakthrough pain.

If you stop using Cynril

You should normally stop taking Cynril when you no longer have any breakthrough pain. You must however continue to take your usual opioid pain-relieving medicine to treat your persistent cancer pain as advised by your doctor, unless your doctor tells you to stop. You may experience withdrawal symptoms similar to the possible side effects of Cynril when discontinuing Cynril. If you experience withdrawal symptoms or if you are concerned about your pain relief you should contact your doctor. Your doctor will evaluate if you need medicine to reduce or eliminate the withdrawal symptoms.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can have side effects, although not everybody gets them. If you notice any of these, contact your doctor. The most serious side effects are shallow breathing, low blood pressure and shock. **You or your carer should REMOVE the Cynril unit from your mouth, contact your doctor immediately and call for emergency help if you experience any of the following serious side effects- you may need urgent medical attention:**

Becoming very sleepy or having slow and/ or shallow breathing.

Difficulty in breathing or swelling of the tongue, lip or throat which may be early signs of serious allergic reaction.

Note to carers:

If you see that the patient taking Cynril has slow breathing or if you have a hard time waking the person up, take the following steps IMMEDIATELY:

- Using the handle, remove the Cynril unit from the person's mouth and keep it out of reach of children or pets until the Cynril unit is disposed of.
- CALL FOR EMERGENCY HELP

If you feel excessively dizzy, sleepy or otherwise ill while taking Cynril, use the handle to remove the Cynril unit and dispose of it according to the instructions given in this leaflet (see section 5). Then contact your doctor for further directions on using Cynril.

Contact your doctor if you experience a combination of the following symptoms Nausea, vomiting, loss of appetite, tiredness, weakness, dizziness and low blood pressure. Together these symptoms may be a sign of a potentially life-threatening condition called adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones

Very common side effects (may affect more than 1 in 10 people):

- Vomiting, nausea / discomfort, constipation, stomach (abdominal) pain.
- Asthenia (weakness), sleepiness, dizziness, headache.
- Shortness of breath.

Common side effects (may affect up to 1 in 10 people):

- Confusion, anxiety, seeing or hearing things that are not there (hallucinations), depression, mood swings.
- Feeling unwell
- Muscle jerks, feeling of dizziness or "spinning", loss of consciousness, sedation, tingling or numbness, difficulty coordinating movements, increased or altered sensitivity to touch, convulsions (fits).
- Dry mouth, mouth inflammation, tongue problems (eg burning sensation or ulcers), taste alteration.
- Wind, abdominal bloating, indigestion, decreased appetite, weight loss.
- Blurred or double vision.
- Sweating, skin rash, itchy skin.
- Difficulty passing urine.
- Accidental injury (e.g. falls).

Uncommon side effects (may affect up to 1 in 100 people):

- Tooth decay, paralysis of the gut, (which may cause side effects such as stomach cramps, being sick, loss of bowel movements and being unable to pass wind), mouth ulcers, gum bleeding.
- Coma, slurred speech.
- Abnormal dreams, feeling detached, abnormal thinking, excessive feeling of well being.
- Widening of blood vessels.
- Hives.

Not known (frequency cannot be estimated from the available data):

They have also reported the following side effects with the use of Cynril but how often that can occur is not known:

- Receding gums, swollen gums, tooth loss, severe breathing problems, flushing, feeling very warm, diarrhoea, swelling of arms or legs, fatigue, insomnia, pyrexia, withdrawal syndrome (may manifest by the occurrence of the following side effects nausea, vomiting, diarrhoea, anxiety, chills, tremor and sweating).
- Drug dependence (addiction)
- Drug abuse
- Lack of sex hormones (androgen deficiency)
- Delirium (symptoms may include a combination of agitation, restlessness, disorientation, confusion, fear, seeing or hearing things that are not really there, sleep disturbance, nightmares)

Prolonged treatment with fentanyl during pregnancy may cause withdrawal symptoms in the newborn which can be life-threatening (see section 2)

While using Cynril you may experience irritation, pain and ulcers in the application site and gum bleeding.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cynril

The pain-relieving medicine in Cynril is very strong and could be life-threatening if taken accidentally by a child. Cynril must be kept out of sight and reach of children.

- Do not use Cynril after the expiry date shown on the package label and the carton.
- Do not store above 25°C.
- Always keep Cynril in its blister package until you are ready to use it. Do not use if the blister package has been damaged or opened before you are ready to use it.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

How to dispose of Cynril after use

Partially used units of Cynril may still contain enough medicine to be harmful or life-threatening to a child. Even if there is a little or no medicine left on the handle, the handle itself must be properly disposed of as follows:

- If there is no medicine, put the applicator in a waste container that is out of reach of children and pets.
- If any medicine remains on the applicator, put the lozenge under hot running water to dissolve the remainder and then put the applicator in a waste container that is out of reach of children and pets.
- If you do not finish the entire unit of Cynril and can not dissolve the remains of the drug immediately, put the unit of Cynril out of reach of children and pets until you have time to dispose of the partially used unit of Cynril as explained above.
- Do not flush a partially used lozenge, handles, or the blister packaging down the toilet.

6. Contents of the pack and other information

What Cynril contains: The active substance is fentanyl. Each individual lozenge contains either 200, 400, 600, 800, 1200 or 1600 micrograms of fentanyl (as citrate).

The other ingredients are:

Lozenge:

Dextrates hydrated, citric acid, disodium hydrogenphosphate, artificial flavour berry (tapioca starch, arabic gum (E-414), magnesium stearate.

Edible glue used to attach the lozenge to the applicator:

Based food starch modified maize, hydrated dextrates, water.

Applicator:

ABS resin

Printing ink: Ethanol, Water, Purified Shellac (E904), Acetone, FD&C Blue No.1 (E133 Brilliant Blue FCF), Ammonium Hydroxide (E527)

What Cynril looks like and contents of the pack

Cynril is a system for administering medication directly through the lining of the mouth. Each unit consists of a white to slightly yellowish cylindrical lozenge attached to a handle for oromucosal application.

The unit is normally white, however, during storage can acquire a slightly mottled appearance. This does not affect in any way the action of the medicine.

Cynril is available in six different doses: 200, 400, 600, 800, 1200 and 1600 micrograms. The dose is marked on the white lozenge in the applicator in the blister and on the carton to ensure that you use the appropriate medication and dosage. Each dose is associated with a specific color.

Each blister package contains one unit of Cynril supplied in boxes of 1, 3, 15 or 30 individual Cynril units.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Fontus Health Ltd
60 Lichfield Street
Walsall
WS4 2BX

United Kingdom

Manufacturer:

PRASFARMA,
S.L.C/ Sant Joan 11-15
08560
Manlleu (Barcelona)
Spain

This medicinal product is authorised in the Member States of the EEA under the following names:

Netherlands - Fentanyl CF 200/ 400/ 600/ 800/ 1200/ 1600 µg, zuigtabletten met integrale applicator voor oromucosaal gebruik

Germany - Fentanyl Ribosepharm 200/400/600/800/1200/1600 Mikrogramm Lutschtablette, gepresst mit integriertem Applikator zur Anwendung in der Mundhöhle

This leaflet was last revised in 11/2019