Package leaflet: Information for the user

ACTIQ® 200 micrograms compressed lozenge with integral oromucosal applicator

ACTIQ® 400 micrograms compressed lozenge 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 ACTIQ is and what it is used for
2. What you need to know before you use ACTIQ
3. How to use ACTIQ
4. Possible side effects
5. How to store ACTIQ
6. Contents of the pack and other information

1. What ACTIQ is and what it is used for

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

Do NOT use ACTIQ:
- 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 ACTIQ, because it may increase the risk that breathing could become 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 (MAO) inhibitors (medicines for severe depression) or have taken them in the past 2 weeks (see section 2 under “Talk to your doctor or pharmacist **BEFORE** using ACTIQ if:”).
- If you are taking a medicine which contains sodium oxybate.
- 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 ACTIQ if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist BEFORE using ACTIQ.

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

Repeated use of ACTIQ may result in the drug being less effective (you become accustomed to it) or becoming dependent on it. Your doctor will monitor you for signs of these conditions.

Talk to your doctor or pharmacist **BEFORE** using ACTIQ 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 use benzodiazepines (see section 2 under ”Other medicines and ACTIQ”). Using benzodiazepines can increase the chances of getting serious side effects including death.
- 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 ACTIQ” and “Other medicines and ACTIQ”). The use of these medicines with ACTIQ can lead to a **serotonin syndrome a potentially life-threatening condition** (see section 2 under “Other medicines and ACTIQ”).
- You have ever abused or been dependent on opioids or any other drug, alcohol or illegal drugs.
- You have ever developed adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones, or lack of sex hormones (androgen deficiency) with opioid use, (see section 4 under “Serious side effects’’).
- You drink alcohol; please refer to section ACTIQ with food, drink and alcohol.

Your doctor may need to check you more closely if:
- You or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs (“addiction”).
- You are a smoker.
- You have ever had problems with your mood (depression, anxiety or a personality disorder) or have been treated by a psychiatrist for other mental illnesses.

Consult your doctor **WHILE** using ACTIQ if:
- 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 exhibit signs of dental decay. ACTIQ contains approximately 1.89 grams of sugar; frequent use exposes you to an increased risk of dental decay that may be serious. It is important to take good care of your teeth during treatment with ACTIQ. Visit your dentist regularly during treatment.
- 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.
- Sleep-related breathing disorders: ACTIQ can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.
- Repeated use of ACTIQ may lead to dependence and abuse which may result in life-threatening
- overdose. If you have concern that you may become dependent on ACTIQ, it is important that you consult your doctor.

Seek **URGENT** medical advice if:
- You experience symptoms such as difficulty in breathing or dizziness, swelling of the tongue, lip or throat while using ACTIQ. These might be early symptoms of a serious allergic reaction (anaphylaxis, hypersensitivity; see section 4 under “Serious side effects”)

Children and adolescents
ACTIQ is not recommended for children and adolescents below 16 years of age.

Other medicines and ACTIQ
Do not use this medicine and tell your doctor or pharmacist:
- if you are taking 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, 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 Do NOT use ACTIQ and “Talk to your doctor or pharmacist **BEFORE** using ACTIQ if:”)..

Tell your doctor or pharmacist before using ACTIQ 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:
- Concomitant use of ACTIQ 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 ACTIQ 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 (such as sleeping pills, medicines to treat anxiety, some medicines to treat allergic reactions (antihistamines), or tranquillisers) 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.
- Some muscle relaxants - such as baclofen, diazepam (see also section “Warnings and precautions”).
- Any medicines that might affect how your body breaks down ACTIQ - such as ritonavir or other medicines that help control HIV infection, other so-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’ such as rifampin or rifabutin (medicines for bacterial infections), carbamazepine, phenobarbital or phenytoin (medicines used to treat convulsions/fits).
- Certain types of strong pain killers, called partial agonist/antagonists e.g. buprenorphine, nalbuphine 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.
- Some painkillers for nerve pain (gabapentin and pregabalin).
- 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 ACTIQ can lead to serotonin syndrome a potentially life-threatening condition (see section 2 under “Talk to your doctor or pharmacist **BEFORE** using ACTIQ if:” and “Do NOT use ACTIQ:”). 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 ACTIQ is suitable for you.

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

ACTIQ with food, drink and alcohol
- ACTIQ may be used before or after meals. However do not use during meals.
- You may drink some water before using ACTIQ to help moisten your mouth. However, do not drink or eat anything while using ACTIQ.
- Do not drink grapefruit juice while using ACTIQ. This is because it may affect the way your body breaks down ACTIQ.
- Do not drink alcohol while using ACTIQ. It can increase the chances of getting serious side effects including death.

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

Pregnancy
ACTIQ should not be used during pregnancy unless you have discussed this with your doctor.
If ACTIQ is used for a long time during pregnancy, there is a risk of the new-born child having withdrawal symptoms which might be life-threatening if not recognized and treated by a doctor (see section 4 under “Other side effects with frequency not known’’).

You should not use ACTIQ during child-birth because fentanyl may cause breathing difficulties 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 ACTIQ if you are breast-feeding. You should not start breast-feeding until at least 5 days after the last dose of ACTIQ.

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 ACTIQ.
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 ACTIQ before driving or using any tools or machines.

ACTIQ contains glucose
Contains 1,89 g glucose per dose. This should be taken into account in patients with diabetes mellitus. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine. May be harmful to the teeth.

ACTIQ contains sucrose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine. May be harmful to the teeth.

ACTIQ contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per lozenge, that is to say essentially ‘sodium-free’.

3. How to use ACTIQ

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 ACTIQ, your doctor will work with you to find the dose that will relieve your breakthrough pain. It is very important that you use ACTIQ exactly as the doctor tells you.
- Do not change doses of ACTIQ 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 gets into your body
When you place the lozenge 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 ACTIQ. However, while you and the doctor are finding out the dose that controls your breakthrough pain, you may not get enough pain relief 30 minutes after starting to use one ACTIQ unit (15 minutes from when you finish using the ACTIQ unit). If this happens, your doctor may allow you to use a second ACTIQ 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.

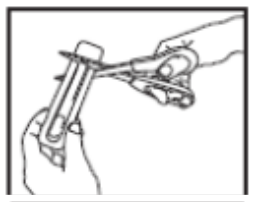
While the right dose is being found, you may need to have more than one strength of ACTIQ units at home. However, keep only the strengths of ACTIQ units you need in the house. This is to stop possible confusion or overdose. Talk to your pharmacist about how to dispose of any ACTIQ units you do not need.

How many units to use
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 ACTIQ 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.

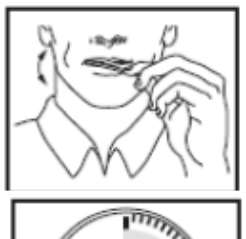
You must let your doctor know immediately if you are using ACTIQ more than four times per day, as a change may be required to your treatment regimen. Your doctor may change the treatment for your persistent pain; when your persistent pain is controlled, your doctor may need to change the dose of ACTIQ. If your doctor suspects ACTIQ-related increased sensitivity to pain (hyperalgesia), a reduction of your ACTIQ dose may be considered (see section 2 under “Warnings and precautions”). For the most effective relief, let your doctor know about your pain and how ACTIQ is working for you, so that the dose can be changed if needed.

How to use the medicine

Opening the pack – each ACTIQ unit is sealed in its own blister pack.



- Open the pack when you are ready to use it. Do not open it in advance.
- Hold the blister pack with the printed side away from you.
- Hold the short tab end of the blister pack.
- Put scissors close to the end of ACTIQ unit and cut the long tab end completely off (as shown).
- Separate the printed backing from the blister pack and pull the printed backing completely off the blister pack.
- Remove the ACTIQ unit from the blister pack and put the lozenge in your mouth straight away.



Using the ACTIQ unit

- Put the lozenge between your cheek and gum.
- Using the handle, keep moving the lozenge round in your mouth, especially along your cheeks. Twirl the handle often.
- To get the most effective relief, finish the lozenge 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 blood levels 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 ACTIQ
Once a dose is found that effectively controls your pain, do not use more than four ACTIQ units each day. If you think you might need to use more than four ACTIQ units per day, talk to your doctor straight away.

How many ACTIQ units you should use
Do not use more than two units to treat any single episode of breakthrough pain.

If you use more ACTIQ than you should
The most common side effects of using too much 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 ACTIQ is slow and/or shallow breathing. This can occur if your dose of ACTIQ is too high or if you take too much ACTIQ.

- If this happens, get medical help straight away.

What to do if a child or adult accidentally takes ACTIQ
If you think someone has accidentally taken ACTIQ, 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 ACTIQ
If you still have the breakthrough pain, you may use ACTIQ as your doctor has told you. If the breakthrough pain has stopped, do not use ACTIQ until the next breakthrough pain episode.

If you stop using ACTIQ
You should discontinue ACTIQ 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. You may experience withdrawal symptoms similar to the possible side effects of ACTIQ when discontinuing ACTIQ. 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 cause side effects, although not everybody gets them. If you notice any of these, contact your doctor.

Serious side effects

- The most serious side effects are shallow breathing, low blood pressure and shock.
  You or your carer should REMOVE the ACTIQ 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 dizziness, 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 using ACTIQ has slow and/or shallow breathing or if you have a hard time waking the person up, take the following steps IMMEDIATELY:

- Using the handle, remove the ACTIQ unit from the person’s mouth and keep it out of the reach of children or pets until it is disposed of.
- CALL FOR EMERGENCY HELP.
- While waiting for emergency help, if the person seems to be breathing slowly, prompt them to breathe every 5-10 seconds.

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

- **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.

- Prolonged treatment with fentanyl during pregnancy may cause withdrawal symptoms in the newborn which can be life-threatening (see section 2 under “Pregnancy and breast-feeding”).

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

- Vomiting, nausea/feeling sick, constipation, stomach (abdominal) pain
- Asthenia (weakness), sleepiness, dizziness, headaches
- Shortness of breath

Common: 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 (for example, 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 (for example, falls)

Uncommon: may affect up to 1 in 100 people

- Tooth decay (that can lead to teeth removal), paralysis of the gut, mouth ulcers, gum bleeding
- Coma, slurred speech
- Abnormal dreams, feeling detached, abnormal thinking, excessive feeling of well being
- Widening of blood vessels
- Hives

Frequency not known
The following side effects have also been reported with the use of ACTIQ lozenge but it is not known how often they may occur:

- Receding gums, inflammation of the gum, 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).
- Lack of sex hormones (androgen deficiency)
- Drug dependence (addiction)
- Drug abuse
- Delirium (symptoms may include a combination of agitation, restlessness, disorientation, confusion, fear, seeing or hearing things that are not really there, sleep disturbance, nightmares).
- trouble breathing during sleep
- bleeding at the site of application

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

Whilst using ACTIQ you may experience irritation, pain and ulcer at 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 HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ACTIQ

- The pain-relieving medicine in ACTIQ is very strong and could be life-threatening if taken accidentally by a child. Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and package label after EXP. The expiry date refers to the last day of that month.
- Do not store above 30°C.
- Store in protective blister until ready to use.
- Do not use this medicine if you notice that 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 ACTIQ after use
Partially used ACTIQ lozenge may 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 the medicine is totally gone, throw the handle away in a waste container that is out of reach of children and pets.
- If any medicine remains on the handle, place the lozenge under hot running water to dissolve the remainder and then throw the handle away in a waste container that is out of the reach of children and pets.
- If you do not finish the entire lozenge and you cannot immediately dissolve the remaining medicine, put the lozenge out of the reach of children and pets until such a time as you can dispose of the partially used lozenge as instructed above.
- Do not flush partially used lozenge, handles, or the blister packaging down the toilet.

6. Contents of the pack and other information

What ACTIQ contains:
The active substance is fentanyl. Each lozenge contains either:

- 200 micrograms fentanyl (as citrate),
- 400 micrograms fentanyl (as citrate)

The other ingredients are:
Product imported from Italy;
Lozenge: dextrates hydrated (equivalent to about 1.89 grams of glucose),, citric acid anhydrous, disodium phosphate anhydrous, artificial berry flavour (maltodextrin, propylene glycol, artificial flavours, and triethylcitrate), magnesium stearate.
Edible glue used to attach the lozenge to the handle.
Modified maize based food starch (E 1450), confectioner’s sugar (as sucrose and maize starch), water, purified.
Imprinting ink: de-ionised water, de-waxed white shellac, propylene glycol, blue synthetic coal tar dye (E 133), ammonium hydroxide (E 527) for pH adjustment.

Product imported from Greece;
Lozenge: dextrates hydrated (equivalent to about 1.89 grams of glucose),
citric acid, disodium phosphate, artificial berry flavour (maltodextrin, propylene glycol, artificial flavours and triethylcitrate), magnesium stearate.
Edible glue used to attach the lozenge to the handle: modified maize based food starch (E 1450), confectioner's sugar (as sucrose and maize starch), water.
Imprinting ink: water, de-waxed white shellac, propylene glycol, blue synthetic coal tar dye (E133), ammonium hydroxide (E 527) for pH adjustment.

What ACTIQ looks like and contents of the pack
ACTIQ consists of a white to off-white solid lozenge attached to a handle for oromucosal application. The lozenge may appear slightly mottled on storage. This is due to slight changes in the flavouring agent of the product and does not affect how the product works in any way. ACTIQ exists in 2 different strengths: 200 and 400 micrograms. The dosage strength is marked on the white lozenge, on the handle, on the blister package and on the carton to ensure that you are using the right medicine. Each strength is associated with a specific colour. ACTIQ lozenges are supplied in individual blister packages. Blister packages are supplied in cartons with 15 or 30 individual ACTIQ units.
Not all pack sizes may be marketed.

Parallel Product Authorisation Numbers:
PPA0465/407/001, PPA0465/407/002

Product procured from within the EU, repackaged and distributed by the parallel product authorization holder:
PCO Manufacturing Ltd., Unit 10, Ashbourne Business Park, Rath, Ashbourne, Co. Meath, Ireland.

Manufacturer
Cephalon France, 5 rue Charles Martigny, 94700 Maisons-Alfort-France or Teva Pharmaceuticals Europe B.V., Swensweg 5 2031 GA Haarlem, The Netherlands or Merckle GmbH, Ludwig-Merckle-Straße 3, 89143 Blaubeuren, Germany.
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