



Qutenza[®]
(capsaicin) 8% topical system

Not an actual
patient.

Ask your doctor
how an in-office application may provide up to
3 months of relief from diabetic nerve pain of
the feet or post-shingles nerve pain

INDICATION

QUTENZA[®] (capsaicin) 8% topical system is indicated in adults for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet.

IMPORTANT SAFETY INFORMATION

Treatment with QUTENZA must be performed only by a healthcare provider. You should never apply or remove QUTENZA yourself.

**Please see additional Important Safety Information inside.
Please see accompanying full Prescribing Information.**

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About QUTENZA

Something different awaits

The journey of finding relief from diabetic nerve pain of the feet and post-shingles nerve pain can be a frustrating one – from the constant feeling of pain, to the trail of treatment methods that didn't improve your symptoms.

But taking the step to talk to your doctor about QUTENZA could take you one step closer to getting the pain relief you've been looking for.

What medications are used to treat diabetic nerve pain of the feet and post-shingles nerve pain?

There are several medications approved by the Food and Drug Administration (FDA) for diabetic nerve pain of the feet and post-shingles nerve pain. These include oral medications and topicals. Please speak to your doctor for more information about your condition.

What is QUTENZA?

QUTENZA is a topical system that contains capsaicin that may provide up to **3 months of pain relief** for patients with diabetic nerve pain of the feet and post-shingles nerve pain. **QUTENZA is the first and only treatment of its kind** to deliver prescription-strength capsaicin directly into the skin.

IMPORTANT SAFETY INFORMATION (cont)

Contraindications

None

Warnings and Precautions

- Do not touch QUTENZA or items exposed to capsaicin. Touching QUTENZA and then accidentally touching other areas of your body can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.

Please see additional Important Safety Information throughout.

MAY PROVIDE UP TO 3 MONTHS OF PAIN RELIEF

Qutenza[®]
(capsaicin) 8% topical system

ABOUT QUTENZA

QUTENZA for diabetic nerve pain of the feet



30-minute application on the feet



Up to 4 topical systems may be used at a time



60-minute application on the skin



Treatment may be repeated **every 3 months** or as warranted by the return of pain (not more frequently than every 3 months)

Is QUTENZA proven to work?

In clinical studies, **QUTENZA has been shown to relieve pain for up to 3 months** in people with diabetic nerve pain of the feet and post-shingles nerve pain. QUTENZA has been shown to be effective for patients who are already taking other pain medicines. QUTENZA is unlikely to interact with other medicines you may be taking. Like any medicine, QUTENZA may not work for everyone. Only you and your doctor can decide if QUTENZA is right for you.

How quickly might QUTENZA work for me?

In a clinical study, after one application of QUTENZA, patients with diabetic nerve pain of the feet experienced **pain relief after 19 days versus 72 days** for patients who received a placebo.

In a different clinical study, some patients with post-shingles nerve pain began to feel **pain relief after 1 week**.

In clinical studies, some patients did not respond to the first treatment of QUTENZA, but **did respond to the second treatment with QUTENZA**.

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

- QUTENZA is not for use near eyes or mucous membranes. Do not sniff or inhale near QUTENZA as this may cause you to cough or sneeze.
- If any of these side effects become severe, tell your healthcare provider immediately.

Please see accompanying full Prescribing Information.



About QUTENZA (cont)

What are the most common side effects of QUTENZA?

The most common side effects are application site redness, application site pain, and application site itching.

Why does QUTENZA have to be applied by my doctor or a healthcare professional?



QUTENZA contains **prescription-strength capsaicin** capable of producing severe irritation of the eyes, mucous membranes, respiratory tract, and skin. **Only a physician or healthcare professional** under the close supervision of a physician is to administer and handle QUTENZA. While administering QUTENZA, special gloves are required and must be disposed of properly to prevent accidental contact.



Your blood pressure may be monitored periodically during and following treatment because pain during the treatment may cause your blood pressure to increase.

Tell your physician or healthcare professional if you have experienced any recent heart problems prior to QUTENZA treatment.

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

- Even though a numbing medicine is used on the skin before applying QUTENZA, some patients may still experience substantial pain during the treatment. Tell your healthcare provider if you are experiencing pain; a cool compress or medicine for the pain can be provided to help lessen your discomfort.

Please see additional Important Safety Information throughout.

What should I discuss with my physician or healthcare professional before using QUTENZA?

Tell your physician or healthcare professional if you:



Have high blood pressure that is not well controlled by medicine, or have had recent heart problems, stroke, or other vascular problems. Your physician or healthcare professional may monitor your blood pressure periodically during and following the treatment.



Not an actual patient.

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

- QUTENZA can cause serious side effects, including pain and increases in blood pressure during or right after treatment.
- Your healthcare provider should check your blood pressure during treatment with QUTENZA.

Please see accompanying full Prescribing Information.



What to expect during QUTENZA treatment

Is there pain during the QUTENZA application?



Some pain and burning during and following the treatment is common, due to the prescription-strength capsaicin in QUTENZA. It's important that you **tell your physician or healthcare professional how you are feeling** during the application process. If you experience pain, **tell your physician or healthcare professional. Your healthcare professional may use cold packs or pain medicine to reduce treatment-related discomfort.** Also, because the pain may cause an increase in blood pressure, your physician or healthcare professional may monitor your blood pressure periodically during and following the treatment.

What can I expect during my QUTENZA application?



For QUTENZA, temporary increases in pain may be common on the day of treatment. Pain increases that occur during QUTENZA application **usually begin to decrease after QUTENZA removal.** On average, for most patients in clinical trials, pain subsided by the end of the treatment day.

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

- If you have high blood pressure that is not well controlled by medicine, or have had recent heart problems, stroke, or other vascular problems, you may be at increased risk and should discuss with your doctor whether QUTENZA is right for you.
- Tell your doctor if you have reduced sensation in the feet. You may notice that you have less feeling for hot or sharp pain where QUTENZA was applied, but this is usually minor and temporary.

Side Effects

In all clinical trials, the most common drug-related side effects of QUTENZA were redness, pain, or itching where QUTENZA was applied. You should tell your doctor if any side effects bother you or do not go away.

Please see additional Important Safety Information throughout.

What else should I know about QUTENZA?



Do not touch QUTENZA during treatment, as this may irritate your eyes, mucous membranes, respiratory tract, and skin.



The areas treated with QUTENZA may be sensitive to heat, so you may wish to avoid hot showers or baths, direct sunlight, and vigorous exercise for a few days following treatment.



Not an actual patient.
QUTENZA is not indicated for patients under 18 years of age.

IMPORTANT SAFETY INFORMATION (cont)

Adverse Event Reporting

Physicians, other healthcare providers, and patients are encouraged to voluntarily report adverse events involving drugs or medical devices. To make a report you can:

- In the U.S., visit www.fda.gov/medwatch or call 1-800-FDA-1088; or
- For QUTENZA, you may also call 1-877-900-6479 and select option 1, or press zero on your keypad to talk to an operator to direct your call.

For more information, ask your healthcare provider or pharmacist.

Please see accompanying full Prescribing Information.



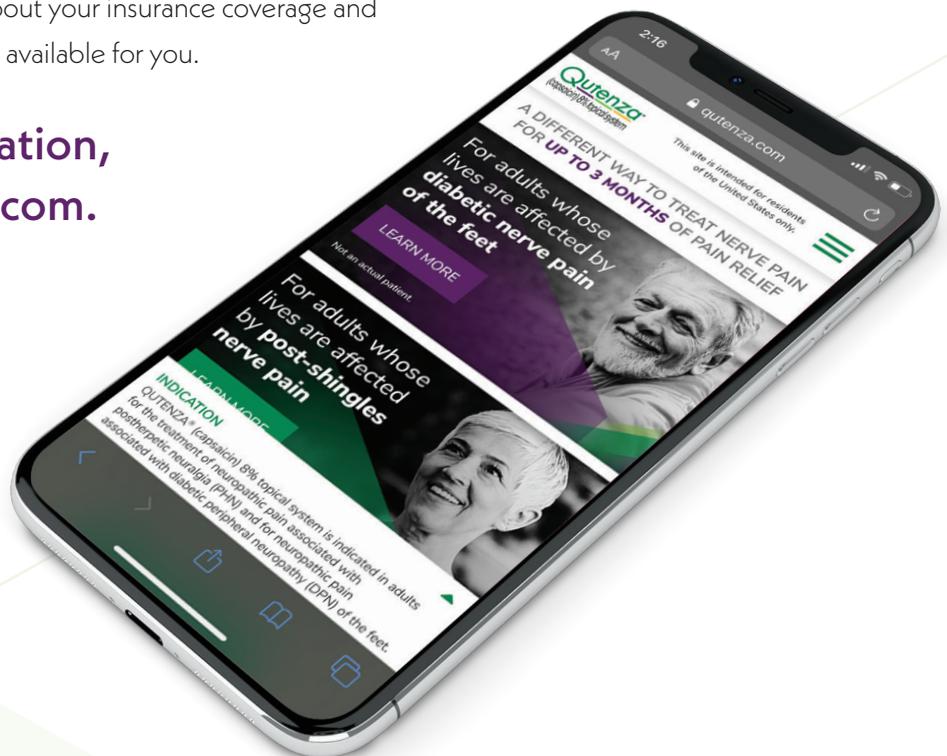
QUTENZA access support

QUTENZA is covered under Medicare Part B as a medical benefit.

If you are under 65 years old and commercially insured, you may be eligible for a medical benefit for QUTENZA.

Talk to your doctor about your insurance coverage and whether a medical benefit is available for you.

For more information, visit QUTENZA.com.



Important Safety Information

INDICATION

QUTENZA[®] (capsaicin) 8% topical system is indicated in adults for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet.

IMPORTANT SAFETY INFORMATION

Treatment with QUTENZA must be performed only by a healthcare provider. You should never apply or remove QUTENZA yourself.

Contraindications

None

Warnings and Precautions

- Do not touch QUTENZA or items exposed to capsaicin. Touching QUTENZA and then accidentally touching other areas of your body can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.
- QUTENZA is not for use near eyes or mucous membranes. Do not sniff or inhale near QUTENZA as this may cause you to cough or sneeze.
- If any of these side effects become severe, tell your healthcare provider immediately.
- Even though a numbing medicine is used on the skin before applying QUTENZA, some patients may still experience substantial pain during the treatment. Tell your healthcare provider if you are experiencing pain; a cool compress or medicine for the pain can be provided to help lessen your discomfort.
- QUTENZA can cause serious side effects, including pain and increases in blood pressure during or right after treatment.
- Your healthcare provider should check your blood pressure during treatment with QUTENZA.

- If you have high blood pressure that is not well controlled by medicine, or have had recent heart problems, stroke, or other vascular problems, you may be at increased risk and should discuss with your doctor whether QUTENZA is right for you.
- Tell your doctor if you have reduced sensation in the feet. You may notice that you have less feeling for hot or sharp pain where QUTENZA was applied, but this is usually minor and temporary.

Side Effects

In all clinical trials, the most common drug-related side effects of QUTENZA were redness, pain, or itching where QUTENZA was applied. You should tell your doctor if any side effects bother you or do not go away.

Adverse Event Reporting

Physicians, other healthcare providers, and patients are encouraged to voluntarily report adverse events involving drugs or medical devices. To make a report you can:

- In the U.S., visit www.fda.gov/medwatch or call 1-800-FDA-1088; or
- For QUTENZA, you may also call 1-877-900-6479 and select option 1, or press zero on your keypad to talk to an operator to direct your call.

For more information, ask your healthcare provider or pharmacist.

Please see accompanying full Prescribing Information.

Abou

**Diabetic
Nerve Pain
of the Feet**

Qutenza[®]
(capsaicin) 8% topical system

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DIABETIC NERVE PAIN OF THE FEET

Not an actual patient.



Diabetic nerve pain of the feet and you: Explaining the pain

What happens when diabetic nerve pain of the feet occurs

Diabetic nerve pain of the feet, also known as painful diabetic peripheral neuropathy (PDPN) of the feet, occurs if **nerves are damaged** as a result of diabetes. Damaged **nerves cannot correctly transmit signals from the skin to the brain**, causing the signals to become exaggerated, and creating the chronic pain you may be feeling.

Although diabetic nerve pain can affect any nerve, **it's most commonly felt in the feet.**

That is why your doctor has prescribed QUTENZA, which works differently to treat diabetic nerve pain of the feet with capsaicin, an active ingredient that desensitizes the nerve right at the site of pain.



Patients have described diabetic nerve pain of the feet as "shooting" or "stabbing"



A 30-minute, in-office application

IMPORTANT SAFETY INFORMATION

Treatment with QUTENZA must be performed only by a healthcare provider. You should never apply or remove QUTENZA yourself.

Contraindications

None

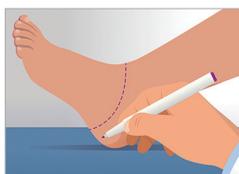
Warnings and Precautions

- Do not touch QUTENZA or items exposed to capsaicin. Touching QUTENZA and then accidentally touching other areas of your body can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.

Please see additional Important Safety Information throughout.

QUTENZA application guide

What you can expect



Step 1: Identify - Your physician or healthcare provider will **identify and mark the treatment area** on your skin and examine your feet prior to the application. If necessary, your hair will be clipped in and around the identified treatment area to ensure QUTENZA will stick. The treatment area will then be washed with mild soap and water, and dried thoroughly.



Step 2: Numb - A topical **anesthetic will be applied** to reduce discomfort associated with the application of QUTENZA. The topical anesthetic will be removed with a dry wipe, the treatment area will be gently washed with mild soap and water, and dried thoroughly.



Step 3: Apply - QUTENZA is applied to your skin for **30 minutes**. A dressing, such as rolled gauze, may be used to ensure QUTENZA maintains contact with the treatment area. QUTENZA can be wrapped around the top, bottom, or side of each foot to completely cover the treatment area. During the treatment, you must not touch QUTENZA or the treatment area. Touching QUTENZA and then accidentally touching other areas of your body can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.



Step 4: Remove - After 30 minutes have passed, your physician or healthcare provider will **gently and slowly remove** QUTENZA.



Step 5: Cleanse - After QUTENZA is removed, a **Cleansing Gel will be applied** to the treatment area for at least one minute. The Cleansing Gel will then be removed with a dry wipe, the treatment area will be gently washed with mild soap and water, and dried thoroughly.

NOTE: The treatment area may be sensitive to heat (eg, hot showers/baths, direct sunlight, vigorous exercise) for a few days after application.

About

**Post-Shingles
Nerve Pain**

Qutenza[®]
(capsaicin) 8% topical system

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Not an actual patient.

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POST-SHINGLES NERVE PAIN



Post-shingles nerve pain and you: Explaining the pain

What happens when post-shingles nerve pain occurs

Post-shingles nerve pain, also known as postherpetic neuralgia (PHN), occurs if **nerves are damaged** due to a previous herpes zoster infection, or shingles. Damaged nerves **cannot correctly transmit signals** from the skin to the brain, which can cause the chronic pain you may be feeling.

Symptoms of post-shingles nerve pain are often limited or **localized to the area of skin where the shingles outbreak first occurred**, often in the band around your trunk, usually on one side of the body. Less common symptoms of post-shingles nerve pain have included itching, numbness, or feeling of “pins and needles.”

That is why your doctor has prescribed QUTENZA, which works differently to treat post-shingles nerve pain with capsaicin, an active ingredient that desensitizes the nerve right at the site of pain.



Patients have described post-shingles nerve pain as “shooting” or “stabbing”



A 60-minute, in-office application

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

- QUTENZA is not for use near eyes or mucous membranes. Do not sniff or inhale near QUTENZA as this may cause you to cough or sneeze.
- If any of these side effects become severe, tell your healthcare provider immediately.
- Even though a numbing medicine is used on the skin before applying QUTENZA, some patients may still experience substantial pain during the treatment. Tell your healthcare provider if you are experiencing pain; a cool compress or medicine for the pain can be provided to help lessen your discomfort.
- QUTENZA can cause serious side effects, including pain and increases in blood pressure during or right after treatment.
- Your healthcare provider should check your blood pressure during treatment with QUTENZA.

Please see additional Important Safety Information throughout.

QUTENZA application guide

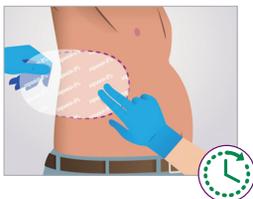
What you can expect



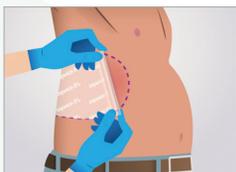
Step 1: Identify - Your physician or healthcare provider will **identify and mark the treatment area** on your skin prior to the application. If necessary, your hair will be clipped in and around the identified treatment area to ensure QUTENZA will stick. The treatment area will then be washed with mild soap and water, and dried thoroughly.



Step 2: Numb - A topical **anesthetic will be applied** to reduce discomfort associated with the application of QUTENZA. The topical anesthetic will be removed with a dry wipe, the treatment area will be gently washed with mild soap and water, and dried thoroughly.



Step 3: Apply - QUTENZA **is applied to your skin for 60 minutes**. A dressing, such as rolled gauze, may be used to ensure QUTENZA maintains contact with the treatment area. During the treatment, you must not touch QUTENZA or the treatment area. Touching QUTENZA and then accidentally touching other areas of your body can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.



Step 4: Remove - After 60 minutes have passed, your physician or healthcare provider will **gently and slowly remove** QUTENZA.



Step 5: Cleanse - After QUTENZA is removed, **a Cleansing Gel will be applied** to the treatment area for at least one minute. The Cleansing Gel will then be removed with a dry wipe, the treatment area will be gently washed with mild soap and water, and dried thoroughly.

NOTE: The treatment area may be sensitive to heat (eg, hot showers/baths, direct sunlight, vigorous exercise) for a few days after application.

AN IN-OFFICE APPLICATION THAT MAY
PROVIDE UP TO 3 MONTHS OF PAIN RELIEF

Qutenza[®]
(capsaicin) 8% topical system

Up to 3 months of pain relief

30-minute application for diabetic
nerve pain of the feet and 60-minute
application for post-shingles nerve pain



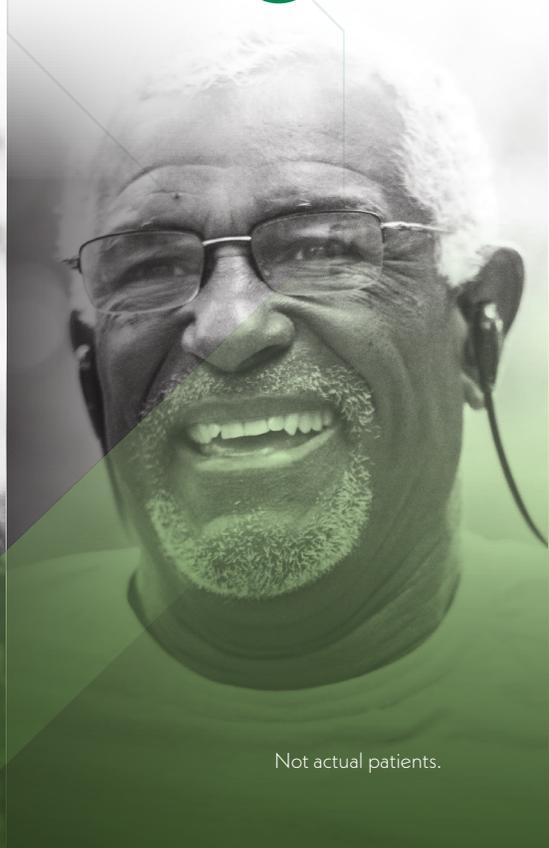
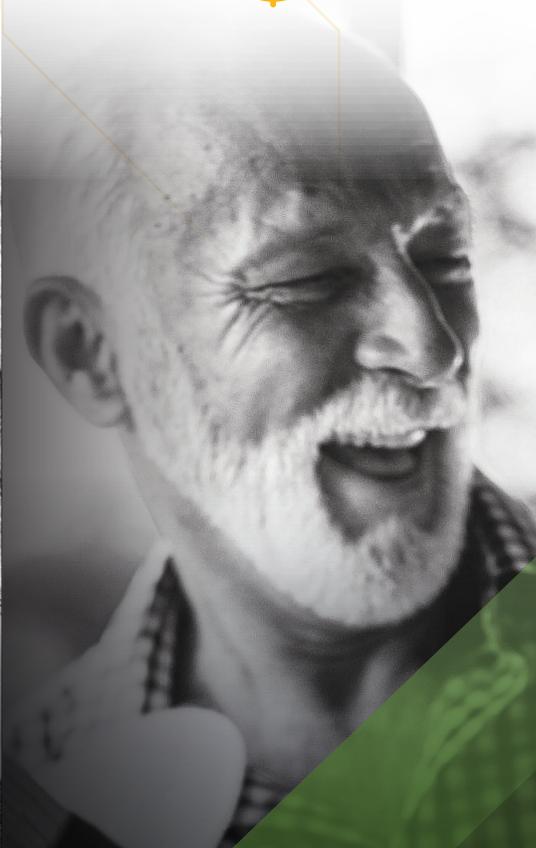
Acts locally

Treat diabetic nerve pain of the
feet and post-shingles nerve pain
at the site of pain



No drug-drug interactions

QUTENZA can be used
alone or in combination
with other treatments



Not actual patients.

INDICATION

QUTENZA[®] (capsaicin) 8% topical system is indicated in adults for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet.

IMPORTANT SAFETY INFORMATION

Treatment with QUTENZA must be performed only by a healthcare provider. You should never apply or remove QUTENZA yourself.

**Please see additional Important Safety Information inside.
Please see accompanying full Prescribing Information.**



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R_x only. For topical use only.

HIGHLIGHTS OF PRESCRIBING INFORMATION
 These highlights do not include all the information needed to use QUTENZA safely and effectively. See full prescribing information for QUTENZA.
QUTENZA® (capsaicin) topical system
Initial U.S. Approval: 2009

RECENT MAJOR CHANGES

Indications and Usage, Neuropathic pain associated with diabetic peripheral neuropathy of the feet (1)	7/2020
Dosage and Administration (2)	7/2020
Dosage and Administration (2.1, 2.3)	5/2020
Warnings and Precautions (5.1, 5.2)	5/2020
Warnings and Precautions (5.4)	7/2020

INDICATIONS AND USAGE

QUTENZA is a TRPV1 channel agonist indicated for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet. (1)

DOSAGE AND ADMINISTRATION

- Only physicians or health care professionals under the close supervision of a physician are to administer QUTENZA. (2.1)
- Administer QUTENZA in a well-ventilated treatment area. (2.1)
- Wear nitrile (not latex) gloves when handling QUTENZA and when cleaning treatment areas. (2.1)
- Use of a face mask and protective glasses is advisable for healthcare providers. (2.1)
- Do not use QUTENZA on broken skin. (2.1)
- PHN: Apply up to four topical systems for 60 minutes. (2.2)
- DPN: Apply up to four topical systems for 30 minutes on the feet. (2.2)
- Repeat every 3 months or as warranted by the return of pain (not more frequently than every three months). (2.2)
- See Dosage and Administration, Instructions for Use, for detailed instructions on QUTENZA administration. (2.3)

DOSAGE FORMS AND STRENGTHS

- QUTENZA contains 8% capsaicin (640 mcg per cm²). Each QUTENZA contains a total of 179 mg of capsaicin. (3)

CONTRAINDICATIONS

- None

WARNINGS AND PRECAUTIONS

Severe Irritation with Unintended Capsaicin Exposure: Capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin. (5.1)

- Do not use near eyes or mucous membranes.
- Wear nitrile gloves and avoid touching items or surfaces that the patient may later touch. (5.1)
- If irritation of eyes or airway occurs, remove the affected individual from the vicinity of QUTENZA and flush the mucous membranes or eyes with water.
- If skin not intended to be treated comes into contact with QUTENZA, apply Cleansing Gel and then wipe off with dry gauze.
- Thoroughly clean all areas and items exposed to QUTENZA and dispose of properly.

Application-Associated Pain: Patients may experience substantial procedural pain and burning upon application of QUTENZA and following removal of QUTENZA. Prepare to treat acute pain during and following the application procedure with local cooling (such as an ice pack) and/or appropriate analgesic medication. (5.2)

Increase in Blood Pressure: Transient increases in blood pressure may occur with QUTENZA treatment. Monitor blood pressure during and following the treatment procedure. (5.3)

Sensory Function: Reductions in sensory function, which were generally minor and temporary, have been reported following administration of QUTENZA. All patients with sensory deficits should be assessed for signs of sensory deterioration or loss prior to each application of QUTENZA. If sensory loss occurs, treatment should be reconsidered. (5.4)

ADVERSE REACTIONS

The most common adverse reactions (≥5% and greater than control) in all controlled clinical trials are application site erythema, application site pain, and application site pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Averitas Pharma at 1-877-900-6479 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

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*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
 QUTENZA is indicated in adults for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet.

2 DOSAGE AND ADMINISTRATION

- 2.1 Important Dosage and Administration Instructions**
- Do not dispense QUTENZA to patients for self-administration or handling. Only physicians or healthcare professionals under the close supervision of a physician are to administer and handle QUTENZA.
 - Unintended exposure to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin in healthcare providers and others [see *Warnings and Precautions (5.1)*].
 - Because unintended exposure to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin, when administering QUTENZA, it is important to follow these procedures:
 - Administer QUTENZA in a well-ventilated treatment area.
 - Wear only nitrile gloves when handling QUTENZA or any item that makes contact with QUTENZA, and when cleaning capsaicin residue from the skin. Do not use latex gloves as they do not provide adequate protection.
 - Use of a face mask and protective glasses is advisable for healthcare providers.
 - Keep QUTENZA in the sealed pouch until immediately before use.
 - Use QUTENZA only on dry, intact (unbroken) skin.
 - In patients treated for neuropathic pain associated with diabetic peripheral neuropathy, a careful examination of the feet should be undertaken prior to each application of QUTENZA to detect skin lesions related to underlying neuropathy or vascular insufficiency. [see *Warnings and Precautions (5.4)*].
 - During administration, avoid unnecessary contact with any items in the room, including items that the patient may later have contact with, such as horizontal surfaces and bedsheets.
 - Aerosolization of capsaicin can occur upon rapid removal of QUTENZA. Therefore, remove QUTENZA gently and slowly by rolling the adhesive side inward [see *Warnings and Precautions (5.1)*].
 - Immediately after use, clean all areas that had contact with QUTENZA and properly dispose of QUTENZA, associated packaging, Cleansing Gel, gloves, and other treatment materials in accordance with local biomedical waste procedures.
 - If QUTENZA is cut, ensure unused pieces are properly disposed of.

- 2.2 Dosing**
- The recommended dose of QUTENZA for neuropathic pain associated with postherpetic neuralgia is a single, 60-minute application of up to four topical systems.
 - The recommended dose of QUTENZA for neuropathic pain associated with diabetic peripheral neuropathy is a single, 30-minute application on the feet of up to four topical systems.

Treatment with QUTENZA may be repeated every three months or as warranted by the return of pain (not more frequently than every three months).

2.3 Instructions for Use
USE IN NEUROPATHIC PAIN ASSOCIATED WITH POSTHERPETIC NEURALGIA (60-MINUTE APPLICATION TIME)
Prepare

- Administer QUTENZA in a well-ventilated treatment area.
- Put on nitrile (not latex) gloves. Use of a face mask and protective glasses is advisable for healthcare providers.
- Inspect the pouch. Do not use if the pouch has been torn or damaged.

Identify

- The treatment area (painful area including areas of hypersensitivity and allodynia) must be identified by a physician or healthcare professional and marked on the skin.



- If necessary, clip hair (do not shave) in and around the identified treatment area to promote QUTENZA adherence.
- QUTENZA can be cut to match the size and shape of the treatment area. Gently wash the treatment area with mild soap and water, and dry thoroughly.

Anesthetize

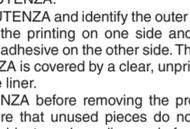
- Pre-treat with a topical anesthetic to reduce discomfort associated with the application of QUTENZA.
- Apply topical anesthetic to the entire treatment area and surrounding 1 to 2 cm, and keep the local anesthetic in place until the skin is anesthetized prior to the application of QUTENZA.



- Remove the topical anesthetic with a dry wipe. Gently wash the treatment area with mild soap and water, and dry thoroughly.

Apply

- Tear open the pouch along the three dashed lines and remove QUTENZA.
- Inspect QUTENZA and identify the outer surface backing layer with the printing on one side and the capsaicin-containing adhesive on the other side. The adhesive side of QUTENZA is covered by a clear, unprinted, diagonally cut release liner.
- Cut QUTENZA before removing the protective release liner. Ensure that unused pieces do not make contact with other objects and are disposed of appropriately.
- The diagonal cut in the release liner is to aid in its removal. Peel a small section of the release liner back and place the adhesive side of QUTENZA on the treatment area.
- While you slowly peel back the release liner from under the QUTENZA with one hand, use your other hand to smooth QUTENZA down onto the skin.



- Remove the topical anesthetic with a dry wipe. Gently wash the treatment area with mild soap and water, and dry thoroughly.
- Tear open the pouch along the three dashed lines and remove QUTENZA.
- Inspect QUTENZA and identify the outer surface backing layer with the printing on one side and the capsaicin-containing adhesive on the other side. The adhesive side of QUTENZA is covered by a clear, unprinted, diagonally cut release liner.
- Cut QUTENZA before removing the protective release liner. Ensure that unused pieces do not make contact with other objects and are disposed of appropriately.
- The diagonal cut in the release liner is to aid in its removal. Peel a small section of the release liner back and place the adhesive side of QUTENZA on the treatment area.
- While you slowly peel back the release liner from under the QUTENZA with one hand, use your other hand to smooth QUTENZA down onto the skin.
- QUTENZA can be wrapped around the dorsal, lateral and plantar surfaces of each foot to completely cover the treatment area.



- Once QUTENZA is applied, leave in place for 60 minutes (PHN).
- To ensure QUTENZA maintains contact with the treatment area, a dressing, such as rolled gauze, may be used. Remove the nitrile gloves after the application.
- Instruct the patient not to touch QUTENZA or the treatment area.

Remove

- Put on nitrile (not latex) gloves. Remove QUTENZA by gently and slowly rolling inward.



Cleanse

- After removal of QUTENZA, generously apply Cleansing Gel to the treatment area and leave on for at least one minute. Remove Cleansing Gel with a dry wipe and gently wash the area with mild soap and water. Dry thoroughly.



- Dispose of all treatment materials as described [see *Dosage and Administration (2.1)*].
- Inform the patient that the treated area may be sensitive for a few days to heat (e.g., hot showers/baths, direct sunlight, vigorous exercise).



- If necessary, clip hair (do not shave) in and around the identified treatment area to promote QUTENZA adherence.
- QUTENZA can be cut to match the size and shape of the treatment area. Gently wash the treatment area with mild soap and water, and dry thoroughly.

Anesthetize

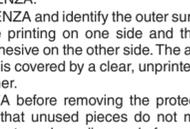
- Pre-treat with a topical anesthetic to reduce discomfort associated with the application of QUTENZA.
- Apply topical anesthetic to the entire treatment area and surrounding 1 to 2 cm, and keep the local anesthetic in place until the skin is anesthetized prior to the application of QUTENZA.



- Remove the topical anesthetic with a dry wipe. Gently wash the treatment area with mild soap and water, and dry thoroughly.

Apply

- Tear open the pouch along the three dashed lines and remove QUTENZA.
- Inspect QUTENZA and identify the outer surface backing layer with the printing on one side and the capsaicin-containing adhesive on the other side. The adhesive side of QUTENZA is covered by a clear, unprinted, diagonally cut release liner.
- Cut QUTENZA before removing the protective release liner. Ensure that unused pieces do not make contact with other objects and are disposed of appropriately.
- The diagonal cut in the release liner is to aid in its removal. Peel a small section of the release liner back and place the adhesive side of QUTENZA on the treatment area.
- While you slowly peel back the release liner from under the QUTENZA with one hand, use your other hand to smooth QUTENZA down onto the skin.
- QUTENZA can be wrapped around the dorsal, lateral and plantar surfaces of each foot to completely cover the treatment area.



- Once QUTENZA is applied, leave in place for 30 minutes on the feet (DPN).
- To ensure QUTENZA maintains contact with the treatment area, a dressing, such as rolled gauze, may be used. Remove the nitrile gloves after the application.
- Instruct the patient not to touch QUTENZA or the treatment area.



- Once QUTENZA is applied, leave in place for 30 minutes on the feet (DPN).
- To ensure QUTENZA maintains contact with the treatment area, a dressing, such as rolled gauze, may be used. Remove the nitrile gloves after the application.
- Instruct the patient not to touch QUTENZA or the treatment area.

Remove

- Put on nitrile (not latex) gloves. Remove QUTENZA by gently and slowly rolling inward.



Cleanse

- After removal of QUTENZA, generously apply Cleansing Gel to the treatment area and leave on for at least one minute. Remove Cleansing Gel with a dry wipe and gently wash the area with mild soap and water. Dry thoroughly.



- Dispose of all treatment materials as described [see *Dosage and Administration (2.1)*].
- Inform the patient that the treated area may be sensitive for a few days to heat (e.g., hot showers/baths, direct sunlight, vigorous exercise).

3 DOSAGE FORMS AND STRENGTHS
 QUTENZA topical system contains 8% capsaicin (640 mcg per cm²). Each topical system contains a total of 179 mg of capsaicin. Each topical system is 14 cm x 20 cm (280 cm²) and consists of an adhesive side containing the active substance and an outer surface backing layer. The adhesive side is covered with a removable, clear, unprinted, diagonally cut, release liner. The outer surface of the backing layer is imprinted with “capsaicin 8%.”

4 CONTRAINDICATIONS
 None.

5 WARNINGS AND PRECAUTIONS
5.1 Severe Irritation with Unintended Capsaicin Exposure
 Unintended exposure to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.

- Eye and Mucous Membrane Exposure**
- Do not apply QUTENZA to the face, eyes, mouth, nose, or scalp to avoid risk of exposure to eyes or mucous membranes.
 - Accidental exposure to the eyes and mucous membranes can occur from touching QUTENZA or items exposed to capsaicin and then touching the eyes and mucous membranes.
 - Wear nitrile gloves when administering QUTENZA and avoid unnecessary contact with items in the room, including items that the patient may later have contact with, such as horizontal surfaces and bedsheets.
 - If irritation of eyes or mucous membranes occurs, remove the affected individual from the vicinity of QUTENZA and flush eyes and mucous membranes with cool water.

Respiratory Tract Exposure

- Aerosolization of capsaicin can occur upon rapid removal of QUTENZA. Therefore, remove QUTENZA gently and slowly by rolling the adhesive side inward [see *Dosage and Administration (2.1, 2.3)*].
- Inhalation of airborne capsaicin can result in coughing or sneezing. If irritation of airways occurs, remove the affected individual from the vicinity of QUTENZA. Provide supportive medical care if shortness of breath develops.

Skin Exposure

- If skin not intended to be treated is exposed to QUTENZA, apply Cleansing Gel for one minute and wipe off with dry gauze. After the Cleansing Gel has been wiped off, wash the area with soap and water.

Thoroughly clean all areas that had contact with QUTENZA and properly dispose of QUTENZA, associated packaging, Cleansing Gel, gloves, and other treatment materials in accordance with local biomedical waste procedures [see *Dosage and Administration (2.1, 2.3)*].

5.2 Application-Associated Pain
 Even following use of a local anesthetic prior to administration of QUTENZA, patients may experience substantial procedural pain and burning upon application of QUTENZA and following removal of QUTENZA. Prepare to treat acute pain during and following the application procedure with local cooling (such as an ice pack) and/or appropriate analgesic medication.

5.3 Increase in Blood Pressure
 In clinical trials, transient increases in blood pressure occurred during or shortly after exposure to QUTENZA. The changes averaged less than 10 mm Hg, although some patients had greater increases and these changes lasted for approximately two hours after QUTENZA removal. Increases in blood pressure were unrelated to the pretreatment blood pressure but were related to treatment-related increases in pain. Monitor blood pressure periodically during and following the treatment procedure and provide adequate support for treatment-related pain.

Patients with unstable or poorly controlled hypertension, or a recent history of cardiovascular or cerebrovascular events, may be at an increased risk of adverse cardiovascular effects. Consider these factors prior to initiating QUTENZA treatment.

5.4 Sensory Function
 Reductions in sensory function have been reported following administration of QUTENZA. Decreases in sensory functions are generally minor and temporary (including to thermal and other harmful stimuli). All patients with pre-existing sensory deficits should be clinically assessed for signs of sensory deterioration or loss prior to each application of QUTENZA. If sensory deterioration or loss is detected or pre-existing sensory deficit worsens, continued use of QUTENZA treatment should be reconsidered.

6 ADVERSE REACTIONS
 The following serious adverse reactions are discussed elsewhere in the labeling:

- Severe Irritation Due to Accidental Exposure of Eyes, Skin, Respiratory Tract, and Mucous Membranes [see *Warning and Precautions (5.1)*]
- Application-Associated Pain [see *Warnings and Precautions (5.2)*]
- Increase in Blood Pressure [see *Warnings and Precautions (5.3)*]
- Sensory Function Reduction [see *Warning and Precautions (5.4)*]

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

Across all controlled and uncontrolled clinical trials, 2848 patients have received QUTENZA. A total of 924 patients received more than one treatment application and 732 patients were followed for 48 weeks or longer. A total of 590 DPN patients and 1112 PHN patients have received QUTENZA across all controlled and uncontrolled clinical trials. Among patients treated with QUTENZA, 1% discontinued prematurely due to an adverse event.

Most Common Adverse Reactions in all Controlled Clinical Trials
 In all controlled clinical trials, adverse reactions occurring in ≥5% of patients in the QUTENZA group and at an incidence at least 1% greater than in the control group were application site erythema, application site pain, and application site pruritus. The majority of application site reactions were transient and self-limited. Transient increases in pain were commonly observed on the day of treatment in patients treated with QUTENZA. Pain increases occurring during QUTENZA application usually began to resolve after QUTENZA removal. On average, pain scores returned to baseline by the end of the treatment day and then remained at or below baseline levels. A majority of QUTENZA-treated patients in clinical trials had adverse reactions with a maximum intensity of “mild” or “moderate.”

Postherpetic Neuralgia (PHN)
 Table 1 summarizes all adverse reactions, regardless of causality, occurring in >1% of patients with PHN in the QUTENZA group for which the incidence was at least 1% greater than in the control group.

TABLE 1: Adverse Reaction Incidence (%) in Controlled Double-blind Trials in Postherpetic Neuralgia (Events in >1% of QUTENZA-treated Patients and at Least 1% Greater in the QUTENZA Group than in the Control Group)

Body System Preferred Term	QUTENZA 60 minutes (N=622) %	Control 60 minutes (N=495) %
General Disorders and Administration Site Conditions		
Application site erythema	63	54
Application site pain	42	21
Application site pruritus	6	4
Application site papules	6	3
Application site edema	4	1
Application site swelling	2	1
Application site dryness	2	1
Infections and Infestations		
Nasopharyngitis	4	2
Bronchitis	2	1
Sinusitis	3	1
Gastrointestinal Disorders		
Nausea	5	2
Vomiting	3	1
Skin and Subcutaneous Tissue Disorder		
Pruritus	2	< 1
Vascular Disorders		
Hypertension	2	1

Less common adverse reactions (<1%) with QUTENZA observed during PHN clinical trials included: palpitations, tachycardia, eye pruritus, application site reactions (such as urticaria, paresthesia, dermatitis, hyperesthesia).

Neuropathic Pain Associated with Diabetic Peripheral Neuropathy (DPN)

Table 2 summarizes all adverse reactions, regardless of causality, occurring in >1% of patients with DPN in the QUTENZA group for which the incidence was at least 1% greater than in the control group.

TABLE 2: Adverse Reaction Incidence (%) in Double-blind Controlled Trials in Neuropathic Pain Associated with Diabetic Peripheral Neuropathy (Events in >1% of QUTENZA-treated Patients and at Least 1% Greater in the QUTENZA Group than in the Control Group)

Body System Preferred Term	QUTENZA 30 minutes (N=186) %	Control 30 minutes (N=183) %
General Disorders and Administration Site Conditions		
Application site reactions		
Burning sensation	14	3
Application site pain	10	2
Erythema	2	0
Injury, Poisoning and Procedural Complications		
Excoriation	2	0
Musculoskeletal and Connective Tissue Disorders		
Pain in extremity	11	6
Nervous System Disorders		
Headache	3	2
Respiratory, Thoracic and Mediastinal Disorders		
Upper respiratory symptoms		
Upper respiratory tract infection	4	< 1
Cough	2	< 1
Vascular Disorders		
Hypertension	2	< 1

Less common adverse reactions (<1%) with QUTENZA observed during DPN clinical trials included: dizziness, dysesthesia, blister.

6.2 Postmarketing Experience

Because adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been identified during post approval use of QUTENZA: second-degree burn and scarring; accidental exposure (including eye pain, cough, eye and throat irritation).

7 DRUG INTERACTIONS

No clinical drug interaction studies have been performed.

Data from *in vitro* cytochrome P450 inhibition and induction studies show that capsaicin does not inhibit or induce liver cytochrome P450 enzymes at concentrations which far exceed those measured in blood samples. Therefore, interactions with systemic medicinal products are unlikely.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Capsaicin is negligibly absorbed systemically following topical administration of QUTENZA, and maternal use is not expected to result in the fetal exposure to QUTENZA. In animal reproductive studies, no evidence of malformations were observed when capsaicin was administered daily by the topical route to pregnant rats and rabbits during the period of organogenesis at doses of up to 11- and 37-times, respectively, the maximum recommended human dose (MRHD) of QUTENZA at 716 mg capsaicin per day (4 topical systems containing 179 mg/topical system). In a peri- and postnatal development study, no adverse effects were observed when capsaicin was administered daily by the topical route to rats during implantation to weaning at doses of up to 11-times the MRHD (*see Data*).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

There was no evidence of fetal malformations in embryofetal developmental toxicological studies conducted in pregnant rats and rabbits in which QUTENZA (rats) or capsaicin liquid (rabbits) were applied once daily for a 3-hour duration during the period of fetal organogenesis at doses up to 11-times (rat, 32 mg QUTENZA /day) and 37-times (rabbit, 260 mg capsaicin/day) the MRHD based on a C_{max} exposure comparison.

In a peri- and postnatal reproduction toxicology study, pregnant female rats were treated with QUTENZA at doses up to 32 mg QUTENZA/rat/day applied once daily for a 3-hour duration during gestation and lactation (from Gestation Day 7 through Lactation Day 20). Analyses of milk samples on Day 14 of the lactation period demonstrated measurable levels of capsaicin in the dam's milk at all dose levels. There were no effects on survival, growth, learning and memory tests (passive avoidance and water maze), sexual maturation, mating, pregnancy, and fetal development in the offspring of mothers treated with capsaicin up to 32 mg QUTENZA /rat/day (11-times the MRHD based on C_{max} exposure).

8.2 Lactation

Risk Summary

Capsaicin is negligibly absorbed systemically by the mother following topical administration of QUTENZA, and breastfeeding is not expected to result in exposure of the infant to QUTENZA [*see Clinical Pharmacology (12.3)*]. There are no data on the effects of capsaicin on milk production. To minimize potential direct exposure of QUTENZA to the breastfed infant, avoid applying QUTENZA directly to the nipple and areola.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for QUTENZA and any potential adverse effects on the breastfed infant from QUTENZA or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Infertility

In a fertility and reproductive toxicology study, administration of QUTENZA at 13-times the MRHD to male rats for 3 hours/day for 49 days resulted in a statistically significant reduction in the number and percent of motile sperm; however, these reductions did not adversely affect fertility [*see Nonclinical Toxicology (13.1)*]. As this animal model has a large excess of sperm-generating capacity relative to the threshold necessary for fertilization, the lack of an effect on fertility in this species is of unknown clinical significance for males of reproductive potential treated with the MRHD.

8.4 Pediatric Use

The safety and effectiveness of QUTENZA in patients younger than 18 years of age have not been studied.

8.5 Geriatric Use

In controlled clinical trials of QUTENZA in neuropathic pain associated with postherpetic neuralgia, 75% of patients were 65 years and older and 43% of patients were 75 years and older. The safety and effectiveness were similar in geriatric patients and younger patients. No dose adjustments are required in geriatric patients.

10 OVERDOSAGE

There is no clinical experience with QUTENZA overdose in humans.

There is no specific antidote for overdose with capsaicin. In case of suspected overdose, remove QUTENZA gently, apply Cleansing Gel for one minute, wipe off with dry gauze, and gently wash the area with soap and water. Use supportive measures and treat symptoms as clinically warranted.

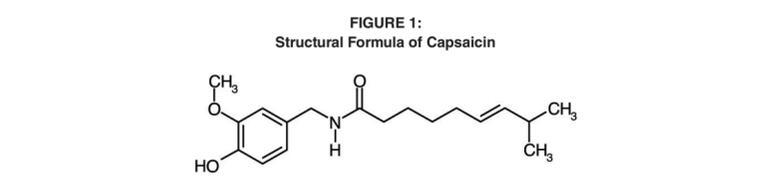
11 DESCRIPTION

QUTENZA (capsaicin) 8% topical system contains capsaicin in a localized dermal delivery system. The capsaicin in QUTENZA is a synthetic equivalent of the naturally occurring compound found in chili peppers. Capsaicin is soluble in alcohol, acetone, and ethyl acetate and very slightly soluble in water.

QUTENZA is a single-use topical system stored in a foil pouch. Each QUTENZA is 14 cm x 20 cm (280 cm²) and consists of a polyester backing film coated with a drug-containing silicone adhesive mixture and covered with a removable polyester release liner.

The backing film is imprinted with "capsaicin 8%." Each QUTENZA contains a total of 179 mg of capsaicin (8% in adhesive, 80 mg per gram of adhesive) or 640 micrograms (mcg) of capsaicin per square cm of topical system.

The empirical formula is C₁₈H₁₇NO₃, with a molecular weight of 305.42. The chemical compound capsaicin [(E)-8-methyl-N-vanillyl-6-nonenamide] is an activating ligand for transient receptor potential vanilloid 1 receptor (TRPV1) and it has the following structure:



QUTENZA contains the following inactive ingredients: diethylene glycol monoethyl ether, dimethicone, ethyl cellulose, polyester film, silicone adhesive, and white ink.

QUTENZA is supplied with a Cleansing Gel which is used to remove residual capsaicin from the skin after treatment. Cleansing Gel consists of the following ingredients: butylated hydroxyanisole, carbomer copolymer, edetate disodium, polyethylene glycol, purified water, and sodium hydroxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Capsaicin is an agonist for the transient receptor potential vanilloid 1 receptor (TRPV1), which is an ion channel-receptor complex expressed on nociceptive nerve fibers in the skin. Topical administration of capsaicin causes an initial enhanced stimulation of the TRPV1-expressing cutaneous nociceptors that may be associated with painful sensations. This is followed by pain relief thought to be mediated by a reduction in TRPV1-expressing nociceptive nerve endings [*see Clinical Pharmacology (12.2)*]. Over the course of several months, there may be a gradual re-emergence of painful neuropathy thought to be due to TRPV1 nerve fiber reinnervation of the treated area.

12.2 Pharmacodynamics

Two studies evaluated the pharmacodynamic effects of QUTENZA on sensory function and epidermal nerve fiber (ENF) density in healthy volunteers. Consistent with the known pharmacodynamic effects of capsaicin on TRPV1-expressing nociceptive nerve endings, reduced ENF density and minor changes in cutaneous nociceptive function (heat detection and sharp sensation) were noted one week after exposure to QUTENZA. ENF density reduction and sensory changes were fully reversible.

12.3 Pharmacokinetics

Pharmacokinetic data in humans showed transient, low (<5 ng/mL) systemic exposure to capsaicin in about one-third of PHN patients following 60-minute applications of QUTENZA. The highest plasma concentration of capsaicin detected was 4.6 ng/mL and occurred immediately after QUTENZA removal. Most quantifiable levels were observed at the time of QUTENZA removal and were below the limit of quantitation 3 to 6 hours after QUTENZA removal. No detectable levels of metabolites were observed in any subject.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Adequate carcinogenicity studies have not been conducted with QUTENZA or capsaicin.

Mutagenesis

Capsaicin was not mutagenic in the Ames, mouse micronucleus, and chromosomal aberration in human peripheral blood lymphocytes assays. As with other catechol-containing compounds (e.g., dopamine), capsaicin showed a weak mutagenic response in the mouse lymphoma assay.

Impairment of Fertility

A fertility and reproductive toxicology study was conducted in rats with exposure to QUTENZA daily for 3 hours/day beginning 28 days before cohabitation, through cohabitation, and continuing through the day before sacrifice (approximately 49 days of treatment). The results revealed a statistically significant reduction in the number and percent of motile sperm. Sperm motility obtained from the vas deferens was reduced in all capsaicin treatment groups (16, 24 and 32 mg QUTENZA/rat/day). Though a "no effect" level was not determined, dose levels used in the study correspond to a 13- to 28-fold exposure margin over the mean C_{max} associated with the MRHD. Sperm counts were reduced in the vas deferens or cauda epididymis in the 24 and 32 mg QUTENZA/rat/day dose groups (79% and 69%, respectively) compared to the placebo topical system-treated control group; however, these reductions did not adversely affect fertility. As this animal model has a large excess of sperm-generating capacity relative to the threshold necessary for fertilization, the lack of an effect on fertility in this species is of unknown significance for human risk assessment.

14 CLINICAL STUDIES

14.1 Postherpetic Neuralgia

The efficacy of QUTENZA was established in two 12-week, double-blind, randomized, dose-controlled, multicenter clinical trials. These studies enrolled patients with postherpetic neuralgia (PHN) persisting for at least 6 months following healing of herpes zoster rash and a baseline score of 3-9 on an 11-point Numerical Pain Rating Scale (NPRS) ranging from 0 (no pain) to 10 (worst possible pain). QUTENZA and a control topical system were each applied as a single, 60-minute application. The control used in these studies looked similar to QUTENZA but contained a low concentration of the active ingredient, capsaicin (3.2 mcg/cm², 0.04% w/w), to retain blinding regarding the known application site reactions of capsaicin (such as burning and erythema). The baseline mean pain score across the 2 studies was approximately 6.0. Patients who entered the study on stable doses of pain-control medications were required to keep dosing stable throughout the duration of the study. Approximately half of the patients were taking concomitant medications, including anticonvulsants, non-SSRI antidepressants, or opioids for their PHN at study entry. Prior to application, a topical anesthetic was applied to the treatment area for 60 minutes. Patients were permitted to use local cooling and additional analgesic medications for treatment-related discomfort as needed through Day 5. Patients recorded their pain daily in a diary.

PHN Study 1: In this 12-week study, the QUTENZA group demonstrated a greater reduction in pain compared to the control group during the primary assessment at Week 8. The percent change in average pain from baseline to Week 8 was -18% (±2%) for the low-dose control and -29% (±2%) for QUTENZA.

For various degrees of improvement in pain from baseline to study endpoint, Figure 2 shows the fraction of patients achieving that degree of improvement. The figure is cumulative, so that patients whose change from baseline is, for example, 50%, are also included at every level of improvement below 50%. Patients who did not complete the study through Week 12 or who showed no improvement at Week 12 were assigned 0% improvement. Some patients experienced a decrease in pain as early as Week 1, which persisted throughout the study. The proportion of patients experiencing ≥30% reduction in pain intensity from baseline for each week through Week 12 is shown in Figure 3.

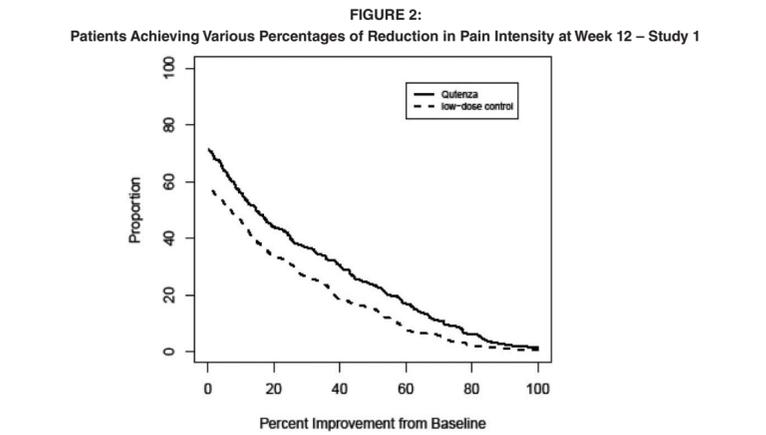
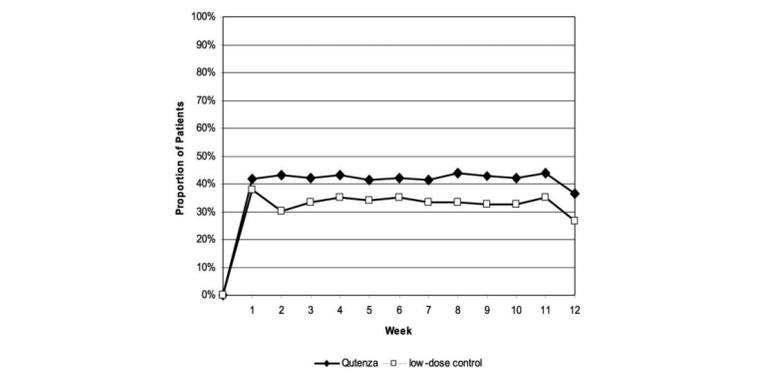


FIGURE 3:
Weekly Proportion of Patients Achieving ≥30% Pain Intensity Reduction – Study 1*



*The same patients may not have responded at each timepoint.

PHN Study 2: In this 12-week study, the QUTENZA group demonstrated a greater reduction in pain compared to the control group during the primary assessment at Week 8. The percent change in average pain from baseline to Week 8 was -26% (±2%) for the low-dose control and -33% (±2%) for QUTENZA.

For various degrees of improvement in pain from baseline to study endpoint, Figure 4 shows the fraction of patients achieving that degree of improvement. The figure is cumulative, so that patients whose change from baseline is, for example, 50%, are also included at every level of improvement below 50%. Patients who did not complete the study through Week 12 or who showed no improvement at Week 12 were assigned 0% improvement. Some patients experienced a decrease in pain as early as Week 1, which persisted throughout the study. The proportion of patients achieving ≥30% reduction in pain intensity from baseline for each week through Week 12 is shown in Figure 5.

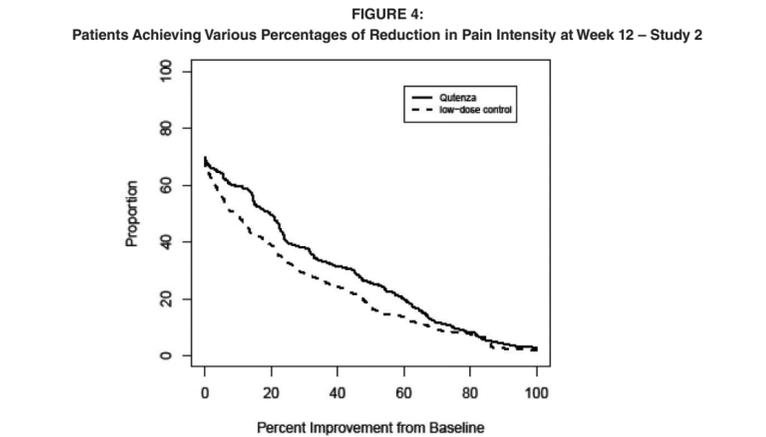
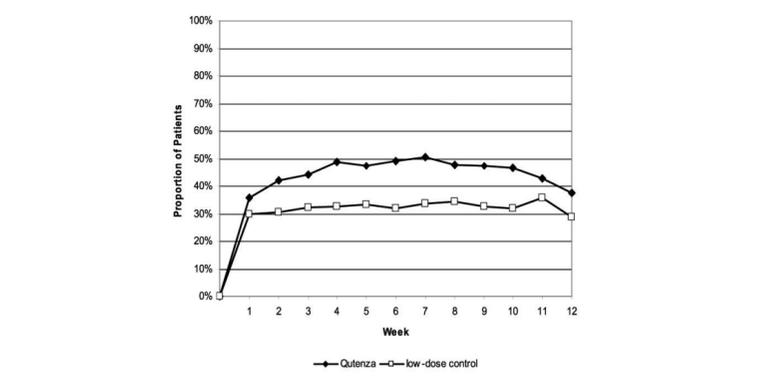


FIGURE 5:
Weekly Proportion of Patients Achieving ≥30% Pain Intensity Reduction – Study 2*



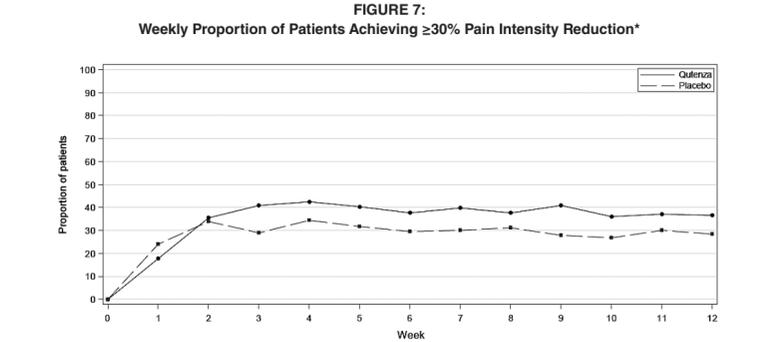
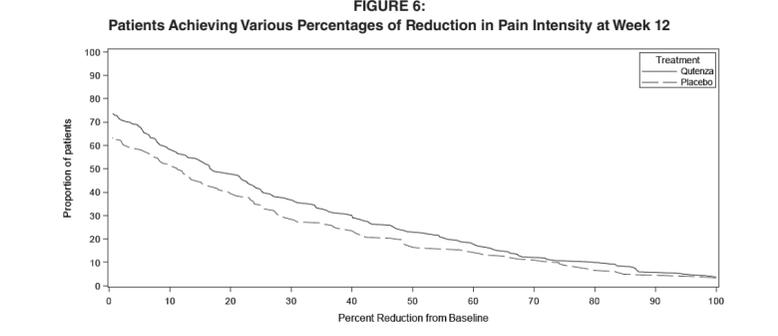
*The same patients may not have responded at each timepoint.

14.2 Neuropathic Pain Associated with Diabetic Peripheral Neuropathy

The efficacy of QUTENZA was established in one 12-week, double-blind, randomized, placebo-controlled, multicenter study. This study enrolled patients with neuropathic pain associated with diabetic peripheral neuropathy (DPN) diagnosed at least 1 year prior to screening and an average pain score of ≥ 4 over the baseline period on an 11-point Numerical Pain Rating Scale (NPRS) ranging from 0 (no pain) to 10 (worst possible pain). QUTENZA and placebo were each applied as a single, 30-minute application. The placebo used in this study was similar to QUTENZA but did not contain an active ingredient. The baseline mean pain score in this study was 6.51 (SD 1.45) and was similar in both groups. Patients who entered the study on stable doses of pain-control medications were required to keep dosing stable throughout the duration of the study. Use of opioid medication other than short-acting rescue medication was not allowed during the study. Concomitant medications for neuropathic pain associated with DPN were taken during the study by 47.2% of the patients and included anticonvulsants and non-SSRI antidepressants. Prior to application, a topical anesthetic was applied to the treatment area for 60 minutes. Patients were permitted to use local cooling and additional analgesic medications for treatment-related discomfort as needed through Day 5. Patients recorded their pain daily.

In this 12-week study, the percent change in average pain from baseline to Week 12 was higher in the QUTENZA group compared to the placebo group. The percent change in average pain from baseline to Week 12 was -22% (±3%) for placebo and -30% (±3%) for QUTENZA. The least-squares mean change was -1.92 on the 11-point NPRS scale for QUTENZA, vs -1.37 for placebo, a least-squares mean difference of -0.56 (95% CI -0.98, -0.14).

For various degrees of improvement in pain from baseline to study endpoint, Figure 6 shows the fraction of patients achieving that degree of improvement. The figure is cumulative, so that patients whose change from baseline is, for example, 50%, are also included at every level of improvement below 50%. Patients who did not complete the study through Week 12 or who showed no improvement at Week 12 were assigned 0% improvement. The proportion of patients experiencing ≥30% reduction in pain intensity from baseline for each week through Week 12 is shown in Figure 7.



*The same patients may not have responded at each timepoint.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

QUTENZA (capsaicin) 8% topical system is a single-use topical system stored in a sealed pouch (NDC 72512-920-00). QUTENZA is 14 cm x 20 cm (280 cm²) and consists of an adhesive side containing the active substance and an outer surface backing layer. The adhesive side is covered with a removable, clear, unprinted, diagonally cut, release liner. The outer surface of the backing layer is imprinted with "capsaicin 8%".

Cleansing Gel is provided in a 50 g tube.

QUTENZA is available in the following presentations:

 Carton of 1 topical system and 50 g tube of Cleansing Gel (NDC 72512-928-01).

 Carton of 2 topical systems and 50 g tube of Cleansing Gel (NDC 72512-929-01).

16.2 Storage

Store carton between 20°C to 25°C (68°F to 77°F). Excursions between 15°C and 30°C (59°F and 86°F) are allowed.

Keep QUTENZA in the sealed pouch until immediately before use.

16.3 Handling and Disposal

Unintended exposure to capsaicin can cause severe irritation of eyes, skin, respiratory tract, and mucous membranes. Wear nitrile (not latex) gloves while administering QUTENZA. Use of a face mask and protective glasses is advisable. Immediately after use, dispose of used and unused QUTENZA, QUTENZA clippings, associated packaging, Cleansing Gel, and all other potentially contaminated treatment supplies in accordance with local biomedical waste procedures [*see Dosage and Administration (2), Warnings and Precautions (5.1)*].

17 PATIENT COUNSELING INFORMATION

- Inform patients that accidental exposure to capsaicin from touching QUTENZA or items exposed to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.
- Instruct patients not to touch their eyes and other unintended target area and that if irritation of eyes or airways occurs, or if any of the side effects become severe, to notify their doctor immediately.
- Inform patients that the treated area may be sensitive to heat (e.g., hot showers/bath, direct sunlight, vigorous exercise) for a few days following treatment.
- Inform patients that they may be given medication to treat acute pain during and after the QUTENZA application procedure.
- Inform patients that as a result of treatment-related increases in pain, small transient increases in blood pressure may occur during and shortly after QUTENZA treatment and that blood pressure will be monitored during the treatment procedure. Instruct patients to inform the physician if they have experienced any recent cardiovascular events.

Manufactured for Averitas Pharma, Inc., Morristown, NJ 07960, USA
by Lohmann Therapie-Systeme AG (LTS), Andernach, Germany



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