**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

Qutenza 179 mg cutaneous patch

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 280 $cm^2$ cutaneous patch contains a total of 179 mg of capsaicin or 640 micrograms of capsaicin per $cm^2$ of patch.

Excipient with known effect
Each 50 g tube of cleansing gel for Qutenza contains 0.2 mg/g butylhydroxyanisole (E320).

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Cutaneous patch.

Each patch is 14 cm x 20 cm (280 $cm^2$) 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. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Qutenza is indicated for the treatment of peripheral neuropathic pain in adults either alone or in combination with other medicinal products for pain.

### 4.2 Posology and method of administration

The Qutenza cutaneous patch should be applied by a physician or by a health care professional under the supervision of a physician.

Posology

Qutenza should be applied to the most painful skin areas (using up to a maximum of 4 patches). The painful area should be determined by the physician and marked on the skin. Qutenza must be applied to intact, non-irritated, dry skin, and allowed to remain in place for 30 minutes for the feet (e.g. HIV-associated neuropathy, painful diabetic peripheral neuropathy) and 60 minutes for other locations (e.g. postherpetic neuralgia). Qutenza treatments may be repeated every 90 days, as warranted by the persistence or return of pain.

The treatment area may be pre-treated with a topical anaesthetic or the patient may be administered an oral analgesic prior to application of Qutenza to reduce potential application related discomfort. The topical anaesthetic should be applied to cover the entire Qutenza treatment area and surrounding 1 to 2 cm. The topical anaesthetic or oral analgesic should be used in accordance with the medicinal product's instructions for use. In clinical trials, patients were pre-treated with topical lidocaine (4%), lidocaine (2.5%)/prilocaine (2.5%) or with 50 mg of tramadol. The anaesthetic cream should be removed prior to applying Qutenza and the skin washed and dried thoroughly.

*Renal and/or hepatic impairment*

No dose adjustment is required for patients with renal or hepatic impairment.

*Paediatric population*

The safety and efficacy of Qutenza in children from birth to 18 years has not been established. No data are available.

Method of administration

Cutaneous use only.

*Precautions to be taken before handling or administering the medicinal product*

Nitrile gloves should be worn at all times while handling Qutenza and cleaning treatment areas. Latex gloves should NOT be worn as they do not provide adequate protection. Use of a mask and protective glasses is recommended , particularly during application and removal of the patch.

These precautions should be taken to avoid unintentional contact with the patches or other materials that have come in contact with the treated areas. This may result in transient erythema and burning sensation (with mucous membranes being particularly susceptible), eye pain, eye and throat irritation and cough.

Patches should not be held near eyes or mucous membranes.

If necessary, hairs in the affected area should be clipped to promote patch adherence (do not shave). The treatment area(s) should be gently washed with soap and water. Following hair removal and washing, the skin should be thoroughly dried.

*Instructions for use*

Qutenza is a single use patch and can be cut to match the size and shape of the treatment area. Qutenza should be cut prior to removal of the release liner. The release liner should NOT be removed until just prior to application. There is a diagonal cut in the release liner to aid in its removal. A section of the release liner should be peeled and folded and the adhesive side of the printed patch placed on the treatment area. The patch should be held in place. The release liner should slowly and carefully be peeled from underneath with one hand while the patch should simultaneously be smoothed onto the skin with the other to ensure that there is complete contact between the patch and the skin, with no air bubbles and no moisture.

When treating feet, Qutenza patches can be wrapped around the dorsal, lateral and plantar surfaces of each foot to completely cover the treatment area.

To ensure Qutenza maintains contact to the treatment area, stretchable socks or rolled gauze may be used.

The Qutenza patches should be removed gently and slowly by rolling them inward to minimize the risk of aerosolisation of capsaicin. After removal of Qutenza, cleansing gel should be applied liberally to the treatment area and left on for at least one minute. Cleansing gel should be wiped off with dry gauze to remove any remaining capsaicin from the skin. After the cleansing gel has been wiped off, the area should be gently washed with soap and water.

Acute pain during and following the procedure should be treated with local cooling (such as a cool compress) and oral analgesics (e.g. short-acting opioids).

For instructions on handling and disposal of the treatment materials see section 6.6.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

## 4.4 Special warnings and precautions for use

Health care professionals should wear nitrile gloves when handling patches and when cleansing treatment areas (see section 4.2). It is advisable to administer Qutenza in a well ventilated treatment area.

Dermal assessment

Qutenza should be used only on dry, intact (unbroken) skin and not on the face, above the hairline of the scalp, and/or in proximity to mucous membranes. In patients with painful diabetic peripheral neuropathy, a careful visual examination of the feet should be undertaken prior to each application of Qutenza and at subsequent clinic visits to detect skin lesions related to underlying neuropathy and vascular insufficiency.

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 sharp stimuli), however, a single case of persistent hypoesthesia has been reported in clinical studies in painful diabetic neuropathy. For this case a relationship with Qutenza could not be excluded. Caution should be exercised in patients with reduced sensation in the feet and in those at increased risk for such changes in sensory function. All patients with pre-existing sensory deficits should be clinically assessed for signs of sensory loss to prior to each application of Qutenza. If sensory loss is detected or worsens, Qutenza treatment should be reconsidered.

Monitoring and management of application site reactions

Application site reactions, such as transient local applications site burning, pain, erythema and pruritus are common or very common. In addition, there have been reported cases of burns, including second degree burns, in patients treated with capsaicin patches. See section 4.8. In patients reporting severe pain, the patch should be removed and the skin examined for chemical burn.

Unintended exposure

If Qutenza comes in contact with skin not intended to be treated, cleansing gel should be applied for one minute and wiped off with dry gauze to remove any remaining capsaicin from the skin surface. After the cleansing gel has been wiped off, the area should be gently washed with soap and water. If burning of eyes, skin, or airway occurs, the affected individual should be removed from the vicinity of Qutenza. Eyes or mucous membranes should be flushed or rinsed with water. Appropriate medical care should be provided if shortness of breath develops.

Increase in blood pressure

As a result of treatment-related increases in pain, transient increases in blood pressure (on average < 8.0 mm Hg) may occur during and shortly after the Qutenza treatment. Blood pressure should be monitored during the treatment procedure. For patients with unstable or poorly controlled hypertension or a history of cardiovascular disease, the risk of adverse cardiovascular events due to the potential stress of the procedure should be considered prior to initiating Qutenza treatment. Particular attention should be given to diabetic patients with comorbidities of coronary artery disease, hypertension and cardiovascular autonomic neuropathy.

Treatment-related discomfort

Patients experiencing pain during and after patch application should be provided with supportive treatment such as local cooling or oral analgesics (i.e. short acting opioids).

Patients using high doses of opioids may not respond to oral opioid analgesics when used for acute pain during and following the treatment procedure. A thorough history should be reviewed prior to initiating treatment and an alternative pain reduction strategy put in place prior to Qutenza treatment in patients with suspected high opioid tolerance.

Cleansing gel

The cleansing gel for Qutenza contains butylhydroxyanisole, which may cause local skin reactions (e.g. contact dermatitis) or irritation of the eyes and mucous membranes.

## 4.5 Interaction with other medicinal products and other forms of interaction

No formal interaction studies with other medicinal products have been performed as only transient low levels of systemic absorption have been shown to occur with Qutenza.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of capsaicin in pregnant women.
Based on human pharmacokinetics, which show transient, low systemic exposure to capsaicin, the likelihood that Qutenza increases the risk of developmental abnormalities when given to pregnant women is very low. However, caution should be exercised when prescribing to pregnant women.

Breast-feeding

It is unknown whether capsaicin/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of capsaicin/metabolites in milk (for details see 5.3).

A risk to the newborns/infants cannot be excluded.

Breast-feeding should be discontinued during treatment with Qutenza.

Fertility

There is no data in humans available on fertility. A reproductive toxicology study in rats showed a reduction in the number and percent of motile sperm and the number of pregnancies (see section 5.3).

## 4.7 Effects on ability to drive and use machines

Qutenza has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

Summary of the safety profile

Of the 1826 patients treated with Qutenza in randomized controlled trials, 1089 (59.6%) reported adverse reactions considered related to the medicinal product by the investigator. The most commonly reported adverse reactions were transient local application site burning, pain, erythema and pruritus.

Adverse reactions were transient, self limiting and usually mild to moderate in intensity. In all controlled trials, the discontinuation rate due to adverse reactions was 2.0% for patients receiving Qutenza and 0.9% for patients receiving control.

Tabulated list of adverse reactions

In Table 1 below all adverse reactions, which occurred at an incidence greater than control and in more than one patient in controlled clinical trials in patients with postherpetic neuralgia (PHN), painful Human Imunodeficiency Virus – Associated Neuropathy (HIV-AN) and painful diabetic peripheral neuropathy, are listed by system organ class and frequency: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100) and not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

**Table 1: Tabulated list of adverse reactions**

| System organ class and frequency | Adverse reaction |
|---|---|
| **Infections and infestations** | |
| Uncommon | Herpes zoster |
| **Nervous system disorders** | |
| Common | Burning sensation |
| Uncommon | Dysgeusia, hypoaesthesia |
| **Eye disorders** | |
| Uncommon | Eye irritation |
| **Cardiac disorders** | |
| Uncommon | First degree atrio-ventricular (AV) block, tachycardia, palpitations |
| **Vascular disorders** | |
| Uncommon | Hypertension |
| **Respiratory, thoracic and mediastinal disorders** | |
| Uncommon | Cough, throat irritation |
| **Gastrointestinal disorders** | |
| Uncommon | Nausea |
| **Skin and subcutaneous tissue disorders** | |
| Uncommon | Pruritus |
| **Musculoskeletal and connective tissue disorders** | |
| Common | Pain in extremity |
| Uncommon | Muscle spasms |
| **General disorders and administration site conditions** | |
| Very common | Application site pain, application site erythema |
| Common | Application site pruritus, application site papules, application site vesicles, application site oedema, application site swelling, application site dryness |
| Uncommon | Application site urticaria, application site paraesthesia, application site dermatitis, application site hyperaesthesia, application site inflammation, application site reaction, application site irritation, application site bruising, peripheral oedema |
| **Investigations** | |
| Uncommon | Increased blood pressure |
| **Injury, poisoning and procedural complications** | |
| Not known | Burns second degree, accidental exposure (including eye pain, eye and throat irritation and cough) |

Description of selected adverse reactions

Temporary, minor changes in heat detection (1°C to 2°C) and sharp sensations were detected at the Qutenza application site in clinical trials with healthy volunteers.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

### 4.9 Overdose

No case of overdose has been reported. Qutenza is required to be administered by a physician or under the supervision of a physician. Therefore, overdosing is unlikely to occur. Overdose may be associated with severe application site reactions, e.g. application site pain, application site erythema, application site pruritus. In case of suspected overdose, the patches should be removed gently, cleansing gel should be applied for one minute and then wiped off with dry gauze and the area should be gently washed with soap and water. Supportive measures should be taken as clinically needed. There is no antidote to capsaicin.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics, other local anaesthetics, ATC code: N01BX04

Mechanism of action

Capsaicin, or 6-nonenamide, N-[(4-hydroxy-3-methoxyphenyl) methyl]-8-methyl, (6E), is a highly selective agonist for the transient receptor potential vanilloid 1 receptor (TRPV1). The initial effect of capsaicin is the activation of TRPV1-expressing cutaneous nociceptors, which results in pungency and erythema due to the release of vasoactive neuropeptides.

Pharmacodynamic effects

Following capsaicin exposure, cutaneous nociceptors become less sensitive to a variety of stimuli. These later-stage effects of capsaicin are frequently referred to as “desensitization” and are thought to underlie the pain relief. Sensations from non TRPV1-expressing cutaneous nerves are expected to remain unaltered, including the ability to detect mechanical and vibratory stimuli. Capsaicin-induced alterations in cutaneous nociceptors are reversible and it has been reported and observed that normal function (the detection of noxious sensations) returns within weeks in healthy volunteers.

Clinical efficacy and safety

Efficacy of a single 30-minute application of Qutenza to the feet has been shown in controlled clinical trials conducted in patients with painful Human Imunodeficiency Virus – Associated Neuropathy (HIV-AN) and painful diabetic peripheral neuropathy. Efficacy of a single 60-minute application of Qutenza to locations other than the feet has been shown in controlled clinical trials conducted in patients with postherpetic neuralgia (PHN). Pain reduction was observed at week 1 in PHN, week 2 in HIV-AN and week 3 in painful diabetic peripheral neuropathy. For all three aetiologies efficacy was maintained throughout the 12-week study period. For painful diabetic peripheral neuropathy consistent and reproducible efficacy has been demonstrated with repeated treatments during a 52-week period.

The safety profile of Qutenza in diabetic patients was consistent with that seen in the non-diabetic population.

Qutenza has been shown to be effective when used alone or when used in combination with systemic medicinal products for neuropathic pain.

### 5.2 Pharmacokinetic properties

The capsaicin contained in Qutenza is intended for delivery into the skin. *In vitro* data (active substance dissolution and skin permeation assays) demonstrate that the rate of release of capsaicin

from Qutenza is linear during the application time. Based on *in vitro* studies, approximately 1% of capsaicin is estimated to be absorbed into the epidermal and dermal layers of skin during one-hour applications. As the amount of capsaicin released from the patch per hour is proportional to the surface area of application, this amounts to an estimated total maximum possible dose for a 1000 $cm^2$ area of application of approximately 7 mg. Assuming 1000 $cm^2$ of patch area delivers approximately 1% of capsaicin from the patch to a 60 kg person, the maximum potential exposure to capsaicin is approximately 0.12 mg/kg, once every 3 months.

According to the EC Scientific Committee on Food, the average European oral intake of capsaicin is 1.5 mg/day (0.025 mg/kg/day for a 60 kg person) and the highest dietary exposure is 25 to 200 mg/day (up to 3.3 mg/kg/day for a 60 kg person).

Pharmacokinetic data in humans showed transient, low (< 5 ng/ml) systemic exposure to capsaicin in about one third of PHN patients, in 3% of patients with painful diabetic peripheral neuropathyand in no HIV-AN patients following 60-minute applications of Qutenza. No data are available following 30-minute treatments. In general, the proportions of PHN patients with systemic exposure to capsaicin increased with larger treatment areas and with longer treatment durations. The highest concentration of capsaicin detected in patients treated for 60 minutes was 4.6 ng/mL, which occurred immediately after Qutenza removal. Most quantifiable levels were observed at the time of Qutenza removal, with a clear trend towards disappearance by 3 to 6 hours after Qutenza removal. No detectable levels of metabolites were observed in any subject.

A population pharmacokinetic analysis of patients treated for 60 and 90 minutes indicated that capsaicin levels in plasma peaked around 20 minutes after Qutenza removal and declined very rapidly, with a mean elimination half-life of about 130 minutes.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, single-dose toxicity, and repeated-dose toxicity.

Genotoxicity studies performed with capsaicin show a weak mutagenic response in the mouse lymphoma assay and negative responses in the Ames, mouse micronucleus and chromosomal aberrationin human peripheral blood lymphocytes assays.

A carcinogenicity study performed in mice indicates that capsaicin is not carcinogenic.

A reproductive toxicology study conducted in rats showed a statistically significant reduction in the number and percent of motile sperms in rats treated 3 hours/day beginning 28 days before cohabitation, through cohabitation and continuing through the day before sacrifice. Although neither statistically significant nor dose dependent, the Fertility Index and the number of pregnancies per number of rats in cohabitation were reduced in all capsaicin-treated groups.

A teratology study conducted in rabbits did not show any potential for embryofetal toxicity. Delays in skeletal ossification (reductions in ossified metatarsals) were observed in a rat teratology study at dose levels higher than human therapeutic levels; the significance of this finding for humans is unknown. Peri- and post-natal toxicology studies, conducted in rats do not show potential for reproductive toxicity. Lactating rats exposed to Qutenza daily for 3 hours showed measurable levels of capsaicin in the mothers' milk.

A mild sensitization was seen in a cutaneous sensitization study with guinea pigs.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Patch

*Matrix:*
silicone adhesives
diethylene glycol monoethyl ether
silicone oil
ethylcellulose N50 (E462)

*Backing layer:*
polyester backing film
printing ink containing Pigment White 6

*Removable protective layer:*
polyester release liner

Cleansing gel

macrogol 300
carbomer
purified water
sodium hydroxide (E524)
disodium edetate
butylhydroxyanisole (E320)

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

4 years.

After opening sachet: apply Qutenza within 2 hours.

## 6.4 Special precautions for storage

Qutenza cutaneous patch: Store flat in the original sachet and carton. Store below 25°C.

Cleansing gel: Store below 25°C.

## 6.5 Nature and contents of container

The Qutenza patch is stored in a paper coated aluminium foil sachet with acrylnitrile-acrylic acid copolymer heat seal layer.

Qutenza is available in a kit containing one or two individually sealed Qutenza patches and a 50 g tube of cleansing gel.

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

Health care professionals should wear nitrile gloves when handling patches and cleansing treatment areas. The use of a mask and protective glasses is recommended, see section 4.2.

Used and unused patches and all other materials that have been in contact with the treated area should be disposed of immediately after use by sealing them in a polyethylene medical waste bag and placing in an appropriate medical waste container.

## 7. MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

## 8. MARKETING AUTHORISATION NUMBERS

EU/1/09/524/001-002

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 May 2009
Date of latest renewal: 15 May 2014

## 10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) http://www.ema.europa.eu

# ANNEX II

**A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

## A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

GP Grenzach Produktions GmbH
Emil-Barell-Strasse 7
D-79639 Grenzach-Wyhlen
Germany

## B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

## C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- Periodic Safety update Reports

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

## D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2. of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

The MAH shall agree the details of an educational programme for health care practitioners with the National Competent Authorities and implement such programme nationally before launch.
This educational programme will include:

- recommendations regarding the general handling and disposal measures for Qutenza
  - administration of capsaicin should only be done under medical supervision
  - because of the risk of accidental exposure, the use of nitrile gloves, a mask and protective glasses are recommended
  - administration of Qutenza in a well ventilated area to reduce the risk of occupational exposure
- instructions regarding the administration of Qutenza
- warnings and precautions, including the need:

- to undertake a visual examination of the feet prior to each application of Qutenza and at subsequent clinic visits to detect skin lesions related to underlying neuropathy and vascular insufficiency in patients with painful diabetic peripheral neuropathy
- to be aware of the risk of reductions in sensory function which are generally minor and temporary (including to thermal and sharp stimuli) following administration of Qutenza
- to use caution when administering Qutenza in patients with reduced sensation in the feet and in those at increased risk for such changes in sensory function
- to clinically assess patients for increased sensory loss prior to each application of Qutenza in all patients with pre-existing sensory deficits. If sensory loss is detected or worsens, Qutenza treatment should be reconsidered
- to monitor blood pressure during the treatment procedure
- to provide supportive treatment if patients experience increased pain during Qutenza administration
- in patients with unstable or poorly controlled hypertension or cardiovascular disease: to evaluate, prior to initiating Qutenza treatment, the risk of adverse cardiovascular eventsdue to the potential stress of the procedure. Particular attention should be given to diabetic patients with comorbidities of coronary artery disease, hypertension and cardiovascular autonomic neuropathy
- in patients using high doses of opioids and with suspected high opioid tolerance: to put in place an alternative pain reduction strategy prior to initiating Qutenza treatment, as these patients may not respond to oral opioid analgesics when used for acute pain during and following the treatment procedure
- to warn patients about the risk of causal local reactions (e.g. contact dermatitis) and of irritation of the eyes and mucous membranes associated with the cleansing gel of Qutenza.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON OF 1 OR 2 PATCHES**

## 1. NAME OF THE MEDICINAL PRODUCT

Qutenza 179 mg cutaneous patch
capsaicin

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 280 $cm^2$ cutaneous patch contains a total of 179 mg of capsaicin or 640 micrograms of capsaicin per $cm^2$ of patch.

## 3. LIST OF EXCIPIENTS

Patch

*Matrix:*
silicone adhesives
diethylene glycol monoethyl ether
silicone oil
ethylcellulose N50 (E462)

*Backing layer:*
polyester backing film
printing ink containing Pigment White 6

*Removable protective layer:*
polyester release liner

Cleansing gel

macrogol 300
carbomer
purified water
sodium hydroxide (E524)
disodium edetate
butylhydroxyanisole (E320)

See package leaflet for further information.

## 4. PHARMACEUTICAL FORM AND CONTENTS

1 sachet containing 1 cutaneous patch and 1 tube of cleansing gel (50 g).

2 sachets, each containing 1 cutaneous patch and 1 tube of cleansing gel (50 g).

## 5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.

Cutaneous use.

**Instructions for use**

**1.** Nitrile gloves should be worn when handling patches and cleansing treatment areas.

**2.** Outline treatment area. Clip excessive hair. Clean treatment area.

*If topical anaesthetic is used prior to patch application proceed with 3, otherwise move to 5.*

**3**. Apply topical anaesthetic to treatment area. Wait up to 60 minutes, or according to product's instructions for use.

**4**. Remove anaesthetic. Gently clean with soap and water and dry thoroughly.

**5**. Cut patch to match treatment area size. Place non-glossy side up while preparing. Do not remove release liner from the patch until ready for application.

**6**. Remove patch release liner and apply to the skin. Keep in place for 30 or 60 minutes depending on the location of treatment. Gauze wraps or socks may be used to promote contact between patch and skin.

**7**. Use of a mask and protective glasses is recommended when applying and removing the patch, and applying cleansing gel afterwards. Wait for one minute and then wipe skin clean with dry gauze. Gently clean treated area with soap and water.

For more detailed instructions, please refer to the Summary of Product Characteristics or the package leaflet.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING, IF NECESSARY

## 8. EXPIRY DATE

EXP
Use the patch within 2 hours of opening the sachet.

## 9. SPECIAL STORAGE CONDITIONS

Store flat in the original sachet and carton. Store below 25°C.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of used and unused patches, gauze wipes and all other materials placed in contact with the treated area by sealing in a polyethylene bag and placing in an appropriate medical waste container.

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/524/001 1 patch
EU/1/09/524/002 2 patches

## 13. BATCH NUMBER

Lot

## 14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**

**SACHET OF ONE PATCH**

## 1. NAME OF THE MEDICINAL PRODUCT

Qutenza 179 mg cutaneous patch
capsaicin

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 280 $cm^2$ cutaneous patch contains a total of 179 mg of capsaicin or 640 micrograms of capsaicin per $cm^2$ of patch .

## 3. LIST OF EXCIPIENTS

Patch

*Matrix:*
silicone adhesives
diethylene glycol monoethyl ether
silicone oil
ethylcellulose N50 (E462)

*Backing layer:*
polyester backing film
printing ink containing Pigment White 6

*Removable protective layer:*
polyester release liner

See the package leaflet for further information

## 4. PHARMACEUTICAL FORM AND CONTENTS

One cutaneous patch

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Cutaneous use.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP
Use the patch within 2 hours of opening the sachet.

## 9. SPECIAL STORAGE CONDITIONS

Store flat in the original sachet and carton. Store below 25°C.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of used and unused patches, gauze wipes and all other materials placed in contact with the treated area by sealing in a polyethylene bag and placing in an appropriate medical waste container.

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

## 12. MARKETING AUTHORISATION NUMBERS

EU/1/09/524/001 1 patch
EU/1/09/524/002 2 patches

## 13. BATCH NUMBER

Lot

## 14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**

**TUBE OF CLEANSING GEL - LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT

Cleansing Gel for use with Qutenza

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

## 3. LIST OF EXCIPIENTS

Contains macrogol 300, carbomer, purified water, sodium hydroxide (E524), disodium edetate and butylhydroxyanisole (E320); See package leaflet for further information.

## 4. PHARMACEUTICAL FORM AND CONTENTS

50 g

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use. See the package leaflet for further information.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP

## 9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of cleansing gel tube by sealing in a polyethylene bag along with other used Qutenza components and placing in an appropriate medical waste container.

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Grünenthal GmbH
Zieglerstraße 6
52078 Aachen
Germany

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/524/001 1 patch
EU/1/09/524/002 2 patches

## 13. BATCH NUMBER

Lot

## 14. GENERAL CLASSIFICATION FOR SUPPLY

## 15. INSTRUCTIONS ON USE

## 16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

**B. PACKAGE LEAFLET**

**Package leaflet: Information for the user**

**Qutenza 179 mg cutaneous patch**
capsaicin

**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.
- 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. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**


## 1. What Qutenza is and what it is used for

Qutenza contains capsaicin and belongs to a group of medicines called anaesthetics.
Qutenza is indicated for the treatment of peripheral neuropathic pain in adults either alone or in combination with other medicinal products for pain.

Qutenza is used to relieve pain in people who have nerve pain due to damaged nerves in the skin. Damaged nerves in your skin may occur as a result of a variety of diseases such as shingles, HIV infection, diabetes, certain medicines and other conditions. You may experience pain relief between 1 and 3 weeks after treatment.

## 2. What you need to know before Qutenza is used

**Do not use Qutenza**

- if you are allergic to capsaicin, chilli peppers or any other ingredients of this medicine (listed in section 6).

**Warnings and precautions**

Talk to your doctor before using Qutenza

Do not use Qutenza on any part of your head or face.

Do not use Qutenza on broken skin or open wounds.

Do not touch Qutenza or other materials that have come in contact with the treated areas as it may cause burning and stinging. Do not touch your eyes, mouth or other sensitive areas as it may cause irritation and pain. Sniffing or inhaling close to the Qutenza patches may cause coughing, throat irritation or sneezing.

It is usual for the skin to sting or become red and burn during and after Qutenza treatment for a short while. Because of the pain, your blood pressure may go up and therefore, your doctor will measure your blood pressure several times during your treatment. If you experience a lot of pain, your doctor will apply local cooling or give you medicine for pain. If you experience very severe pain, ask your doctor to remove the patch.

Generally small, short-term changes in the ability to feel when something is hot or sharp have been seen after use of capsaicin.

If you have unstable or poorly controlled high blood pressure or had heart problems, your doctor will consider the risk of side effects to your heart or blood pressure due to the potential stress of the procedure before treating you with Qutenza.

If you are using high doses of opioids, you may not respond to oral opioid analgesics when used for acute pain during and following the treatment procedure. In this case, your doctor will use other measures to reduce your pain following Qutenza treatment.

**Children and adolescents**

Qutenza is not recommended for treatment in patients under 18 years of age.

**Other medicines and Qutenza**

Qutenza acts locally on your skin and is not expected to influence other medicines. Tell your doctor if you are taking, have recently taken or might take any other medicines.

**Qutenza with food and drink**

Food or drink are not expected to influence Qutenza as it acts locally on your skin.

**Pregnancy and breast-feeding**

Qutenza should be used with caution if you are pregnant and/or breastfeeding. If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby ask your doctor for advice before taking this medicine.

**Driving and using machines**

There are no studies of the effects of Qutenza on the ability to drive and use machines. When using Qutenza, only very small amounts of the active substance may be present in the blood stream for a very short time. Therefore, Qutenza is unlikely to have any direct effects on your ability to concentrate or your ability to drive or use machinery.

**Cleansing gel for Qutenza contains butylhydroxyanisole**

The cleansing gel for Qutenza contains butylhydroxyanisole which may cause local skin reactions (e.g. contact dermatitis), or irritation of the eyes and mucous membranes.

## 3. How to use Qutenza

No more than 4 patches should be used at the same time.

Qutenza should only be applied by your doctor or by a nurse under the supervision of your doctor.

Qutenza is for use on your skin.

Your doctor will mark the most painful areas on your skin with a pen or marker.

Before placing the Qutenza patches on the skin, the treatment area(s) will be washed with soap and water and dried. Hair in treatment areas will be clipped.

Before placing the Qutenza patches on the skin, your doctor or nurse may apply a numbing gel or cream or give you an oral pain medicine to reduce potential stinging. The gel or cream should be removed prior to applying Qutenza and the skin washed and dried thoroughly.

Your doctor or nurse may wear gloves, and sometimes a mask and protective glasses, while handling the Qutenza patches. Do not sniff or inhale close to the Qutenza patches as this may cause coughing or sneezing.

Qutenza may be cut into smaller pieces to fit the treatment area. Your doctor or nurse will remove the patches after 30 minutes if you're being treated for nerve pain on your feet or 60 minutes if you're being treated for nerve pain on other parts of your body. Do not touch the patch with your hands as it may cause burning and stinging.

It may take between 1 to 3 weeks before you experience pain relief with Qutenza. If after that time you still have a lot of pain, please talk to your doctor.

Qutenza therapy may be repeated at 90-day intervals, if necessary.

You may be given pain medicines to take for the pain you experience with Qutenza therapy.

It is common for the skin to sting or become red and burn during Qutenza treatment.

Disposable socks may be worn on top of the Qutenza patches if your feet are being treated.

Sometimes your doctor or nurse may put a bandage on top of the Qutenza patch to keep the patch firmly on your skin.

At the end of the Qutenza treatment your doctor or nurse will clean the treated skin with cleansing gel from a tube supplied with the kit. Cleansing gel will be left on your skin for one minute and then wiped off to remove any remaining medicine that may be left on your skin after treatment. After the cleansing gel has been wiped off, the area will be gently washed with soap and water.

**Do not touch your eyes, mouth or other sensitive areas.** If you accidentally touch the Qutenza patch or treated skin before cleansing gel is applied it may burn and/or sting. Call your doctor immediately.

Do not attempt to remove the patch yourself. Your doctor or nurse will remove it for you.

Do not take Qutenza patches away from the clinic.

Do not use Qutenza patches at home.

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

**If Qutenza is used longer than it should**

Overdosing is unlikely to occur. However, if Qutenza is applied longer than it should you might experience severe application site reactions like pain, redness and itching.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**Contact your doctor straightaway** if the following effects happen:

- If you feel that your heart is beating too fast, too slow or is beating abnormally.
    - Uncommon: may affect up to 1 in 100 people

- Deep redness on the area where the patch is applied, blistering/oozing of the skin, skin which becomes very painful to touch, swollen, wet or shiny. In a small number of cases, these may be signs of a second degree burn and need urgent attention.
    - Frequency not known: frequency cannot be estimated from the available data

**Tell your doctor** if the following side effects occur or get worse:

- Redness or pain on the area where the patch is applied which lasts for more than a day.
    - Very common side effects: may affect more than 1 in 10 people

- Itching, bumps, blisters, swelling, dryness on the area where the patch is applied,burning sensation, pain in limbs.
    - Common side effects: may affect up to 1 in 10 people

- Wheals, prickling sensation, inflammation, increased or decreased skin sensation, skin reaction, irritation, bruising on the area where the patch is applied.
    - Uncommon side effects: may affect up to 1 in 100 people

- Decreased taste, reduced sensations in limbs, , eye irritation, cough, throat irritation, nausea, itching, muscle spasms, shingles, swelling of limbs.
    - Uncommon side effects: may affect up to 1 in 100 people

- Accidental exposure (including eye pain, eye and throat irritation and cough).
    - Frequency not known: frequency cannot be estimated from the available data

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Qutenza

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 after EXP. The expiry date refers to the last day of that month.

Qutenza cutaneous patch: Store flat in original sachet and carton. Store below 25°C.

Cleansing gel: Store below 25°C.

After opening the sachet, Qutenza should be applied within 2 hours.

Disposal of used and unused Qutenza patches.

These items may sting your fingers if you touch them. Your doctor or nurse will put them in a polyethylene bag before safely discarding them. Qutenza patches and treatment-related materials should be disposed of properly.

## 6. Contents of the pack and other information

### What Qutenza contains

The active substance is capsaicin. Each 280 $cm^2$ patch contains a total of 179 mg of capsaicin or 640 micrograms of capsaicin per $cm^2$ of patch (8% w/w).

The other ingredients of the Qutenza cutaneous patch are:

*Matrix:*
silicone adhesives
diethylene glycol monoethyl ether
silicone oil
ethylcellulose N50 (E462)

*Backing layer:*
polyester backing film
printing ink containing Pigment White 6

*Removable protective layer:*
polyester release liner

The Qutenza patch is supplied with a tube of cleansing gel, which contains no active substance.

Cleansing gel contains:

macrogol 300
carbomer
purified water
sodium hydroxide (E524)
disodium edetate
butylhydroxyanisole (E320)

### What Qutenza looks like and contents of the pack

Qutenza is a cutaneous patch for use on your skin.

Each patch is 14 cm x 20 cm (280 $cm^2$) 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%’.

Each Qutenza carton contains 1 or 2 sachets and 1 tube of cleansing gel (50 g). Not all pack sizes may be marketed.

### Marketing Authorisation Holder

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**This leaflet was last revised in**

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

The following information is intended for medical or healthcare professionals only:

A complete Summary of Product Characteristics (SPC) is provided with this leaflet.