Each 280 cm^2 cutaneous patch contains a total of 179 mg capsaicin or 640 µg of capsaicin per cm^2 of patch (8 % *w/w*).

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

QUTENZA (8 % *w/w*) Cutaneous Patch and Cleansing gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 280 cm^2 cutaneous patch contains a total of 179 mg capsaicin or 640 µg of capsaicin per cm^2 of patch (8 % *w/w*).

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

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 associated with:

- Postherpetic neuralgia in adults
- Human Immunodeficiency Virus associated neuropathy in adults

4.2 Posology and method of administration

The **QUTENZA** cutaneous patch should be applied by a medical practitioner or by a healthcare professional under

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the supervision of a medical practitioner.

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 medical practitioner 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) 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 should be pre-treated with a topical anaesthetic prior to application of **QUTENZA** to reduce 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 should be used in accordance with the product's instructions for use. In clinical trials, patients were pre-treated with topical lidocaine (lignocaine) 4 % or lidocaine (lignocaine) 2,5 % /prilocaine (2,5 %) for 60 minutes.

Renal and/or hepatic impairment

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

Paediatric population

QUTENZA is not recommended for use in children and adolescents due to lack of data on safety and efficacy.

Method of administration

Precautions to 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.

Patches should not be held near eyes or mucous membranes.

Direct contact with **QUTENZA**, used gauze or used cleansing gel should be avoided.

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

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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 **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 minimise 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 capsaicin or to any of the inactive ingredients of **QUTENZA** (see section 6.1).

4.4 Special warnings and precautions for use

Healthcare professionals should wear nitrile gloves when handling patches and cleansing treatment areas.

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.

Care must be taken to avoid unintentional contact with the patches or other materials that have come in contact with the treated areas. Exposure of the skin to capsaicin results in transient erythema and burning sensation, with mucous membranes being particularly susceptible. Inhalation of airborne capsaicin can result in coughing or

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sneezing. Used patches should be disposed of immediately after use in an appropriate medical waste container (see section 6.6).

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.

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.

Patients experiencing increased pain should be provided with supportive treatment such as local cooling or oral analgesics (i.e., short acting opioids). For patients with unstable or poorly controlled hypertension or a recent history of cardiovascular events, the risk of adverse cardiovascular reactions due to the potential stress of the procedure should be considered prior to initiating **QUTENZA** treatment.

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 in place prior to **QUTENZA** treatment in patients with suspected high opioid tolerance.

Changes in sensory function (e.g., heat detection) have been reported following administration of capsaicin. Patients with increased risk for adverse reactions due to minor changes in sensory function should be cautious when using **QUTENZA**.

Care must be taken to avoid unintentional contact with the patches or other materials that have come in contact with the treated areas. Exposure of the skin to capsaicin results in transient erythema and burning sensation, with mucous membranes being particularly susceptible. Inhalation of airborne capsaicin can result in coughing or sneezing. Used patches should be disposed of immediately after use in an appropriate medical waste container (see section 6.6)**.**

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.

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4.5 Interaction with other medicines and other forms of interaction

No formal interaction studies with other medicines have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

Lactation

QUTENZA must be kept away from contact with babies. Mothers must not breastfeed their babies on the day of application.

Fertility

There is no data in humans available on fertility.

4.7 Effects on ability to drive and use machines

When **QUTENZA** has been applied to hands or feet, changes in sensation may impair the ability to drive or to use machines.

4.8 Undesirable effects

a. Summary of safety profile

Of the 1,327 patients treated with **QUTENZA** in randomised controlled trials, 883 (67 %) reported adverse reactions considered related to the medicinal product by the investigator. The most commonly reported adverse reactions were transient local applications site burning, pain, erythema and pruritus.

b. 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 PHN and painful HIV-AN, are listed by system organ class and frequency: very common (≥ 1/10), common (≥ 1/100 to < 1/10) and uncommon (≥ 1/1,000 to < 1/100).
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Treatment-emergent related adverse reaction incidence in controlled trials

System organ class	**Adverse reaction**

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and frequency	
Infections and infestations	
Uncommon	Herpes zoster
Nervous system disorders	
Uncommon	Dysgeusia, hypoesthaesia, burning sensation
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	
Uncommon	Pain in extremity, 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

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Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Treatment:

QUTENZA is required to be administered by a medical practitioner or under the supervision of a medical practitioner.

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.

Symptoms:

Overdose may be associated with severe application site reactions, e.g. application site pain, application site erythema, application site pruritus.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.4**.** Local anaesthetics

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 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.

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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 “desensitisation” 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 12 weeks in healthy volunteers.

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.

Pharmacokinetic data in humans showed transient, low (< 5 ng/ml) systemic exposure to capsaicin in about one third of Postherpetic Neuralgia (PHN) patients, in 3 % of patients with Painful Diabetic Neuropathy (PDN) and in no Human Immunodeficiency Virus Associated Neuropathy (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.

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Patch

Matrix:

Diethylene glycol monoethyl ether

Ethylcellulose N50 (E462)

Silicone adhesives

Silicone oil

Backing layer:

Polyester backing film

Printing ink containing pigment white 6

Removable protective layer:

Polyester release liner

Cleansing Gel

Butylhydroxyanisole (E320)

Carbomer

Disodium edentate

Macrogol 300

Purified water

Sodium hydroxide (E524)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Cutaneous patch: 48 months

Cleansing gel: 48 months

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6.4 Special precautions for storage

QUTENZA cutaneous patch**:** Store flat in the original sachet and carton. Store at or below 25 °C.

Cleansing gel: Store at or 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

Healthcare professionals should wear nitrile gloves when handling patches and cleansing treatment areas.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road, Erand Gardens

Midrand 1685

South Africa

8. REGISTRATION NUMBER

45/4/1099

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 September 2016

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10. DATE OF REVISION OF THE TEXT

11 February 2022