1. Name of the medicinal product
N-CAPCIN CREAM

2. Qualitative and quantitative composition
Capsaicin 0.025%w/w
Methyl salicylate 5.10%w/w
Menthol 5.44%w/w
For the full list of excipients, see section 6.1

3. Pharmaceutical form
Prolonged transdermal cream

4. Clinical particulars
4.1 Therapeutic indications
For the symptomatic relief of pain associated with joint and musculoskeletal.
4.2 Posology and method of administration
For topical administration to unbroken skin
Adults and children over 12:
Apply only a small amount of cream (pea size) to affected area once time daily. These applications should be evenly spaced throughout the waking hours and not more often than once a day. The cream should be gently rubbed in, there should be no residue left on the surface. N-CAPCIN CREAM may cause transient burning on application. The burning is observed more frequently when application schedules of more than once time daily are used. Hands should be washed immediately after application of N-CAPCIN CREAM unless hands and fingers are being treated. N-CAPCIN CREAM should not be applied near the eyes. Pain relief usually begins within the first four week of treatment and increases with continuing regular application for the next two to eight weeks.
Elderly
The adult does is appropriate
Children
Not suitable for use in children under 12 years old.
4.3 Contraindications
N-CAPCIN CREAM is contra-indicated on broken or irritated skin.
N-CAPCIN CREAM is contra-indicated in patients with known hypersensitivity to capsaicin, salicylates, menthol or any other excipients used in this product.
4.4 Special warnings and precautions for use
Skin irritation has been reported following application of N-CAPCIN CREAM. The hands should be washed immediately after application of the cream, unless the hands are the treated areas, in which case, they should be washed 30 minutes after application
Contact with eyes and mucous membranes should be avoided.
Patients should avoid taking a hot bath or shower just before or after applying N-CAPCIN CREAM, as it can enhance the burning sensation.
Patients and carers should avoid inhalation of vapours from the cream, as transient irritation of the mucous membranes of the eyes and respiratory tract (including exacerbation of asthma) has been reported.
Keep N-CAPCIN CREAM away from the eyes.

Medical advice should be sought if the condition worsens, or clears up then recurs.
Tight bandages should not be applied on top of N-CAPCIN CREAM.

4.5 Interaction with other medicinal products and other forms of interaction

Applying capsaicin formulation may induce coughing in patient taking angiotensin converting enzyme inhibitor

Capsaicin has synergistic effects with other drugs like lidocaine and amitriptyline when applied locally at the same time

There have been report that topical salicylates may potentiate the anticoagulant effects of warfarin. Menthol has also been reported to interact with warfarin (when taken orally), decreasing its effectiveness.

4.6 Fertility, pregnancy and lactation

Capsaicin can crosses the placenta and may pass into breast milk exerts a toxic effect on the peripheral nerves of fetuses. There is no,or inadequate evidence of safety in human pregnancy or lactation. As a precautionary measure, N-CAPCIN CREAM should only be used during pregnancy or lactation when their is no safer alternative.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

N-CAPCIN CREAM may cause skin irritation or transient burning on application. This burning is observed more frequently when application schedules of more than once time daily are utilised. The burning can be enhanced if too much cream is used and if it is applied just before or after a bath or shower.

Irritation of the mucous membranes of the eyes and respiratory tract (such as nasal and throat irritation) on application of N-CAPCIN CREAM has been reported rarely, resulting in symptoms such as coughing, sneezing and runny eyes. These events are usually mild and self-limiting. There have been a few reports of dyspnoea, wheezing and exacerbation of asthma.

If an adverse reaction occurs discontinue use immediately. Known side effects of menthol – contact dermatitis or eczema, hypersensitivity reactions characterized by urticaria, flushing and headache.

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.

4.9 Overdose

When used externally as directed, overdose is unlikely. However, symptoms of systemic salicylate poisoning have been reported after the application of salicylates to large areas of skin or for prolonged periods. Salicylism may also occur in the unlikely event of large quantities being ingested.

Salicylate poisoning

Common features include vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities whit bounding pulses, increased respiratory rate and hyperventilation. Some degree of acid-base disturbance is present in most cases.

A mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) is usual in adults and children over the age of four years. In children aged four years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common.
Acidosis may increase salicylate transfer across the blood brain barrier.
Uncommon features include haematemesis, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopaenia, increased INR/ PTR, intravascular coagulation, renal failure and non-cardiac pulmonary oedema.
Central nervous system features including confusion, disorientation, coma and convulsions are less common in adults than in children.

Management

Activated charcoal may be administered if significant quantities have been ingested within an hour of presentation. The plasma salicylate concentration should be measured, although the severity of poisoning cannot be determined from this alone and the clinical and biochemical features must be taken into account. Elimination is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate. The urine pH should be monitored. Correct metabolic acidosis with intravenous 8.4% sodium bicarbonate (first check serum potassium). Forced diuresis should not be used since it does not enhance salicylate excretion and may cause pulmonary oedema.

Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700mg/L (5.1mmol/L), or lower concentrations associated with severe clinical or metabolic features.
Patients under ten years or over 70 have increased risk of salicylate toxicity and may require dialysis at an earlier stage.

Menthol
Ingestion of significant quantities of menthol is reported to cause symptoms including severe abdominal pain, nausea, vomiting, vertigo, ataxia, drowsiness, and coma. Gastric lavage may be considered if the patient presents within 1 hour of ingestion; any convulsions must be controlled first. Activated charcoal may be given orally.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Topical products for joint and muscular pain, Capsaicin and similar agents, ATC code: M02AB01.
Although the precise mechanism of action of capsaicin is not fully understood, current evidence suggests that capsaicin exerts an analgesic effect by depleting and preventing reaccumulation of Substance P in peripheral sensory neurons. Substance P is thought to be the principal chemomediator of pain impulses from the periphery to the central nervous system. Methyl salicylate has the actions of the salicylates. It is readily absorbed through the skin and has counter-irritant properties. Menthol relieves itching, dilates the vessels causing a sensation of coldness followed by an analgesic effect.

5.2 Pharmacokinetic properties

Absorption after topical application is unknown. Average consumption of dietary spice from capsicum fruit has been estimated at 2.5g/ person/ day in India and 5.0g/ person/ day in Thailand. Capsaicin content in capsicum fruit is approximately 1% therefore dietary intake of capsaicin may range from 0.5-1mg/kg/day for a 50kg person. Application of two tubes of N-CAPCIN CREAM 0.025% (25g) each week results in 3.21mg/ day topical exposure. Assuming 100% absorption in a 50kg person, daily exposure would be 0.064mg/kg which is approximately one seventh to one eighth of the above mentioned dietary intake.

The data from *in vitro* study, the cumulative amount of N-CAPCIN is 2-4 fold of available capsaicin cream. As well as zero order kinetic profile, the frequency of use may be reduced to once daily.

5.3 Preclinical safety data

The available animal toxicity data relating to capsicum, capsicum extracts and capsaicin do not suggest that, in usual doses, they pose any significant toxicity hazard to man. Thus, in both single and repeat dosing studies which have been reported, capsicum extracts and capsicum are generally well-tolerated at many times even the highest estimated human intakes. The safety of N-CAPCIN CREAM for use in human pregnancy has not been established since no formal reproduction studies have been performed in either animals or man. However, there is no reason to suspect from human or animal studies currently available that any adverse effects in humans are likely.

Studies reported in the published literature which relate to potential genotoxic and carcinogenic action of capsaicin have produced inconclusive and conflicting data. However, it is unlikely that capsaicin, in the quantities absorbed transdermally from N-CAPCIN CREAM, will pose any significant hazard to humans.

6. Pharmaceutical particulars

6.1 List of excipients

Nanoemulsion of capsaicin
Methyl salicylate
Menthol
Carbopol 934
Triethanolamine
White beewax
Glyceryl monosterate
PEG-20 sorbitan beewax
Cetyl alcohol
Sodium lauryl sulfate
Paraben conc.
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 25°C.

Return any unused cream to your doctor or pharmacist.

6.5 Nature and contents of container

Aluminium tubes with epoxyphenolic lining and polypropylene spiked cap containing 25g of N-CAPCIN CREAM.

6.6 Special precautions for disposal and other handling

No special requirements for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Chao Phya Abhaibhubejhr Hospital Foundation Under the Royal Patronage of H.R.H. Princess Bejaratana Rajasuda
32/7 Moo 12
T.Tha-ngam
A.Muang
Prachinburi
25000

8. Marketing authorisation number(s)

0-9930-00130-78-2

9. Date of first authorisation/renewal of the authorisation

24 January 2017

10. Date of revision of the text

16/01/2018

11. Legal category

Herbal medicine