1. Product Name
Rheumon, 5% w/w, topical gel

2. Qualitative and Quantitative Composition
1 g of topical gel contains 50 mg of etofenamate.
For the full list of excipients, see section 6.1.

3. Pharmaceutical Form
Nearly transparent yellowish gel for topical application.

4. Clinical Particulars

4.1 Therapeutic indications
For the external supportive symptomatic treatment of pain in adults:
- caused by acute strains, sprains or bruises in the extremities after blunt trauma such as sports injuries;
- in soft tissue near a joint (e.g. bursa, tendon, cord and joint capsule) in cases of gonarthrosis.

If symptoms persist for longer than 3 days, a doctor must be consulted.

4.2 Dose and method of administration

Dose
Apply Rheumon Gel three times a day. Depending on the size of the painful areas, an about 5 to 10 cm long ribbon (equivalent to about 1.7 to 3.3 g of gel and 75 to 150 mg of etofenamate) will be required.

For treatment of blunt trauma, the maximum daily dose is 9 g of gel, equivalent to 450 mg of etofenamate.

Method of administration
Only for external application to the skin. Do not ingest.

Apply Rheumon Gel in a thin layer on the affected parts of the body and gently rub into the skin.

Before applying a dressing, Rheumon Gel should be left for a few minutes to dry on the skin. The application of an occlusive dressing is not recommended.

Usually, treatment for one week is sufficient. Therapeutic benefit of a longer use has not been verified.
4.3 Contraindications

Rheumon Gel should not be used in the following cases:

- Hypersensitivity to etofenamate or to any of the excipients listed in section 6.1.
- On open injuries, inflammations or infections of the skin as well as on skin eczema or on mucous membranes.
- Final trimester of pregnancy
- Children and adolescents.

4.4 Special warnings and precautions for use

Rheumon Gel should not be applied to the mucous membranes or the eyes.

Rheumon Gel must only be used when certain precautions are taken and only under close medical supervision:

- In patients suffering from asthma, chronic obstructive airway disease, hay fever or chronic swelling of the nasal mucous membranes (so-called nasal polyps), or chronic obstructive airway diseases or chronic airway infections, especially if they are combined with hay-fever-like manifestations;
- In patients with known hypersensitivity to other non-steroidal antiphlogistic/analgesic agents. These patients are rather at risk than other patients to react to Rheumon Gel with symptoms like asthma attacks (so-called analgesic intolerance / analgesic asthma), local swelling of the skin or mucous membranes (so-called Quincke's disease) or urticaria.
- In patients who react allergic (hypersensitive) to other substances; e.g. in form of skin reactions, itching or nettle rash.

Rheumon Gel can cause discoloration or damage to the surface of polished furniture or plastics. The hands should therefore be washed after applying the product, or contact with the above items should be avoided.

4.5 Interaction with other medicines and other forms of interaction

No interactions are known when Rheumon Gel is used correctly.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of etofenamate in pregnant women. Since the impact of prostaglandin synthesis inhibition on human pregnancy has not yet been fully explored, Rheumon Gel should only be used in the first and second trimester of pregnancy after carefully weighing the risk/benefit ratio. The maximum daily dose must not be exceeded (see section 4.2).

Use of Rheumon Gel is contraindicated in the final trimester of pregnancy.

During the last three months of pregnancy, the mechanism of action of these medicinal products may lead to suppression of labor activity, prolongation of pregnancy and to a prolonged birth process, may cause cardiovascular (with premature closure of ductus arteriosus and pulmonary hypertension) and renal (with oliguresis and oligoamnios) toxicity in the child, increased bleeding tendency in mother and child as well as an increased risk of oedema formation in the mother.

Breast-feeding

Due to the fact that etofenamate passes into the breast milk to a small extent, prolonged use of Rheumon Gel by breastfeeding mothers should be avoided, if possible, and the daily dose must
not be exceeded. In order to avoid absorption by the sucking baby, breastfeeding mothers must not use this medicinal product in the region of their breasts.

4.7 Effects on ability to drive and use machines

Rheumon Gel has no influence on the ability to drive or use machinery.

4.8 Undesirable effects

Evaluation of undesirable effects is based on the following frequency information:

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>≥1/10</td>
</tr>
<tr>
<td>Common</td>
<td>≥1/100 to &lt;1/10</td>
</tr>
<tr>
<td>Uncommon</td>
<td>≥1/1000 to &lt;1/100</td>
</tr>
<tr>
<td>Rare</td>
<td>≥1/10,000 to &lt;1/1000</td>
</tr>
<tr>
<td>Very rare</td>
<td>&lt;1/10,000</td>
</tr>
<tr>
<td>Not known</td>
<td>Frequency cannot be estimated from the available data.</td>
</tr>
</tbody>
</table>

Uncommonly, local skin reactions such as reddening of the skin, itching, burning sensation, skin rash, sometimes with pimples or hives, can develop.

In rare cases, Rheumon Gel can cause hypersensitivity reactions or local allergic reactions (contact dermatitis).

If Rheumon Gel is applied on large skin surface areas and over a longer period of time, development of side effects, affecting a specific system of organs or the entire organism, as under circumstances after systemic use of etofenamate-containing drugs, cannot be ruled out.

**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. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

If more than the recommended dose has been applied on the skin, the gel should be removed and the skin be rinsed with water. There is no specific antidote.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory preparations, non-steroids for topical use for joint and muscular pain; ATC code: M02AA06

**Mechanism of action**

Rheumon Gel is a nonsteroidal anti-inflammatory with analgesic properties which has been proved to be effective in well-known animal models by inhibiting prostaglandin synthesis.

5.2 Pharmacokinetic properties

**Absorption**

The bioavailability of products containing etofenamate is subject to great inter-individual and intra-individual fluctuations, essentially resulting from the administration site, skin moisture and
other factors. After cutaneous administration the relative bioavailability, i.e. the systemically available portion of the dose, is in the range of other etofenamate products (up to 20%).

**Distribution**

After 300 mg of etofenamate had been administered to volunteers in the form of Etofenamate gel (5%), maximum plasma etofenamate levels were measured between 12 and 24 hours after administration (21-28 ng/ml).

The protein binding varies between 98% and 99%.

**Elimination**

Etofenamate is excreted in the form of numerous metabolites (hydroxylation, ether and ester cleavage) and their conjugates, 35% renally and to a large extent in the bile and faeces. Enterohepatic circulation probably occurs. Etofenamate is excreted as flufenamic acid at low concentrations in the breast milk.

**5.3 Preclinical safety data**

When etofenamate is applied topically, the absorption quota must be borne in mind in the evaluation of the toxicological data (see section 5.2).

**Acute toxicity**

Investigations of the acute toxicity of etofenamate have been carried out with various forms of administration in rats, mice, guinea-pigs and rabbits. The oral route of administration proved more toxic than the intramuscular route. The intoxication picture is characterized by gastrointestinal disturbances with diarrhea and loss of body weight. These symptoms usually first appear some days after administration of the substance. Death occurs between the 2nd and 14th day of administration of the substance. After sub lethal doses, the animals recovered in the course of about 14 days. Post-mortem examination of the animals that had died revealed peritonitis and ascites.

**Sub chronic and chronic toxicity**

Sub chronic toxicity has been investigated in various animal species. One-year studies with oral administration were carried out in rats (7, 27, 100 mg/kg body weight/day) and primates (7, 26, 100 mg/kg body weight/day). Rats given 100 mg/kg BW/day developed gastrointestinal haemorrhages and ulcers with subsequent peritonitis and increased mortality.

The high dose led to a reduction in body weight, thymus weight and haemoglobin in primates.

**Mutagenic and carcinogenic potential**

In-vitro and in-vivo investigations of gene and chromosome mutation induction produced negative results. The possibility of the substance having a mutagenic effect appears to have been excluded with sufficient reliability.

Long-term studies involving oral administration to rats (7, 21, 63 mg/kg BW/day) and mice (15, 45, 140 mg/kg BW/day) provided no evidence of a tumorigenic potential of etofenamate.

**Local tolerance**

See section 4.8.

**Reproduction toxicity**

Etofenamate crosses the placental barrier.

There is no experience with administration to humans. In animal experiments, the embryotoxic dose was lower than the maternotoxic dose. In rats, there was an increased incidence of dilation of the renal pelvis from a dose of 21 mg/kg BW/day administered orally (days 6-15 p.c.) and an
increased incidence of 14 rib pairs from 7 mg/kg BW/day administered orally (days 6-15 p.c.) in pups whose mothers had been treated.

6. Pharmaceutical Particulars

6.1 List of excipients

Alpha-[hexadecyl,(Z)-octadec-9-en-1-yl]-ω-hydroxypoly(oxyethylene)-8
Macrogol 400
Sodium hydroxide
Carbomer 940
Propan-2-ol
Purified water.

6.2 Incompatibilities

No incompatibilities are known.

6.3 Shelf life

Unopened: 5 years.

After first opening of the tube: 12 weeks.

6.4 Special precautions for storage

Store at or below 30°C.

6.5 Nature and contents of container

Tube. Pack-sizes of 50 g.

6.6 Special precautions for disposal and other handling

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

Rheumon Gel can cause discoloration or damage to the surface of polished furniture or plastics. The hands should therefore be washed after applying the product or contact with the above items should be avoided.

7. Medicines Schedule

Pharmacy Medicine

8. Sponsor Details

Mylan New Zealand Ltd
PO Box 11-183
Ellerslie
AUCKLAND
Telephone 09-579-2792

9. Date of First Approval

2 March 2000
10. Date of Revision of the Text

5 December 2016   Update to SmPC format, updated sponsor details (8)