WARNING: RISK OF SERIOUS CARDIOVASCULAR and GASTROINTESTINAL EVENTS
Cardiovascular Thrombotic Events
Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.
Olfen 1% GEL is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.
Gastrointestinal Bleeding, Ulceration, and Perforation NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal.
These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI event.

1. Name of the medicinal product
Olfen™ 1 % Gel

2. Qualitative and quantitative composition
Active substance: 1 g of gel contains 10 mg of the active substance diclofenac sodium.
Excipients: Antioxidant E223 (sodium metabisulphite), excipients for gel.
For a full list of excipients, see section 6.1.

3. Pharmaceutical form
Gel
Opalescent to slightly turbid, colourless to light yellowish gel with an odour of Isopropanol

4. Clinical Particulars

4.1 Therapeutic indications
For the local symptomatic relief of pain and inflammation in:
- trauma of the tendons, ligaments, muscles and joints, eg due to sprains, strains and bruises
- localised forms of soft tissue rheumatism,

It is recommended that the treatment be reviewed after 14 days in these indications.
- and for the symptomatic therapy of osteoarthritis of small and medium-sized joints close to the skin, such as finger joints, wrists or knees.

In the treatment of osteoarthritis, therapy should be reviewed after 4 weeks.

4.2 Posology and method of administration
Adults and adolescents aged 14 years and over
Depending on the size of the painful site to be treated, 2 to 4 g Olfen 1 % gel (cherry- to walnut-sized amount sufficient to treat an area of about 400–800 cm²) should be applied 3-4 times daily to the affected parts of the body and rubbed in gently.
The duration of use depends on the indication and the success of treatment. It is recommended to reassess the treatment after 2 weeks if the symptoms have not improved. For the treatment of osteoarthritis of superficial joints such as the knee. In the treatment of osteoarthritis, therapy should be reviewed after 4 weeks. Olfen 1 % gel should not be used for more than 14 days. The hands should be washed well after use (except in the treatment of osteoarthritis of the fingers).
Olfen 1 % gel can also be used as adjuvant therapy together with other dosage forms of Olfen.
Children under 14 years
So far, the use and safety of Olfen 1 % gel have not been systematically tested in children under 14 years of age and its use is not recommended.
Children and adolescents:
There are insufficient data on efficacy and safety available for the children and adolescents below 14 years of age (see also contraindications section 4.3). In children aged 14 years

and over, if this product is required for more than 7 days for pain relief or if the symptoms worsen the patient/parents of the adolescent is/are advised to consult a doctor.

4.3 Contraindications

Hypersensitivity to diclofenac or to any of the excipients (e.g. isopropanol or E223 sodium metabisulphite). Olfen 1 % gel is contraindicated in patients in whom acetylsalicylic acid or other non-steroidal anti-inflammatory drugs such as ibuprofen can trigger asthma attacks, urticaria or acute rhinitis.
Olfen 1 % gel is contraindicated during the 3rd trimester of pregnancy (see advice in the section “Pregnancy/Breast-feeding”).
The use in children and adolescents aged less than 14 years is contraindicated.

4.4 Special warnings and precautions for use

Olfen 1 % gel should be applied to intact skin surfaces only and not to skin wounds or open lesions. The eyes and mucous membranes should not come into contact with the preparation.
Olfen 1 % gel must not be used with airtight, occlusive bandages.
The possibility of systemic adverse events from application of Olfen 1 % gel cannot be excluded if the preparation is used on large areas of skin and over a prolonged period (see the product information on systemic forms of diclofenac).

- Concomitant use of oral NSAID's should be cautioned as the incidence of untoward effects, particularly systemic side effects, may increase.

- Olfen 1 % gel should not be co-administered with other products containing diclofenac.

-Olfen 1 % gel should be applied only to intact, non-diseased skin and not to skin wounds or open injuries. It should not be allowed to come into contact with the eyes or mucous membranes, and should not be ingested.

- Discontinue the treatment if a skin rash develops after applying the product.

- Some possibility of gastro-intestinal bleeding in those with a significant history of this condition has been reported in isolated cases.

4.5 Interactions with other medicinal products and other forms of interaction

Due to the low systemic absorption in topical use, the likelihood of interactions is very low. See also the last paragraph of the section “Adverse effects”.

4.6 Fertility, pregnancy and lactation

Pregnancy
No controlled studies are available in pregnant women. Olfen 1 % gel should therefore not be used during pregnancy.
Olfen 1 % gel is contraindicated in the 3rd trimester of pregnancy due to possible premature closure of the ductus arteriosus and possible suppression of uterine contractions. Animal studies have not shown direct or indirect harmful effects with respect to pregnancy, embryofetal development, birth or postnatal development (see “Preclinical data”).
Breast-feeding
It is not known whether topically applied diclofenac passes into breast milk. Therefore, Olfen 1 % gel should not be used in breast-feeding mothers. Where it is strictly indicated, Olfen 1 % gel should not be used in the area of the breast, over large areas of skin or for prolonged periods.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Frequency
“Very common” (>1/10), “common” (>1/100 to <1/10), “uncommon” (>1/1,000 to <1/100), “rare” (>1/10,000 to <1/1,000), “very rare” (<1/10,000).

Immune system disorders
Very rare: hypersensitivity reactions (including urticaria), angio-oedema
Respiratory organs
Very rare: asthma
Skin and subcutaneous tissue disorders:
Common: skin rash, eczema, reddening, dermatitis (including contact dermatitis), pruritus.
Rare: bullous dermatitis
Very rare: photosensitisation, pustular skin rash.
The likelihood of systemic side effects occurring during topical administration of diclofenac is low compared with the frequency of side effects during oral treatment with diclofenac.
When Olfen 1 % gel is used on relatively large areas and for a prolonged period of time, the occurrence of systemic side effects cannot entirely be ruled out. In such cases, the professional information should be consulted for the oral forms of Olfen.

To report any side effect(s):

The National Pharmacovigilance and Drug Safety Centre (NPC)
- Fax: +966-11-205-7662
- Call NPC at +966-11-2038222, Exts: 2317-2356-2353-2354-2334-2340.
- Toll free phone: 8002490000
- E-mail: npc.drug@sfda.gov.sa
- Website: www.sfda.gov.sa/npc

4.9 Overdose
Due to the low systemic absorption of diclofenac when used topically, an overdose is very unlikely.
Adverse effects similar to those of an overdose with diclofenac tablets are to be expected following inadvertent ingestion of Olfen 1 % gel (1 tube of 100 g is equivalent to 1 g diclofenac sodium). Should significant systemic side effects occur as a result of improper use or accidental overdose (e.g. in children), the general therapeutic measures customary for treating intoxication with non-steroidal anti-inflammatory agents must be taken.
Gastric lavage and treatment with activated charcoal may be considered, particular shortly after ingestion.

5. Pharmacological properties

5.1 Pharmacodynamic properties
ATC code: M02AA15
Mechanism of action and pharmacodynamics
Diclofenac is a non-steroidal antic-inflammatory drug (NSAID) with marked analgesic, anti-inflammatory and antipyretic properties.
Olfen 1 % gel is an anti-inflammatory and analgesic preparation for external use.
The colourless, non-greasy gel can be rubbed into skin easily and possesses a soothing, cooling effect due to the aqueous alcoholic base.
The demonstrated inhibition of prostaglandin biosynthesis by diclofenac is regarded as an important component of its mechanism of action.

5.2 Pharmacokinetic properties
Absorption
The amount of diclofenac absorbed through the skin is proportional to the duration of skin contact and to the area of skin covered with diclofenac gel and is dependent on the total topical dose and the hydration of the skin. After topical application of 2.5 g diclofenac gel per 500 cm^2 of skin, about 6% of the diclofenac dose is absorbed, as determined by total elimination via the kidney compared with diclofenac tablets. The absorption of diclofenac is increased three-fold by an occlusive bandage for 10 hours.
Distribution
Following topical administration of Olfen 1 % gel to hand and knee joints, diclofenac is detectable in plasma, synovial tissue and synovial fluid.

Peak plasma concentrations of diclofenac are about 100 times lower after topical application of Olfen 1 % gel than after oral administration of Olfen tablets. Diclofenac is 99.7% bound to serum proteins, primarily albumin (99.4%).

Metabolism

Biotransformation of diclofenac is partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation followed by glucuronidation of most of the resultant phenolic metabolites. Two of these phenolic metabolites are biologically active, although to a much lesser extent than diclofenac.

Elimination

Total systemic clearance of diclofenac from plasma is 263 ± 56 mL/min (mean ± standard deviation) and the terminal plasma half-life is 1 2 h. Four of the metabolites, including the two active metabolites, also have a short plasma half-life of 1 3 h. One metabolite, 3'-hydroxy-4'-methoxy-diclofenac, has a much longer half-life. However, this metabolite is practically inactive.

Diclofenac and its metabolites are predominantly eliminated with the urine.

Kinetics in special clinical situations

No accumulation of diclofenac and its metabolites is to be expected in patients with renal failure.

The kinetics and metabolism of diclofenac in patients with chronic hepatitis or compensated liver cirrhosis are the same as in patients without liver disease.

5.3 Preclinical safety data

Preclinical data from acute and repeated dose toxicity, genotoxicity, mutagenicity and carcinogenicity studies with diclofenac indicated no specific hazard for humans at the recommended therapeutic dosages. No teratogenic effects were found in mice, rats or rabbits. Diclofenac has no effect on the fertility of the parent animals (rat) or prenatal, perinatal and postnatal development of the progeny.

There was no evidence in various studies that diclofenac gel causes phototoxicity or skin sensitisation.

6. Pharmaceutical particulars

6.1 List of excipients

Lactic acid, di-isopropyl adipate, isopropyl alcohol, sodium metabisulphite (E223), hydroxyethylcellulose, hydroxypropylcellulose, purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C.

Instructions for handling

Do not swallow.

Keep out of the sight and reach of children.

6.5 Nature and contents of container

The aluminium tubes contain 20 g, 50 g or 100 g of gel. The tubes have an internal foodstuff compliant epoxy phenolic resin coating and an external polyester coating.

High density polyethylene caps having an opening-spike are used as closure for the tubes.

Not all pack sizes may be marketed.

7. Marketing Authorisation Holder

Acino Pharma AG, Liesberg (Switzerland)

8. Marketing Authorisation Number(s)

4-222-95

9. Date of first authorisation/renewal of the authorization
01.01.1995

10. Date of revision of the text
May 2018