cardiovascular disease, uncontrolled hypertension, or significant risk factors for cardiovascular disease (e.g., hypertension, hyperlipidaemia, diabetes mellitus and smoking) should be treated with Diclofenac only after careful consideration and only at doses ≤100mg daily when treatment continues for more than 4 weeks.

As the cardiovascular risks of Diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used for the shortest duration possible. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially when treatment continues for more than 4 weeks.

Patients should remain alert for the signs and symptoms of serious arteriothrombotic events (e.g., chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be instructed to see a physician immediately in case of such an event.

INTERACTIONS WITH OTHER MEDICAMENTS

Since systemic absorption of Diclofenac from a topical application is very low such interactions are very unlikely. There are no known interactions with Diclofenac Gel but for a list of interactions known with oral diclofenac the data sheet for oral dosage forms should be consulted.

PREGNANCY AND LACTATION

Pregnancy:

The systemic concentration of diclofenac is lower after topical administration, compared to oral formulations. With reference to experience from treatment with NSAIDs with systemic uptake, the following is recommended:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, diclofenac should not be given unless clearly necessary. If diclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the fetus to:
· cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
· renal dysfunction, which may progress to renal failure with oligo-hydroamniosis; The mother and the neonate, at the end of pregnancy, to:
· possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
· inhibition of uterine contractions resulting in delayed or prolonged labour. Consequently, Diclofenac is contraindicated during the third trimester of pregnancy.

Lactation:
Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, at therapeutic doses of Diclofenac Gel no effects on the suckling child are anticipated. Because of a lack of controlled studies in lactating women, the product should only be used during lactation under advice from a healthcare professional. Under this circumstance, Diclofenac Gel should not be applied on the breasts of nursing mothers, nor elsewhere on large areas of skin or for a prolonged period of time.

SIDE EFFECTS
Immune system disorder
Very rare: Hypersensitivity (including urticaria), angioneurotic oedema.

Infections and infestations
Very rare: Rash pustular.

Respiratory, thoracic and mediastinal disorders
Very rare: Asthma.

Skin and subcutaneous tissue disorders
Common: Rash, eczema, erythema, dermatitis (including dermatitis contact), pruritus.
Rare: Dermatitis bullous.
Very rare: Photosensitivity reaction.
Adverse effects: Dermatological: Occasional – rashes or skin eruptions cases of hair loss, bullous eruptions, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome) and photosensitivity reactions have been reported.

Cardiac disorders
Uncommon*: Myocardial infarction, cardiac failure, palpitations, chest pain.
*The frequency reflects data from long-term treatment with a high dose (150mg/ day)

DESCRIPTION OF SELECTED ADVERSE DRUG REACTIONS

Arteriothrombotic events
Meta-analysis and pharmacoepidemiological data point towards an increased risk of arteriothrombotic events (for example myocardial infarction) associated with the use of Diclofenac, particularly at a high dose (150mg daily) and during long-term treatment (see section WARNINGS AND PRECAUTIONS).

Although less likely with the topical administration, some side effects normally associated with systemically administered Diclofenac may also occur.

SYMPTOMS AND TREATMENT OF OVERDOSE

Symptoms

The low systemic absorption of Diclofenac Gel renders overdose very unlikely. However, undesirable effects, similar to those observed following an overdose of diclofenac tablets, can be expected if Diclofenac Gel is inadvertently ingested (1 tube of 100g contains the equivalent of 1000mg of diclofenac sodium). In the event of accidental ingestion, resulting in significant systemic adverse effects, general therapeutic measures normally adopted to treat poisoning with non- steroidal anti-inflammatory medicines should be used. Gastric decontamination and the use of activated charcoal should be considered, especially within a short time of ingestion.

Treatment

Management of overdosage with NSAIDs essentially consists of supportive and symptomatic measures. There is no typical clinical picture resulting from Diclofenac Gel overdosage. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression; specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE

Cutaneous application of Vewodina (Diclofenac Gel BP 1% w/w) has no influence on the ability to drive and use machines.

STORAGE CONDITION

Store at a temperature below 30°C. Keep out or reach of children.

SHELF LIFE
36 months.

DOSAGE FORM AND PACKAGING

Dosage Form: Semi-solid (Gel for topical use)

Packaging Presentation: Vewodina (Diclofenac Gel BP 1% w/w) is a, white to creamish coloured homogeneous gel, free from agglomerates. It contains 1.0% w/w Diclofenac Sodium in 20g, 50 g aluminium tubes with HDPE screw cap.

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