Olfen®-25/50 *Lactab®*
Olfen®-75 SR *Depotabs®*
Olfen®-100 SR *Depocaps®*
Olfen®-50/100 *Rectocaps®*
Olfen®-75 *ampoules i.m.*

Antirheumatic agent with anti-inflammatory and antipyretic properties

Composition

Each *Olfen-25 Lactab* contains:	
Diclofenac sodium:	25 mg
Colour: E 104	
Each *Olfen-50 Lactab* contains:	
Diclofenac sodium:	50 mg
Colour: E 104	
Each *Olfen-75 SR Depotabs* contains:	
Diclofenac sodium:	75 mg
Each *Olfen-100 SR Depocaps* contains:	
Diclofenac sodium:	100 mg
Colour: E 127	
Each *Olfen-50 Rectocaps* contains:	
Diclofenac sodium:	50 mg
Each *Olfen-100 Rectocaps* contains:	
Diclofenac sodium:	100 mg
Each *Olfen-75 ampoule i.m. of 2 ml* contains:	
Diclofenac sodium	75 mg
Lidocaine hydrochloride	20 mg

Properties/Effects

Olfen contains the sodium salt of diclofenac, a nonsteroidal active substance having pronounced antirheumatic, antiinflammatory, analgesic and antipyretic properties. Inhibition of prostaglandin biosynthesis, which has been demonstrated experimentally, is thought to be important for the mechanism of action. Prostaglandins play an essential role in the development of inflammation, pain and fever. The antiinflammatory and analgesic properties become clinically evident in the case of rheumatic disorders in that the symptoms, such as rest pain, pain on motion, morning stiffness, swelling of the joints, are significantly improved and functional ability increases. In post-traumatic/post-operative inflammations, Olfen causes a rapid reduction in spontaneous pain and pain on motion and reduces inflammatory swelling and wound oedema.

For moderate and severe states of pain of a nonrheumatic type, as well, the pronounced analgesic effect was demonstrated in clinical trials. In cases of primary dysmenorrhoea, Olfen can alleviate pain and reduce the extent of bleeding. Olfen (Rectocaps) also has a favourable effect on the symptoms of migraine attacks.

Olfen Lactab are coated with an enteric protective coating.

The Depocaps are suitable for patients for whom the daily dose of 100 mg is appropriate for the symptoms. From the Depocaps, the active ingredient is released over a relatively long period of time, ensuring sustained action. The administration once per day makes particularly long-term treatment with Olfen more simple.

Rectocaps are gelatin capsules for rectal administration. After introduction into the rectum, the gelatin jacket disintegrates within a few minutes. Rectocaps do not irritate the mucosa of the rectum and are thermostable even at elevated temperatures.

The Rectocaps are administered blunt end first. To facilitate the introduction, they are coated with a lubricant. If appropriate, the Rectocaps can be wetted with water prior to introduction.

Olfen ampoules are particularly suitable for the initial therapy of inflammatory and degenerative rheumatic disorders, as well as for the treatment of pain due to inflammations of the nonrheumatic type, whereby the onset of action occurs within 15–30 minutes.

Pharmacokinetics

Absorption

Diclofenac is absorbed rapidly and completely from the Lactab which is resistant to gastric juices.

On average, the mean plasma concentration of 0.92 mg/l (C_{max}) is reached 2.6 hours (t_{max}) after a 50 mg Lactab has been taken. The relation of the plasma concentration to the dose is linear.

When a Lactab is taken during or after a meal, passage through the stomach is slower than in the case of administration on an empty stomach, and may take from 2.5 to 12 hours. However, this does not negatively affect the amount of active ingredient absorbed.

From Depocaps, diclofenac is absorbed completely. As a consequence of the delayed release of active ingredient, the maximum plasma concentrations reached are lower than those after administration of conventional administration forms. On the other hand, measurable concentrations can be detected even after several hours. When a Depocaps is taken during or after a meal, absorption sets in later than when the Depocaps is administered on an empty stomach. However, this does not negatively affect the amount of active ingredient absorbed. After a 100 mg Depocaps has been taken, the mean maximum plasma concentration of 0.43 µg/ml (1.35 µmol/l) is reached on average after about 3.5 hours.

On administration of two 75 mg Olfen SR per day, the mean maximum plasma concentrations reached in the steady state are approximately 489 ± 237 ng/ml.

Distribution

The mean distribution volume of diclofenac is 0.12–0.17 l/kg. Plasma protein binding is more than 99%.

The therapeutic plasma concentration is 0.7–2 µg/ml.

After administration of equivalent doses (mg/kg body weight), the plasma concentrations in children are similar to those of adults. Repeated administration does not change the kinetics. There is no cumulation if the recommended dosage intervals are adhered to.

Diclofenac passes into the synovial fluid, where maximum concentrations are measured 2–4 hours after peak plasma values have been obtained. The apparent elimination half-life from the synovial fluid is 3–6 hours. As a consequence, even 4–6 hours after administration, the concentrations of active ingredient are higher than in the plasma, and they remain higher for up to 12 hours.

Metabolism

About half of the active ingredient is subject to first-pass metabolism. As a result, the areas under the concentration curves (AUC) are, after oral or rectal administration, about half of those after parenteral administration of a dose of the same amount. After oral administration, only 60% of the substance reach the circulation in unmodified form. Biotransformation is partly by glucuronidation of the intact molecule, but mainly by hydroxylation and methoxylation. Two of the phenolic metabolites formed are pharmacologically active, but less so than diclofenac.

Elimination

Diclofenac is eliminated from the plasma with a systemic clearance of 263 ± 56 ml/min (mean ± SD). The terminal half-life is 1–2 hours. Approximately 60% of the administered dose is eliminated via the kidneys in the form of metabolites, and less than 1% in unchanged form. The remainder of the dose is eliminated via the bile in metabolised form.

Kinetics in special clinical situations

Relevant differences in absorption, metabolism and elimination owing to the age of the patients have not been observed.

In the case of patients suffering from impaired kidney function, an increase of the unmodified active substance was not observed when a normal individual dose was administered. If creatinine clearance is less than 10 ml/min, the theoretical steady-state plasma level of the metabolites is approximately four times higher than in healthy people. In spite of this, the metabolites are ultimately eliminated via the bile.

In case of impaired liver function (chronic hepatitis, compensated cirrhosis of the liver), kinetics and metabolism are as in patients with normal hepatic function.

The maximum plasma concentration after administration of Depocaps is within the range of an individual dose of 25 mg, but is more sustained, corresponding to the higher content of active ingredient of the Depocaps.

Indications/possibilities of use

Lactab, Depocaps, Depotabs, Rectocaps

Inflammatory and degenerative, articular and extraarticular rheumatic disorders of muscles, joints, joint capsules, synovial bursae, tendons, synovial sheaths and the spine, such as chronic polyarthritis, arthritis, arthroses, degenerative spondylarthritis, ankylosing spondylitis, soft tissue rheumatism, bursitis, tendovaginitis, tendinitis, lumbago, ischias, cervical syndrome.

Acute gouty arthritis *(Lactab, Rectocaps).*

Painful states of inflammation and swelling after trauma and surgery, for example, in dentistry and orthodontistry, and orthopaedics.

Painful and/or inflammatory states in gynaecology, for example primary dysmenorrhoea, adnexitis.

As an adjuvant in acute painful inflammatory infections of the throat, the nose or the ears, for example pharyngotonsillitis, otitis *(Lactab, Rectocaps).*

In accordance with general medical principles, appropriate therapeutic measures have to be taken for treating the underlying diseases. Fever alone is not an indication.

Ampoules

Intramuscular injection.

Initial treatment of the following conditions:

Exacerbation of inflammatory or degenerative forms of rheumatism: rheumatoid arthritis, ankylosing spondylitis, arthrosis, degenerative spondylarthritis, painful vertebral syndromes, extraarticular rheumatism.

Acute gouty arthritis.

Renal and biliary colic.

Pain, inflammations and swelling after injuries and surgical interventions.

Dosage/use

Lactab, Depocaps, Depotabs and Rectocaps

Adults

The initial daily dose is usually 100–150 mg. In less severe cases and for long-term therapy, 75–100 mg per day are in most cases sufficient.

In general, the daily dose is divided into 2–3 individual administrations, in the case of long-term treatment, for example, 2 × per day 1 Lactab Olfen-50 or 1 × per day 1 Depocaps Olfen-100 or 1 Depotabs Olfen-75 SR. If the symptoms are most severe during the night or in the morning, Olfen-75 SR should preferably be taken in the evening.

Lactab, like Depocaps and Depotabs, are to be taken before a meal, without chewing and with a glass of water.

To prevent pain during the night and morning stiffness, administration of a Rectocaps (50 mg or 100 mg) before going to bed can be combined with Lactab during the day (up to a maximum daily dose of 150 mg).

For primary dysmenorrhoea, the daily dose, adapted individually, is generally 50–150 mg; the initial dose should be selected to be 50–100 mg and is, if required, to be raised over a number of menstruation cycles to a maximum of 200 mg/day. Therapy should be initiated when the first symptoms occur and should continue for a number of days, depending on the symptoms.

Children

Depending on the severity of the disorder, children from the age of 1 are given 0.5–2 mg per kg of body weight per day, divided into 2–3 individual doses. For the treatment of juvenile chronic polyarthritis, the daily dose, divided into a number of individual doses, can be raised to a maximum of 3 mg per kg body weight.

Because of the high content of active ingredient, the use of Olfen Lactab 50 mg, Olfen Depotabs 75 mg, Olfen Depocaps 100 mg and Olfen Rectocaps 50 and 100 mg are not recommended for use in children.

Olfen may not be used for children under the age of 1.

Ampoules

The solution is generally injected by deep intragluteal injection into the upper external quadrant, once daily.

In severe cases (for example colic), it is also possible to administer two injections per day, at an interval of several hours (the injection site should be changed). Alternatively, *it is possible to combine* parenteral administration *with other* forms of Olfen (Lactab, Depocaps, Depotabs, Rectocaps), up to a maximum daily dose of 150 mg. Treatment with Olfen injection should only be carried out for 2 days and, if necessary, be continued with Olfen Lactab or Rectocaps.

Olfen injection is not suitable for children.

Restrictions in use

Contraindications

Gastric and duodenal ulcer. Hypersensitivity to the active ingredient or the excipients. Like other NSAIDs, Olfen is contraindicated for patients in which asthma attacks, urticaria or acute rhinitis have occurred after administration of acetylsalicylic acid or other agents with an inhibitory effect on prostaglandin synthetase.

Rectocaps: proctitis

Olfen may not be used for children under the age of 1.

Precautions

For patients suffering from gastrointestinal complaints, with indications of peptic ulcers in the history, with ulcerative colitis, Crohn's disease or impaired liver function, precise indication and careful medical monitoring is required.

In elderly patients, gastrointestinal bleeding or ulcerations/perforations frequently have serious consequences. They can occur during the treatment at any time, even without warning symptoms and without any indications in the medical history.

In rare cases, where gastrointestinal ulceration or haemorrhage occur during treatment with Olfen, the drug must be discontinued.

As with other NSAIDs, the values of one or more liver enzymes may increase during treatment with Olfen. This has been observed in

the treatment with diclofenac in clinical studies and may occur in about 15% of the patients, but is rarely accompanied by clinical symptoms. The clinical significance of this phenomenon is unknown. In the majority of these cases, these increases are within borderline. Occasionally (in 2.5% of the cases), moderate increases have been observed (≥ 3 – < 8 × upper limit), whereas the incidence of considerable increases (≥ 8 × upper limit) was in the range of about 1%. In the above-mentioned clinical studies, 0.5% of the patients suffered clinically manifest liver damage in addition to elevated liver enzymes. After discontinuation of the medicine, the increased enzyme values generally reverted to normal.

As with other NSAIDs, during long-term therapy with Olfen, the liver function should be monitored regularly.

Olfen should be discontinued in case of prolonged or deteriorating liver dysfunction, if clinical signs and symptoms of liver disease (for example hepatitis) or other manifestations (for example eosinophilia, skin eruptions, etc.) occur. In addition to elevations in liver enzymes, there have been reports of rare cases of serious liver reactions, including jaundice and in individual cases fatal fulminant hepatitis. Hepatitis may occur without prodromal symptoms. In patients suffering from hepatic porphyria, Olfen should be used with care, since the medicine may trigger an attack.

Owing to the important function of the prostaglandins in maintaining kidney circulation, particular care has to be taken in the case of patients suffering from impaired cardiac or renal function; elderly patients; patients taking diuretics, and patients suffering from fluid deficit in the extracellular space owing to any cause, for example during the peri- or post-operative phase of major surgical interventions. If Olfen is used in such cases, it is recommended to monitor kidney function as a precautionary measure. If the therapy is discontinued, the state prior to the treatment is usually reestablished.

Owing to basic medical considerations, care should be taken in the case of elderly patients.

In particular, it is recommended to use the lowest effective dosage for frail elderly patients or patients with a low body weight.

If Olfen is used for a relatively long time, it is recommended–as in the case of other highly active NSAIDs–to monitor kidney and liver function and the blood picture as precautionary measures.

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can occur even if the drug is used for the first time.

Like other NSAIDs, Olfen may inhibit thrombocyte aggregation temporarily. Patients suffering from a coagulation defect should be monitored carefully.

Owing to its pharmacodynamic properties, Olfen–like other NSAIDs–may obscure the symptoms of an infection.

Special note: Patients suffering from vertigo or other disturbances of the central nervous system, including visual disturbances, should not drive vehicles or operate machinery.

Pregnancy/lactation

1st and 2nd trimester: Pregnancy category B.

Animal studies have not shown any risk for the foetus; however, there are no controlled studies of pregnant women.

3rd trimester: Pregnancy category D.

Olfen should not be administered because of premature closure of the ductus arteriosus and possible uterine inertia.

After administration of oral doses of 50 mg at intervals of 8 hours, the amount of the active ingredient of Olfen that passes into the breast milk is so small that no undesirable effects on the infant are to be expected.

Undesirable effects

Digestive tract

Occasional: Epigastric pain, other gastrointestinal symptoms such as nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence, anorexia and local irritation (only in the case of Rectocaps).

Rare: Gastro-intestinal bleeding (haematemesis, melaena, bloody diarrhoea), peptic ulcer with or without bleeding or perforation.

In individual cases: Symptoms in the lower abdomen (for example non-specific haemorragic colitis and exacerbation of ulcerative colitis or Crohn's disease), aphthous stomatitis, glossitis, oesophageal lesion, diaphragm-like intestinal strictures, constipation, pancreatitis, exacerbation of haemorrhoids.

Olfen-75 SR: Chronic inflammatory conditions in the lower intestine, with pseudomembranes and strictures.

Central nervous system

Occasional: Headaches, dizziness, vertigo.

Rare: Tiredness.

In isolated cases: Disturbance of sensation, paraesthesia, memory disturbances, disorientation, sleeplessness, irritability, spasms, depressions, anxiety, nightmares, tremor, psychotic reactions, aseptic meningitis.

Sensory organs

In isolated cases: Visual disturbances (blurred vision, diplopia), impaired hearing, tinnitus, taste disturbances.

Skin

Occasional: Skin eruptions.

Rare: Urticaria.

In isolated cases: Bullous rash, eczema, multiform erythema, Stevens Johnson syndrome, Lyell syndrome (toxic epidermal necrolysis), erythrodermia (exfoliative dermatitis), hair loss, photosensitization, purpura including allergic purpura.

Kidney

Rare: Oedema.

In isolated cases: Acute renal insufficiency, haematuria, proteinuria, interstitial nephritis, nephrotic syndrome, necrotizing papillitis.

Liver

Frequent: Elevation of serum amino transferases (SGOT, SGPT), occasionally to a moderate extent (≥ 3 × upper limit), or considerable (≥ 8 × upper limit) extent.

Rare: Hepatitis with or without jaundice, in individual cases fulminant hepatitis.

Blood

In individual cases: Thrombocytopenia, leukopenia, agranulocytosis, haemolytic anaemia, aplastic anaemia.

Hypersensitivity

Rare: Hypersensitivity reactions (for example bronchospasms, anaphylactic/anaphylactoid systemic reactions including hypotension).

In isolated cases: Vasculitis, pneumonitis.

Other organs

In isolated cases: Impotence (the connection with the use of Olfen is uncertain), palpitations, chest pain, hypertension, cardiac insufficiency.

Local adverse reactions at the injection site (localized pain and indurations; in individual cases: abscesses and localized necroses).

Interactions

Lithium, digoxin

When used concomitantly, Olfen may increase the plasma concentrations of lithium or digoxin.

Diuretics

Like other NSAIDs, Olfen may reduce the efficacy of diuretics. Concomitant treatment with potassium-sparing diuretics may lead hyperkalemia, and it is therefore necessary to determine serum potassium concentration.

Nonsteroidal antirheumatics

The concomitant use of different systemic nonsteroidal an rheumatics or glucocorticoids may promote the occurrence of u desirable effects.

Anticoagulants

Clinical studies have indicated that Olfen does not interfere w the action of anticoagulants. Nevertheless, as a precaution, it recommended to check the desired anticoagulant effect by lab ratory controls when using Olfen and anticoagulants concon tantly. Like other NSAIDs, high doses (200 mg) of diclofenac c reversibly inhibit thrombocyte aggregation.

Antidiabetic agents

Clinical studies have shown that Olfen can be administered co comitantly with oral antidiabetics without interfering with the clinical action. However, there have been individual reports of h poglycaemic and hyperglycaemic reactions after administration Olfen, which have required dosage adjustment to the antidiabet agents.

Methotrexate

Care has to be taken when administering nonsteroidal ant rheumatics less than 24 hours before or after treatment wi methotrexate, since the concentration of methotrexate in the bloo and the toxicity of methotrexate may be increased.

Cyclosporin

The effect of NSAIDs on the prostaglandins of the kidney can in crease the nephrotoxicity of cyclosporin.

Quinolone antibiotics

There have been individual reports of convulsions which are pos sibly the result of concomitant use of quinolones and NSAIDs.

Overdosage

The treatment of acute poisonings with nonsteroidal antirheuma ics consists of supportive or symptomatic measures. Typical clin ical symptoms after overdosage of diclofenac are not known.

The therapeutic measures in cases of overdosage are as follows after swallowing, absorption should be prevented as quickly a possible by gastrolavage and treatment with activated charcoal The treatment of complications such as hypotension, renal insu ficiency, convulsions, gastrointestinal irritation and respiratory de pression is supportive and symptomatic. Specific therapy, such a forced diuresis, dialysis or haemoperfusion, are presumably of lit tle help for eliminating NSAIDs, owing to their high rate of prote binding and their extensive metabolism.

Presentation

Olfen-25

Packings of 30 Lactab

Olfen 50

Packings of 20 Lactab

Olfen-75 SR

Packings of 10 and 30 Depotabs

Olfen-100 SR

Packings of 10 and 20 Depocaps

Olfen-50

Packings of 10 Rectocaps

Olfen-100

Packings of 5 Rectocaps

Olfen-75

Packings of 5 ampoules of 2 ml

Hospital Packings