Bosch For Medical Professional Only

Orthofenac® Tablets/Injection

(D i c l o f e n a c S o d i u m)

آرتھوفینیک ٹیبلیٹس / انجکشن

(ڈائی کلوفینک سوڈیم)

DESCRIPTION:
Diclofenac sodium is a phenyl-acetic acid derivative. It is available as delayed-release (enteric-coated) and sustained release tablets or as a nonsteroidal anti-inflammatory drug for intravenous administration.

Diclofenac sodium is a white to off-white, virtually odorless, crystalline powder. Diclofenac sodium is freely soluble in methanol, soluble in ethanol, and practically insoluble in chloroform and in dilute acid. Diclofenac sodium is sparingly soluble in water. The chemical name is 2-[(2,6-dichlorophenyl)amino] benzeneacetic acid, monosodium salt. The molecular weight is 318.14. Its molecular formula is $C_{14}H_{10}Cl_2NO_2Na$

Composition:
Orthofenac 75mg/3ml Injection:
Each ampoule contains:
Diclofenac Sodium U.S.P. 75mg
(Product Specs.: Bosch.)

Orthofenac 50mg tablets:
Each enteric coated tablet contains:
Diclofenac Sodium U.S.P. ... 50 mg
(Product Specs. U.S.P.)
“Product contains lactose”

Orthofenac SR 100mg tablets:
Each sustained release tablet contains :
Diclofenac Sodium U.S.P. ... 100 mg
(Product Specs. U.S.P.)
“Product contains lactose”

CLINICAL PHARMACOLOGY
Pharmacodynamic properties:
Pharmacotherapeutic category: non-steroidal antinflammatory drugs (NSAIDs):
ATC Code: M01AB05.

Mechansim of action:
Diclofenac has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of ORTHOFENAC, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Diclofenac is a potent inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues.
Diclofenac sodium in-vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

Pharmacokinetic properties:
Absorption
Oral: Absorption is complete but onset is delayed until passage through the stomach, which may be affected by food which delays stomach emptying. The mean peak plasma diclofenac concentration reached at about 2 hours

Intramuscular injection: After administration of 75mg diclofenac by intramuscular injection, absorption sets in immediately, and mean peak plasma concentrations of about 2.558 ± 0.968µg/ml (2.5µg/mL ≡ 8µmol/L) are reached after about 20 minutes. The amount absorbed is in linear proportion to the size of the dose.
Intravenous infusion: When 75mg diclofenac is administered as an intravenous infusion over 2 hours, mean peak plasma concentrations are about 1.875 ± 0.436µg/ml (1.9µg/mL ≡ 5.9µmol/L). Shorter infusions result in higher peak plasma concentrations, while longer infusions give plateau concentrations proportional to the infusion rate after 3 to 4 hours. This is in contrast to the rapid decline in plasma concentrations seen after peak levels have been achieved with oral, rectal or i.m. administration.

Bioavailability:
The area under the concentration curve (AUC) after intramuscular or intravenous administration is about twice as large as it is following oral or rectal administration as this route avoids "first-pass" metabolism. In Oral about half of the administered diclofenac is metabolised during its first passage through the liver

Distribution
The active substance is 99.7% protein bound, mainly to albumin (99.4%).
Diclofenac enters the synovial fluid, where maximum concentrations are measured 2-4 hours after the peak plasma values have been attained. The apparent half-life for elimination from the synovial fluid is 3-6 hours. Two hours after reaching the peak plasma values, concentrations of the active substance are already higher in the synovial fluid than they are in the plasma and remain higher for up to 12 hours.
Diclofenac was detected in a low concentration (100 ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose

Metabolism
Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two phenolic metabolites are biologically active, but to a much lesser extent than diclofenac.

Excretion
Total systemic clearance of diclofenac in plasma is 263 ± 56 mL/min (mean value ± SD). The terminal half-life in plasma is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours.

About 60% of the administered dose is excreted in the urine in the form of the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites through the bile in the faeces.

Specific population
Elderly
No relevant age-dependent differences in the drug's absorption, metabolism or excretion have been observed.

Renal impairment
In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 mL/min, the calculated steady-state plasma levels of the hydroxy metabolites are about 4 times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.

Hepatic impairment
In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

THERAPEUTIC INDICATIONS
Tablets
Adults and elderly
Relief of all grades of pain and inflammation in a wide range of conditions, including:
(i) arthritic conditions: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout,
(ii) acute musculo-skeletal disorders such as periarthritis (for example frozen shoulder), tendinitis, tenosynovitis, bursitis.
(iii) other painful conditions resulting from trauma, including fracture, low back pain, sprains, strains, dislocations, orthopaedic, dental and other minor surgery.

Children
Diclofenac Sodium tablets are not suitable for children.

Ampoules for intra muscular use:
The ampoules are effective in acute forms of pain, including renal colic, exacerbations of osteo- and rheumatoid arthritis, acute back pain, acute gout, acute trauma and fractures, and post-operative pain.

Ampoules used in intravenous infusion:
For treatment or prevention of post-operative pain in the hospital setting.

DOSAGE AND ADMINISTRATION
Adult
75 mg to 150 mg daily in two or three divided doses. The recommended maximum daily dose of diclofenac sodium tablet is 150mg.

Two alternative regimens are recommended:
For the treatment of moderate to severe post-operative pain, 75mg should be infused continuously over a period of 30 minutes to 2 hours. If necessary, treatment may be repeated after 4-6 hours, not exceeding 150mg within any period of 24 hours.

For the prevention of post-operative pain, a loading dose of 25mg-50mg should be infused after surgery over 15 minutes to 1 hour, followed by a continuous infusion of approx. 5mg per hour up to a maximum daily dosage of 150mg.

Elderly:
The lowest effective dosage be used in frail elderly patients or those with a low body weight and the patient should be monitored for GI bleeding during NSAID therapy.

Pediatric Use
Diclofenac Sodium is not suitable for children.

Renal and Hepatic impairment
Diclofenac is contraindicated in patients with renal and hepatic failure. Caution is advised when administering diclofenac to patients with mild to moderate renal and hepatic impairment.

Method of Administration
Orthofenac ampoules (given im or iv) should not be given for more than two days; if necessary, treatment can be continued with Orthofenac tablets or suppositories.

Intramuscular injection: The following directions for intramuscular injection must be adhered to in order to avoid damage to a nerve or other tissue at the injection site. One ampoule once (or in severe cases twice) daily intramuscularly by deep intragluteal injection into the upper outer quadrant. If two injections daily are required it is advised that the alternative buttock be used for the second injection. Alternatively, one ampoule of 75mg can be combined with other dosage forms of Orthofenac (tablets or suppositories) up to the maximum daily dosage of 150mg.

Renal colic: One 75mg ampoule intramuscularly. A further ampoule may be administered after 30 minutes if necessary. The recommended maximum daily dose of Orthofenac is 150mg.

Intravenous Infusion: Immediately before initiating an intravenous infusion, Orthofenac must be diluted with 100-500ml of either sodium chloride solution (0.9%) or glucose solution (5%). Both solutions should be buffered with sodium bicarbonate solution (0.5ml 8.4% or 1ml 4.2%). Only clear solutions should be used.
Orthofenac must not be given as an intravenous bolus injection.

CONTRAINDICATIONS:
- Hypersensitivity to the active substance, sodium metabisulphite or any of the excipients.
- Active, gastric or intestinal ulcer, bleeding or perforation
- History of gastrointestinal bleeding or perforation, relating to previous NSAID therapy
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding)
- Last trimester of pregnancy
- Hepatic failure
- Renal failure
- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease
- Like other non-steroidal anti-inflammatory drugs (NSAIDs), diclofenac is also contraindicated in patients in whom attacks of asthma, angioedema, urticaria or acute rhinitis are precipitated by ibuprofen, acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs.

Specifically for I.V:
- Concomitant NSAID or anticoagulant use (including low dose heparin).
- History of haemorrhagic diathesis, a history of confirmed or suspected cerebrovascular bleeding.
- Operations associated with a high risk of haemorrhage.
- A history of asthma.
- Moderate or severe renal impairment (serum creatinine >160µmol/l).
- Hypovolaemia or dehydration from any cause.

WARNINGS AND PRECAUTIONS
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. The instructions for intramuscular injection should be strictly followed in order to avoid adverse events at the injection site, which may result in muscle weakness, muscle paralysis, hypoaesthesia and injection site necrosis.

Lactose:
Product contains lactose.
Possibility of untoward reaction for patient with celiac disease relating to the use of such excipients. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Gastrointestinal effects:
Gastrointestinal bleeding (haematemesis, melaena), ulceration or perforation which can be fatal has been reported with all NSAIDs including diclofenac and may occur at any time during treatment, with or without warning symptoms or a previous history of serious GI events. If gastrointestinal bleeding or ulceration occurs in patients receiving diclofenac, the drug should be withdrawn. As with all NSAIDs, including diclofenac, close medical surveillance is imperative and particular caution should be exercised when prescribing diclofenac in patients with symptoms indicative of gastrointestinal disorders, or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation.
The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses including diclofenac, and in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation.
Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant use of medicinal products containing low dose acetylsalicylic acid

Hepatic effects:
As with other NSAIDs, including diclofenac, values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac, regular monitoring of hepatic function is indicated as a precautionary measure.
If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), Orthofenac should be discontinued.
Hepatitis may occur with diclofenac without prodromal symptoms.

Caution is called for when using diclofenac in patients with hepatic porphyria, since it may trigger an attack.

Renal effects:
As fluid retention and oedema have been reported in association with NSAIDs therapy, including diclofenac, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery. Monitoring of renal function is recommended as a precautionary measure when using diclofenac in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.

Skin effects:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs. Patients appear to be at the highest risk of these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Orthofenac should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

SLE and mixed connective tissue disease:
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.

Cardiovascular and cerebrovascular effects:
Patients with congestive heart failure (NYHA-I) or patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration. As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.
Appropriate monitoring and advice are required for patients with a history of hypertension and congestive heart failure (NYHA-I) as fluid retention and oedema have been reported in association with NSAID therapy including diclofenac.
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.

Haematological effects:
During prolonged treatment with diclofenac, as with other NSAIDs, monitoring of the blood count is recommended. Orthofenac may reversibly inhibit platelet aggregation Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Pre-existing asthma:
In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions on NSAIDs like asthma exacerbations (so called intolerance to analgesics / analgesics asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients (readiness for emergency). This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.
Like other drugs that inhibit prostaglandin synthetase activity, diclofenac sodium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

Female fertility:
The use of Orthofenac may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Orthofenac should be considered.

DRUG INTERACTIONS:
The following interactions include those observed with diclofenac gastro-resistant tablets and/or other pharmaceutical forms of diclofenac.

Lithium: If used concomitantly, Orthofenac may increase plasma concentrations of lithium Monitoring of the serum lithium level is recommended.

Digoxin: If used concomitantly, Orthofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.
Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of Orthofenac with diuretics and antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis.
Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.

Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored.

Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding. Close monitoring of such patients is required. As with other nonsteroidal anti-inflammatory agents, diclofenac in a high dose can reversibly inhibit platelet aggregation.

Other NSAIDs including cyclooxygenase-2 selective inhibitors and corticosteroids:
Co-administration of diclofenac with other systemic NSAIDs or corticosteroids may increase the risk of gastrointestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs.

Selective serotonin reuptake inhibitors (SSRIs):
Concomitant administration of SSRI's may increase the risk of gastrointestinal bleeding.

Antidiabetics: Orthofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However there have been isolated reports of hypoglycaemic and hyperglycaemic effects necessitating changes in the dosage of the antidiabetic agents during treatment with diclofenac. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

Methotrexate: Diclofenac can inhibit the tubular renal clearance of methotrexate hereby increasing methotrexate levels. Caution is recommended when NSAIDs, including diclofenac, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increase. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.

Ciclosporin: Diclofenac, like other NSAIDs, may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal antiprostagladin effects of both NSAID and calcineurin inhibitor.

Quinolone antibacterials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving an NSAID.

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Colestipol and cholestyramine: These agents can induce a delay or decrease in absorption of diclofenac. Therefore, it is recommended to administer diclofenac at least one hour before or 4 to 6 hours after administration of colestipol/ cholestyramine.

Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac due to inhibition of diclofenac metabolism.

ADVERSE EFFECTS:
Common: Headache, dizziness, Vertigo, Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia, Transaminases increased, Rash, Injection site reaction, injection site pain, injection site induration.
Uncommon: Myocardial infarction, cardiac failure, palpitations, chest pain.
Rare: Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock), Somnolence, tiredness, Asthma (including dyspnoea), Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularly in the elderly), Transaminases increased, Urticaria, Oedema

Very Rare: Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis, Angioneurotic oedema (including face oedema), Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder, Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident, Visual disturbance, vision blurred, diplopia, Tinnitus, hearing impaired, Hypertension, hypotension, vasculitis, Pneumonitis, Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis, Fulminant hepatitis, hepatic necrosis, hepatic failure, Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus, Acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis, Impotence

Not known: Injection site necrosis, Confusion, hallucinations, disturbances of sensation, malaise, Optic neuritis, Kounis syndrome, Ischaemic colitis,

USE IN PREGNANCY AND LACTATION:
PREGNANCY:
During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus 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 the 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, Orthofenac is contra-indicated during the third trimester of pregnancy.

Lactation
Like other NSAIDs, diclofenac passes into breast milk in small amounts. Therefore, diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant

OVERDOSAGE:
Symptoms
Over dosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In the case of significant poisoning acute renal failure and liver damage are possible.
Therapeutic measures
Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and respiratory depression. Special measures such as forced diuresis, dialysis or haemo-perfusion are probably of no help in eliminating NSAIDs, including diclofenac, due to the high protein binding and extensive metabolism. Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life threatening overdose

Special Precautions For Disposal And Other Handling:
Do not use if injection is leaking, solution is cloudy or contains un-dissolved particles.
Do not break, crush or chew the tablet, swallow whole with water.

Shelf life
Tablets: 3 years
Injection: 2 years

Storage and Instructions
Tablets: Protect from heat, sunlight and moisture store between 15°C-30°C.
Injection: Protect from heat & sunlight, store in a cool and dry place at temperature 15°C-25°C.
The expiration date refer to the product correctly stored at the required condtion.
Do not break, crush on chew the tablet, swalllow whole with water.
Keep out of the reach of children.
Do not use if injection is leaking, solution is cloudy or contains un-dissolved particles.
Patients and healthcare professionals can also report suspected adverse drug reaction at
ade@bosch-pharma.com
To be sold on prescription of a registered medical practitioner only.

PRESENTATION:
Orthofenac 50mg Tablets: Cold form & Cold seal alu alu blister pack of 2x10's
Orthofenac SR 100mg Tablets: Cold form & Cold seal alu alu blister pack of 2x15's
Orthofenac 75mg/3ml Injection: Pack of 1x5's ampoules.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات:
انجکشن کو دھوپ اور گرمی سے محفوظ ٹھنڈی اور خشک جگہ پر ۱۵۔۲۵ ڈگری سینٹی گریڈ پر رکھیں۔
انجکشن لیک ہونے، دُھندلا ہونے یا اس میں کوئی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔
ٹیبلیٹس کو دھوپ، گرمی اور نمی سے محفوظ ۱۵۔۳۰ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان میں رکھیں۔
گولی کو توڑے یا چبائے بغیر پانی کے ساتھ نگل لیں۔ بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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