Moveryl®
(Celecoxib)

1. NAME OF THE PRODUCT
Moveryl® (Celecoxib) 100mg Capsules
Moveryl® (Celecoxib) 200mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Moveryl® **100mg Capsules**
Each capsule contains:
Celecoxib USP.....100mg

Moveryl® **200mg Capsules**
Each capsule contains:
Celecoxib USP.....200mg

3. PHARMACEUTICAL FORM
Capsule

Appearance:
Moveryl®**100mg Capsules:** Green opaque cap printed " ***Moveryl*** 100" and ivory opaque body printed "سامی" three times on them.

Moveryl® **200mg Capsules:** Dark blue opaque cap printed "***Moveryl*** 200" and light blue opaque body printed "سامی" three times on them.

4. CLINICAL PARTICULARS
4.1. THERAPEUTIC INDICATIONS:
Moveryl® is indicated in adults for the symptomatic relief in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. The decision to prescribe a selective cyclooxygenase-2 (COX-2) inhibitor should be based on an assessment of the individual patient's overall risks.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:
Posology:
As the cardiovascular risks of Celecoxib 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, especially in patients with osteoarthritis.

Osteoarthritis: The usual recommended daily dose is 200mg taken once daily or in two divided doses. In some patients, with insufficient relief from symptoms, an increased dose of 200mg twice daily may increase efficacy. In the absence of an increase in therapeutic benefit after two weeks, other therapeutic options should be considered.

Rheumatoid arthritis: The initial recommended daily dose is 200mg taken in two divided doses. The dose may, if needed, later be increased to 200mg twice daily. In the absence of an increase in therapeutic benefit after two weeks, other therapeutic options should be considered.

Ankylosing spondylitis: The recommended daily dose is 200mg taken once daily or in two divided doses. In a few patients, with insufficient relief from symptoms, an increased dose of 400mg once daily or in two divided doses may increase efficacy. In the absence of an increase in therapeutic benefit after two weeks, other therapeutic options should be considered. The maximum recommended daily dose is 400mg for all indications.

Special populations:

Elderly (>65 years): As in younger adults, 200mg per day should be used initially. The dose may, if needed, later be increased to 200mg twice daily. Particular caution should be exercised in elderly with a body weight less than 50kg.

Paediatric population: Celecoxib is not indicated for use in children.

CYP2C9 poor metabolisers: Patients who are known, or suspected to be CYP2C9 poor metabolisers based on genotyping or previous history/experience with other CYP2C9 substrates should be administered Celecoxib with caution as the risk of dose dependent adverse effects is increased. Consider reducing the dose to half the lowest recommended dose.

Hepatic impairment: Treatment should be initiated at half the recommended dose in patients with established moderate liver impairment with a serum albumin of 25-35g/l. Experience in such patients is limited to cirrhotic patients.

Renal impairment: Experience with Celecoxib in patients with mild or moderate renal impairment is limited, therefore such patients should be treated with caution.

Method of administration:

For oral use. Celecoxib may be taken with or without food. For patients who have difficulty swallowing capsules, the contents of a Celecoxib capsule can be added to applesauce, rice gruel, yogurt or mashed banana. To do so, the entire capsule contents must be carefully emptied onto a level teaspoon of cool or room temperature applesauce, rice gruel, yogurt or mashed banana and should be ingested immediately with 240ml of water. The sprinkled capsule contents on applesauce, rice gruel or yogurt are stable for up to 6 hours under refrigerated conditions (2-8°C). The sprinkled capsule contents on mashed banana should not be stored under refrigerated conditions and should be ingested immediately.

4.3. CONTRAINDICATIONS:

- Hypersensitivity to the active substance or to any of the excipients.
- Known hypersensitivity to sulphonamide.
- Active peptic ulceration or gastrointestinal (GI) bleeding.
- Patients who have experienced asthma, acute rhinitis, nasal polyps, angioneurotic oedema, urticaria or other allergic type reactions after taking acetylsalicylic acid (aspirin) or other NSAIDs including COX-2 inhibitors.
- In pregnancy and in women of childbearing potential unless using an effective method of contraception.
- Celecoxib has been shown to cause malformations in the two animal species studied. The potential for human risk in pregnancy is unknown, but cannot be excluded.
- Breast-feeding.
- Severe hepatic dysfunction (serum albumin <25 g/l or Child-Pugh score ≥10).
- Patients with estimated creatinine clearance <30ml/min.
- Inflammatory bowel disease.
- Congestive heart failure (NYHA II-IV).
- Established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Gastrointestinal (GI) effects: Upper and lower gastrointestinal complications [perforations, ulcers or bleedings (PUBs)], some of them resulting in fatal outcome, have occurred in patients treated with Celecoxib. Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or acetylsalicylic acid concomitantly, glucocorticoids, patients using alcohol, or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding. There is further increase in the risk of gastrointestinal adverse effects for Celecoxib (gastrointestinal ulceration or other gastrointestinal complications), when Celecoxib is taken concomitantly with acetylsalicylic acid (even at low doses).

Concomitant NSAID use: The concomitant use of Celecoxib and a non-aspirin NSAID should be avoided.

Cardiovascular effects: As the cardiovascular risks of Celecoxib may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. NSAIDs, including COX-2 selective inhibitors, have been associated with increased risk of cardiovascular and thrombotic adverse events when taken long-term. The exact magnitude of the risk associated with a single-dose has not been determined, nor has the exact duration of therapy associated with increased risk. The patient's need for

symptomatic relief and response to therapy should be re-evaluated periodically, especially in patients with osteoarthritis. Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with Celecoxib after careful consideration. COX-2 selective inhibitors are not a substitute for acetylsalicylic acid for prophylaxis of cardiovascular thrombo-embolic diseases because of their lack of antiplatelet effects. Therefore, antiplatelet therapies should not be discontinued.

Fluid retention and oedema: As with other drugs known to inhibit prostaglandin synthesis, fluid retention and oedema have been observed in patients taking Celecoxib. Therefore, Celecoxib should be used with caution in patients with history of cardiac failure, left ventricular dysfunction or hypertension, and in patients with pre-existing oedema from any other reason, since prostaglandin inhibition may result in deterioration of renal function and fluid retention. Caution is also required in patients taking diuretic treatment or otherwise at risk of hypovolemia.

Hypertension: As with all NSAIDS, Celecoxib can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. Therefore, blood pressure should be monitored closely during the initiation of therapy with Celecoxib and throughout the course of therapy.

Hepatic and renal effects: Compromised renal or hepatic function and especially cardiac dysfunction are more likely in the elderly and therefore medically appropriate supervision should be maintained. NSAIDs, including Celecoxib, may cause renal toxicity. Clinical trials with Celecoxib have shown renal effects similar to those observed with comparator NSAIDs. Patients at greatest risk for renal toxicity are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, ACE-inhibitors, angiotensin II receptor antagonists, and the elderly. Such patients should be carefully monitored while receiving treatment with Celecoxib. Some cases of severe hepatic reactions, including fulminant hepatitis (some with fatal outcome), liver necrosis and, hepatic failure (some with fatal outcome or requiring liver transplant), have been reported with Celecoxib. Among the cases that reported time to onset, most of the severe adverse hepatic events developed within one month after initiation of Celecoxib treatment. If during treatment, patients deteriorate in any of the organ system functions described above, appropriate measures should be taken and discontinuation of Celecoxib therapy should be considered.

CYP2D6 inhibition: Celecoxib inhibits CYP2D6. Although it is not a strong inhibitor of this enzyme, a dose reduction may be necessary for individually dose-titrated drugs that are metabolised by CYP2D6.

CYP2C9 poor metabolisers: Patients known to be CYP2C9 poor metabolisers should be treated with caution.

Skin and systemic hypersensitivity reactions: 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 Celecoxib. Patients appear to be at highest risk for 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. Serious hypersensitivity reactions (including anaphylaxis, angioedema and drug rash with eosinophilia and systemic symptoms (DRESS), or hypersensitivity syndrome), have been reported in patients receiving Celecoxib. Patients with a history of sulphonamide allergy or any drug allergy may be at greater risk of serious skin reactions or hypersensitivity reactions. Celecoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

General: Celecoxib may mask fever and other signs of inflammation.

Use with oral anticoagulants: In patients on concurrent therapy with warfarin, serious bleeding events, some of them fatal, have been reported. Increased prothrombin time (INR) with concurrent therapy has been reported. Therefore, this should be closely monitored in patients receiving warfarin/coumarin-type oral anticoagulants, particularly when therapy with Celecoxib is initiated or Celecoxib dose is changed. Concomitant use of anticoagulants with NSAIDS may increase the risk of bleeding. Caution should be exercised when combining Celecoxib with warfarin or other oral anticoagulants, including novel anticoagulants (e.g. apixaban, dabigatran, and rivaroxaban).

Sodium: This medicinal product contains less than 1mmol sodium (23mg) per capsule, that is to say essentially 'sodium-free'.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS:

Pharmacodynamic interactions:

Anticoagulants: Anticoagulant activity should be monitored particularly in the first few days after initiating or changing the dose of Celecoxib in patients receiving warfarin or other anticoagulants since these patients have an increased risk of bleeding complications. Therefore, patients receiving oral anticoagulants should be closely monitored for their prothrombin time INR, particularly in the first few days when therapy with Celecoxib is initiated or the dose of Celecoxib is changed. Bleeding events in association with increases in prothrombin time have been reported, predominantly in the elderly, in patients receiving Celecoxib concurrently with warfarin, some of them fatal.

Anti-hypertensives: NSAIDs may reduce the effect of anti-hypertensive medicinal products including ACE-inhibitors, angiotensin II receptor antagonists, diuretics and beta-blockers. As for NSAIDs, the risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients, patients on

diuretics, or elderly patients) when ACE inhibitors, angiotensin II receptor antagonists, and/or diuretics are combined with NSAIDs, including Celecoxib. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Ciclosporin and Tacrolimus: Co-administration of NSAIDs and ciclosporin or tacrolimus may increase the nephrotoxic effect of ciclosporin or tacrolimus, respectively. Renal function should be monitored when Celecoxib and any of these drugs are combined.

Acetylsalicylic acid: Celecoxib can be used with low-dose acetylsalicylic acid but is not a substitute for acetylsalicylic acid for cardiovascular prophylaxis.

Pharmacokinetic interactions:

Effects of Celecoxib on other drugs:

CYP2D6 Inhibition: Celecoxib is an inhibitor of CYP2D6. The plasma concentrations of drugs that are substrates of this enzyme may be increased when Celecoxib is used concomitantly. Examples of drugs which are metabolised by CYP2D6 are antidepressants (tricyclics and SSRIs), neuroleptics, anti-arrhythmic drugs, etc. The dose of individually dose-titrated CYP2D6 substrates may need to be reduced when treatment with Celecoxib is initiated or increased if treatment with Celecoxib is terminated. Concomitant administration of Celecoxib 200mg twice daily resulted in 2.6-fold and 1.5-fold increases in plasma concentrations of dextromethorphan and metoprolol (CYP2D6 substrates), respectively. These increases are due to Celecoxib CYP2D6 inhibition of the CYP2D6 substrate metabolism.

CYP2C19 Inhibition: In vitro studies have shown some potential for Celecoxib to inhibit CYP2C19 catalyzed metabolism. The clinical significance of this in vitro finding is unknown. Examples of drugs which are metabolised by CYP2C19 are diazepam, citalopram and imipramine.

Methotrexate: In patients with rheumatoid arthritis Celecoxib had no statistically significant effect on the pharmacokinetics (plasma or renal clearance) of methotrexate (in rheumatologic doses). However, adequate monitoring for methotrexate-related toxicity should be considered when combining these two drugs.

Lithium: In healthy subjects, co-administration of Celecoxib 200mg twice daily with 450mg twice daily of lithium resulted in a mean increase in C_{max} of 16% and in AUC of 18% of lithium. Therefore, patients on lithium treatment should be closely monitored when Celecoxib is introduced or withdrawn.

Oral contraceptives: In an interaction study, Celecoxib had no clinically relevant effects on the pharmacokinetics of oral contraceptives (1mg norethisterone/35µgrams ethinylestradiol).

Glibenclamide/tolbutamide: Celecoxib does not affect the pharmacokinetics of tolbutamide (CYP2C9 substrate), or glibenclamide to a clinically relevant extent.

Effects of other drugs on Celecoxib:

CYP2C9 Poor Metabolisers: In individuals who are CYP2C9 poor metabolisers and demonstrate increased systemic exposure to Celecoxib, concomitant treatment with CYP2C9 inhibitors such as fluconazole could result in further increases in Celecoxib exposure. Such combinations should be avoided in known CYP2C9 poor metabolisers.

CYP2C9 Inhibitors and Inducers: Since Celecoxib is predominantly metabolised by CYP2C9 it should be used at half the recommended dose in patients receiving fluconazole. Concomitant use of 200mg single dose of Celecoxib and 200mg once daily of fluconazole, a potent CYP2C9 inhibitor, resulted in a mean increase in Celecoxib C_{max} of 60% and in AUC of 130%. Concomitant use of inducers of CYP2C9 such as rifampicin, carbamazepine and barbiturates may reduce plasma concentrations of Celecoxib.

Ketoconazole and Antacids: Ketoconazole or antacids have not been observed to affect the pharmacokinetics of Celecoxib.

4.6. FERTILITY, PREGNANCY AND LACTATION:

Fertility: Based on the mechanism of action, the use of NSAIDs, including Celecoxib, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women.

Pregnancy: Celecoxib, as with other drugs inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester. Celecoxib is contraindicated in pregnancy and in women who can become pregnant. If a woman becomes pregnant during treatment, Celecoxib should be discontinued.

Breast-feeding: Celecoxib is excreted in the milk of lactating rats at concentrations similar to those in plasma. Administration of Celecoxib to a limited number of lactating women has shown a very low transfer of Celecoxib into breast milk. Women who take Celecoxib should not breast-feed.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Patients who experience dizziness, vertigo or somnolence while taking Celecoxib should refrain from driving or operating machinery.

4.8. UNDESIRABLE EFFECTS:

Adverse drug reactions from post-marketing surveillance as spontaneously reported during a period in which an estimated >70 million patients were treated with Celecoxib (various doses, durations, and indications). Even though these were identified as reactions from post-marketing reports, trial data were consulted to estimate frequency.

Frequencies are based on a cumulative meta-analysis with pooling of trials representing exposure in 38102 patients. The adverse effects are classified below by system organ class according to the following convention: 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), frequency not known.

Infections and infestations: ***Common:*** Sinusitis, upper respiratory tract infection, pharyngitis, urinary tract infection.

Blood and lymphatic system disorders: ***Uncommon:*** Anaemia. ***Rare:*** Leukopenia, thrombocytopenia. ***Very rare:*** Pancytopenia.

Immune system disorders: ***Common:*** Hypersensitivity. ***Very rare:*** Anaphylactic shock, anaphylactic reaction.

Metabolism and nutrition disorders: ***Uncommon:*** Hyperkalaemia

Psychiatric disorders: ***Common:*** Insomnia. ***Uncommon:*** Anxiety, depression, fatigue. ***Rare:*** Confusional state, hallucinations.

Nervous system disorders: ***Common:*** Dizziness, hypertonia, headache. ***Uncommon:*** Cerebral Infarction, paraesthesia, somnolence. ***Rare:*** Ataxia, dysgeusia. ***Very rare:*** Haemorrhage intracranial (including fatal intracranial haemorrhage), meningitis aseptic epilepsy (including aggravated epilepsy), ageusia, anosmia.

Eye disorders: ***Uncommon:*** Vision blurred, conjunctivitis. ***Rare:*** Eye haemorrhage. ***Very rare:*** Retinal artery occlusion, retinal vein occlusion.

Ear and labyrinth disorders: ***Uncommon:*** Tinnitus, hypoacusis.

Cardiac disorders: ***Common:*** Myocardial infarction. ***Uncommon:*** Cardiac failure, palpitations, tachycardia. ***Rare:*** Arrhythmia.

Vascular disorders: ***Very common:*** Hypertension (including aggravated hypertension). ***Rare:*** Pulmonary embolism, flushing. ***Very rare:*** Vasculitis.

Respiratory, thoracic, and mediastinal disorders: ***Common:*** Rhinitis, cough, dyspnoea. ***Uncommon:*** Bronchospasm. ***Rare:*** Pneumonitis.

Gastrointestinal disorders: ***Common:*** Nausea, abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dysphagia. ***Uncommon:*** Constipation, gastritis, stomatitis, gastrointestinal inflammation (including aggravation of gastrointestinal inflammation), eructation. ***Rare:*** Gastrointestinal haemorrhage, duodenal ulcer, gastric ulcer, oesophageal ulcer, intestinal ulcer, and large intestinal ulcer; intestinal perforation; oesophagitis, melaena; pancreatitis, colitis.

Hepatobiliary disorders: ***Uncommon:*** Hepatic function abnormal, hepatic enzyme increased (including increased SGOT and SGPT). ***Rare:*** Hepatitis. ***Very rare:*** Hepatic failure (sometimes fatal or requiring liver transplant), hepatitis fulminant (some with fatal outcome), hepatic necrosis, cholestasis, hepatitis cholestatic, jaundice.

Skin and Subcutaneous tissues disorders: ***Common:*** Rash, pruritus (includes pruritus generalized). ***Uncommon:*** Urticaria, ecchymosis. ***Rare:*** Angioedema, alopecia, photosensitivity. ***Very rare:*** Dermatitis exfoliative,

erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), dermatitis bullous.

Musculoskeletal and connective tissue disorders: ***Common:*** Arthralgia. ***Uncommon:*** Muscle spasms (leg cramps). ***Very rare:*** Myositis.

Renal and urinary disorders: ***Uncommon:*** Blood creatinine increased; blood urea increased. ***Rare:*** Renal failure acute, hyponatraemia. ***Very rare:*** Tubulointerstitial nephritis, nephrotic syndrome, glomerulonephritis minimal lesion.

Reproductive system and breast disorders: ***Rare:*** Menstrual disorder. ***Not known:*** Female (female fertility decreased).

General disorders and administration site conditions: ***Common:*** Influenza-like illness, oedema peripheral/ fluid retention. ***Uncommon:*** Face oedema, chest pain

Injury, poisoning and procedural complications: ***Common:*** Injury (accidental Injury).

4.9. OVERDOSE:

There is no clinical experience of overdose. Single doses up to 1200mg and multiple doses up to 1200mg twice daily have been administered to healthy subjects for nine days without clinically significant adverse effects. In the event of suspected overdose, appropriate supportive medical care should be provided e.g. by eliminating the gastric contents, clinical supervision and, if necessary, the institution of symptomatic treatment. Dialysis is unlikely to be an efficient method of drug removal due to high protein binding.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic drugs, NSAIDs, Coxibs.

ATC code: M01AH01.

Mechanism of action: Celecoxib is an oral, selective, cyclooxygenase-2 (COX-2) inhibitor within the clinical dose range (200-400mg daily).

Cyclooxygenase is responsible for generation of prostaglandins. Two isoforms, COX-1 and COX-2, have been identified. COX-2 is the isoform of the enzyme that has been shown to be induced by pro-inflammatory stimuli and has been postulated to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation, and fever. COX-2 is also involved in ovulation, implantation and closure of the ductus arteriosus, regulation of renal function, and central nervous system functions (fever induction, pain perception and cognitive function). It may also play a role in ulcer healing. COX-2 has been identified in tissue around gastric ulcers in human but its relevance to ulcer healing has not been established. The difference in antiplatelet activity between

some COX-1 inhibiting NSAIDs and COX-2 selective inhibitors may be of clinical significance in patients at risk of thrombo-embolic reactions. COX-2 selective inhibitors reduce the formation of systemic (and therefore possibly endothelial) prostacyclin without affecting platelet thromboxane. Celecoxib is a diaryl-substituted pyrazole, chemically similar to other non-arylamine sulfonamides (e.g. thiazides, furosemide) but differs from arylamine sulfonamides (e.g. sulfamethoxizole and other sulfonamide antibiotics). A dose dependent effect on TxB2 formation has been observed after high doses of Celecoxib. However, in healthy subjects, in small multiple dose studies with 600mg BID (three times the highest recommended dose) Celecoxib had no effect on platelet aggregation and bleeding time compared to placebo.

5.2. PHARMACOKINETICS:

Absorption: Celecoxib is well absorbed reaching peak plasma concentrations after approximately 2-3 hours. Dosing with food (high fat meal) delays absorption of Celecoxib by about 1 hour resulting in a T_{max} of about 4 hours and increases bioavailability by about 20%. In healthy adult volunteers, the overall systemic exposure (AUC) of Celecoxib was equivalent when Celecoxib was administered as intact capsule or capsule contents sprinkled on applesauce. There were no significant alterations in C_{max}, T_{max} or $T_{1/2}$ after administration of capsule contents on applesauce.

Distribution: Plasma protein binding is about 97% at therapeutic plasma concentrations and the drug is not preferentially bound to erythrocytes.

Biotransformation: Celecoxib metabolism is primarily mediated via cytochrome P450 2C9. Three metabolites, inactive as COX-1 or COX-2 inhibitors, have been identified in human plasma i.e., a primary alcohol, the corresponding carboxylic acid and its glucuronide conjugate. Cytochrome P450 2C9 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity, such as those homozygous for the CYP2C9*3 polymorphism.

Elimination: Celecoxib is mainly eliminated by metabolism. Less than 1% of the dose is excreted unchanged in urine. The intersubject variability in the exposure of Celecoxib is about 10-fold. Celecoxib exhibits dose and time-independent pharmacokinetics in the therapeutic dose range. Elimination half-life is 8- 12 hours. Steady state plasma concentrations are reached within 5 days of treatment.

5.3. PRECLINICAL SAFETY DATA:

Non-clinical safety data revealed no special hazard for humans based on conventional studies of repeated dose toxicity, mutagenicity or carcinogenicity. Celecoxib at oral doses ≥ 150mg/kg/day (approximately 2-fold human exposure at 200mg twice daily as measured by AUC0-24), caused an increased incidence of ventricular septal defects, a rare event, and foetal alterations, such

as ribs fused, sternebrae fused and sternebrae misshapen when rabbits were treated throughout organogenesis. A dose-dependent increase in diaphragmatic hernias was observed when rats were given celecoxib at oral doses ≥ 30mg/kg/day (approximately 6-fold human exposure based on the AUC0-24 at 200mg twice daily) throughout organogenesis. These effects are expected following inhibition of prostaglandin synthesis. In rats, exposure to celecoxib during early embryonic development resulted in pre-implantation and post-implantation losses, and reduced embryo/foetal survival. Celecoxib was excreted in rat milk. In a peri-post natal study in rats, pup toxicity was observed. In a two-year toxicity study, an increase in nonadrenal thrombosis was observed in male rat at high doses.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:

***Moveryl*® 100mg Capsules:**

- Sodium starch glycolate
- Dicalcium phosphate dihydrate
- Polyvinyl pyrrolidone
- Sodium lauryl sulphate
- Magnesium stearate
- Purified water
- Hard gelatine capsule

***Moveryl*® 200mg Capsules:**

- Sodium starch glycolate
- Polyvinyl pyrrolidone
- Sodium lauryl sulphate
- Magnesium stearate
- Purified water
- Hard gelatine capsule

6.2. INCOMPATIBILITIES:

Not applicable.

6.3. SHELF LIFE:

See expiry on the pack.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

Avoid exposure to heat, light and humidity. Store between 15 to 30°C.
Improper storage may deteriorate the medicine.
Keep out of reach of children.

6.5. NATURE AND CONTENTS OF CONTAINER:

***Moveryl*® 100mg Capsules:** Alu/PVC blister, pack size is 30's.
***Moveryl*® 200mg Capsules:** Alu/PVC blister, pack size is 30's.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL OF A USED PRODUCT:

No special requirement.

6.7. DRUG PRODUCT SPECIFICATIONS:

***Moveryl*® 100mg Capsules:** BP Specs.
***Moveryl*® 200mg Capsules:** BP Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharma.com
Mfg Lic. No. 000072

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

***Moveryl*® 100mg Capsules:** 029771
***Moveryl*® 200mg Capsules:** 029772

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

***Moveryl*® 100mg Capsules:** 12th March, 2003
***Moveryl*® 200mg Capsules:** 12th March, 2003

10. DATE OF REVISION OF THE TEXT

موورل کیپسول
(سیلیکوکسِب)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو گرمی، روشنی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری

سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی۔