DOMI INJECTION

DESCRIPTION: A clear colourless to yellowish solution.

COMPOSITION:
DOMI INJ 5 MG (1 ML AMP) : Each ml contains Midazolam HCl equivalent to Midazolam 5mg
DOMI INJ 15 MG (3 ML AMP) : Each ml contains Midazolam HCl equivalent to Midazolam 5mg
DOMI INJ 5 MG (5 ML AMP) : Each ml contains Midazolam HCl equivalent to Midazolam 1mg

PHARMACODYNAMICS: Midazolam is a drug acting on psychic function, behaviour, or experience which alters the mental state by affecting the neurophysiological and biochemical activity of the functional units of the CNS, or in the pharmacological sense, as narcotics.
Benzodiazepines appear to intensify the physiological inhibitory mechanisms mediated by gamma-aminobutyric acid (GABA), the most common inhibitory neurotransmitter in the brain. The effects of Midazolam on the CNS are dependent on the dose administered, the route of administration and the presence or absence of other premedications. Onset time of sedative effects after I.M. administration is 15 minutes, with peak sedation occurring 30-60 minutes following injection. When used intravenously as a sedative for endoscopic or other short therapeutic or diagnostic procedures, the end point of slurred speech can be attained within 2.8 to 4.8 minutes, depending on the total dose administered and whether or not preceded by narcotic premedications. The time to ind uction of anaesthesia for surgical procedures is variable occurring in approximately 1.5 minutes (0.3 – 8 minutes) when an opioid premedicant has been administered and in 2 to 2.5 minutes without premedication or with a sedative premedication. Approximately 2 hours is required for full recovery from Midazolam induced anaesthesia: however duration of effect is dependent on the dose and other drugs used. Induction of anaesthesia is unsuccessful in approximately 14% of patients with Midazolam alone but in only about 1% when given with an opioid. At doses sufficient to induce sedation, intravenous Midazolam decreases the sensitivity of the ventilatory response to elevated CO_2 tension in normal subjects and in those with chronic obstructive lung disease. The latter are of course at special risk of hypoxia. Sedation with Midazolam has no adverse effects on pulmonary compliance and does not cause bronchoconstriction or significantly affect functional residual capacity or residual volume. Although Midazolam may cause modest decreases in mean arterial pressure, baroreceptor response is not affected and decreases in arterial pressure are accompanied by increases in heart rate. Intravenous Midazolam at doses of 0.15 to 0.2 mg/kg did not have deleterious effects on cardiac haemodynamics. Intravenous administration of Midazolam does not alter intracranial pressure unless the patient is intubated. As with thiopentone, the intracranial pressure rises during intubation. Cerebral blood flow may be reduced by up to 35% which is of the same order as caused by equivalent doses of diazepam. The effect on cerebral metabolism is not clearly established. Midazolam reduces the intraocular pressure to the same degree as thiopentone and diazepam. However, the increase in intraocular pressure after succinylcholine administration or endotracheal intubation is not prevented by Midazolam, thiopentone or diazepam. The pharmacokinetic profile of Midazolam in man is linear over the 0.05 to 0.4 mg/kg dose range. In normal subjects the drug exhibited a short elimination half-life (1 to 2.8 hours), a large volume of distribution (0.8 to 1.86 L/kg) and a rapid plasma clearance (0.24 to 0.73 L/hr/kg).

PHARMACOKINETICS: Pharmacokinetics in special clinical situations: In some intensive care patients, and in some elderly patients given Midazolam i.v. infusion for prolonged sedation, the elimination half-life was found to increase by up to six times. Particular risk factors include being elderly, abdominal pathology, sepsis and poor renal function. In these patients infusion at an unchanged rate resulted in higher plasma levels at steady state. Consequently, the infusion rate should be reduced once a satisfactory clinical response has been obtained.
Bioavailability: The mean absolute bioavailability of Midazolam following I.M. administration is greater than 90%. The mean time of maximum Midazolam plasma concentrations following I.M. dosing occurs within 45 minutes post-administration. Peak concentrations of Midazolam after I.M. administration are about one-half of those achieved after equivalent I.V. doses.
Metabolism: Less than 0.03% is excreted in the urine as intact Midazolam. The drug is rapidly metabolised to 1-hydroxymethyl Midazolam which is conjugated with subsequent excretion in the urine. The half- life of elimination of the active metabolite is similar to Midazolam. The concentration of Midazolam is 10 to 30 fold greater than that of 1-hydroxymethyl Midazolam. Protein binding: 97% of Midazolam becomes bound to plasma proteins. The extent of protein binding does not vary in renal failure.

INDICATION: Intravenously as an agent for conscious sedation prior to short surgical, diagnostic, therapeutic or endoscopic procedures, such as bronchoscopy, gastroscopy, cystoscopy, coronary angiography and cardiac catheterization, either alone or in conjunction with a narcotic. Intravenously for induction of anaesthesia, preliminary to administration of other anaesthetic agents. With the use of a narcotic premedicant, induction of anaesthesia can be attained with a narrower dose range and in a shorter period of time. Sedation in intensive care units by intravenous intermittent administration or continuous infusion. Intramuscularly for preoperative sedation (induction of sleepiness or drowsiness and relief of apprehension) and to impair memory of perioperative events.

RECOMMENDED DOSAGE: Dosage should be individualized and drug should be administered slowly. Lower doses may be required in elderly or debilitated patients or in patients with hepatic or renal insufficiency. Because serious and life-threatening cardiorespiratory adverse events have been reported, provision for monitoring, detection and correction of these reactions must be made for every patient to whom Midazolam injection is administered, regardless of age or health status. The dosage of Midazolam administered should be adjusted according to the type and amount of premedication used.
Intravenously: Midazolam should be administered slowly.
Endoscopic or Cardiovascular Procedures: For conscious sedation, Midazolam can be used either alone or together with a narcotic immediately before the procedure with supplemental doses to maintain the desired level of sedation throughout the procedure. For perioral procedures, the use of an appropriate topical anaesthetic is recommended. For bronchoscopic procedures, the use of a narcotic premedicant is recommended. Individual response will vary with age, physical stature, and concomitant medications, but may also vary independent of these factors.
Titrate dosage to desired sedative end point, such as slurring of speech, with slow administration immediately prior to the procedure. The initial dose should be given over a period of at least 2 minutes. Wait an additional 2 or more minutes to fully evaluate the sedative effect.
When titrating the dose 2 or more minutes should be allowed after each increment.
In healthy adults the initial dose is approximately 2.5 mg. Some patients may respond to as little as 1 mg. Further doses of 1 mg may be given if necessary. A total dose greater than 5 mg is not usually necessary to reach the desired end point.
In cases of severe illness and in elderly patients the initial dose must be reduced to 1 to 1.5 mg. Total doses greater than 3.5 mg are not usually necessary. If a narcotic premedicant or other CNS depressant is used the dose of Midazolam should be lowered by 25% to 30%.
Induction of Anaesthesia: The dosage of Midazolam should be determined by the response of the individual patient. Administration should be by slow intravenous injection until consciousness is lost using approximately 0.15 – 0.2 mg/kg (10 – 15 mg) administered at a rate of approximately 2.5 mg per 10 seconds. Maximum sedation is usually reached after 2-3 minutes but if required a further dose up to a total of 0.35 mg/kg may be administered.
The onset of sedation has not been found to be dose-dependent but the time to recovery is related to the amount of drug administered. Midazolam should be used with narcotic analgesics as it does not have analgesic properties and narcotic analgesics enhance its anaesthetic inducing properties.
Intravenous sedation in ICU: For sedation in ICU, the recommended infusion rate is 0.03-0.2 mg/kg/hour. The dosage should be individualized and Midazolam titrated to the desired state of sedation according to the clinical need, physical status, age and concomitant medication. It may be possible to reduce the dose (infusion rate) once the therapeutic effect has been obtained.
The dosage should be reduced in hypovolaemic, vasoconstricted and hypothermic patients.
After prolonged i.v. administration of Midazolam, abrupt discontinuation of the product may be accompanied by withdrawal symptoms. Therefore, a gradual reduction of Midazolam is recommended. Midazolam can be used in neurosurgical patients with increased intracranial pressure.
Intramuscularly: For preoperative sedation: (induction of sleepiness or drowsiness and relief of apprehension) and to impair memory of perioperative events. For intramuscular use, Midazolam should be injected deep in large muscle mass.
The recommended premedication dose of Midazolam for good risk (ASA Physical I & II) adult patients below the age of 60 years is 0.07 to 0.08 mg/kg I.M. (approximately 5 mg I.M.) administered approximately one hour before surgery.
The dose must be individualized and reduced when I.M. Midazolam is administered to patients with chronic obstructive pulmonary disease, and other higher risk surgical patients, patients 60 or more years of age, and patients who have received concomitantly narcotics or other CNS depressants (see also Adverse Reactions). In a study of patients 60 years or older who did not receive concomitant administration of narcotics, 2 to 3 mg (0.02 to 0.05 mg/kg) of Midazolam produced adequate sedation during the preoperative period. In approximately 25% of patients 1 mg provided satisfactory sedation. As with any potential respiratory depressant, these patients require special observation for signs of cardio-respiratory depression after receiving I.M. Midazolam.
Onset is within 15 minutes, peaking at 30 to 60 minutes. It can be administered concomitantly with atropine sulphate or scopolamine hydrochloride and reduced doses of narcotics.
Dilution and Admixture: Midazolam may be mixed in the same syringe with frequently used premedicants: morphine sulphate, pethidine, atropine sulphate or scopolamine. Midazolam is compatible with saline, glucose 5% and 10% in water, Ringer's solution and compound sodium lactate intravenous infusion (Hartmann's solution). The 15mg/3mL, 5mg/mL, and 5mg/5mL formulations may be diluted to facilitate slow injection.

ROUTE OF ADMINISTRATION: For deep i.m. and i.v. injection.

CONTRAINDICATIONS: Myasthenia gravis, hypersensitivity to benzodiazepines. Midazolam should not be administered to patients in shock or coma, or in acute alcoholic intoxication with depression of vital signs. Benzodiazepines are contraindicated in patients with acute narrow angle glaucoma.

WARNINGS & PRECAUTIONS: Anaphylaxis (Severe allergic reaction) and angioedema (severe facial swelling), which can occur as early as the first time the product is taken. Complex Sleep – Related behaviours which may include sleep driving, making phone calls, preparing and eating food (while asleep).
Intravenous Midazolam should only be used in settings with equipment and skilled personnel for continuous monitoring of cardiorespiratory function and resuscitation procedures. Patients should be continuously monitored for early signs of underventilation or apnoea. Vital signs should continue to be monitored during the recovery period. During intravenous application of Midazolam respiratory depression, apnoea, respiratory arrest and/or cardiac arrest have occurred. In some cases where this was not recognised promptly and treated, hypoxic encephalopathy or death has resulted. These life-threatening incidents may occur especially in elderly patients or patients with pre-existing respiratory insufficiency, especially if the injection is given too rapidly or with excessive doses. Particular care must be used in administering the drug by the IV route to the elderly to very ill patients, high risk surgical patients and to those with significant hepatic impairment, chronic renal insufficiency, or with limited pulmonary reserve because of the possibility that apnoea or respiratory depression may occur. These patients require lower doses whether premedicated or not.
Patients with chronic obstructive pulmonary disease are unusually sensitive to the respiratory depressant effect of Midazolam.
Elderly patients frequently have inefficient function of one or more organ systems and dosage requirements have been shown to be reduced with age. Patients with chronic renal failure and patients with congestive heart failure eliminate Midazolam more slowly.

In some intensive care patients, and in some elderly patients given Midazolam by i.v. infusion for prolonged sedation, the elimination half-life was found to increase by up to six times. (see ***Pharmacokinetics in special situations***).
Particular care should be exercised in the use of intravenous Midazolam in patients with uncompensated acute illnesses, such as severe fluid or electrolyte disturbances.
There have been rare reports of hypotensive episodes requiring treatment during or after diagnostic or surgical manipulations in patients who have received Midazolam. Hypotension occurred more frequently in the conscious sedation studies in patients premedicated with a narcotic.
After prolonged i.v. administration of Midazolam, abrupt discontinuation of the product may be accompanied by withdrawal symptoms. Therefore, a gradual reduction of Midazolam is recommended.
Reactions such as agitation, involuntary movements (including tonic/clonic movements and muscle tremor), hyperactivity and combativeness have been reported. These reactions may be due to inadequate or excessive dosing or improper administration of Midazolam; however, consideration should be given to the possibility of cerebral hypoxia or true paradoxical reactions. Should such reactions occur, the response to each dose of Midazolam and all other drugs, including local anaesthetics, should be evaluated before proceeding.
The hazards of intra-arterial injection of Midazolam solutions into humans are unknown; therefore precautions against unintended intra-arterial injection should be taken. Extravasation should also be avoided. After parenteral administration of Midazolam patients should not be discharged from hospital for at least three hours, and then, if possible, only if accompanied by a responsible person. The decision as to when patients may again engage in activities requiring complete mental alertness, operate hazardous machinery or drive a motor vehicle must be individualized. Gross tests of recovery from the effects of Midazolam cannot be relied upon to predict reaction time under stress. When Midazolam is used with other drugs during anaesthesia, the contribution of these can vary and should also be considered.
Patients should be warned to take extra care as a pedestrian and not to drive a vehicle or operate a machine until the effects of the drug, such as drowsiness, have subsided or until the day after anaesthesia and surgery, whichever is longer. The patient's attendants should be made aware that the patient anterograde amnesia may persist longer than the sedation and therefore patients may not carry out instructions even though they appear to acknowledge them.
Carcinogenesis: Midazolam maleate was administered with diet in mice and rats for 2 years at dosage of 1, 9 and 80 mg/kg/day. In female mice in the highest dose group there was a marked increase in the incidence of hepatic tumours. In high dose male rats there was a small but statistically significant increase in benign thyroid follicular cell tumours. Dosage of 9 mg/kg/day of Midazolam maleate do not increase the incidence of tumours. The pathogenesis of induction of these tumours is not known. These tumours were found after chronic administration, whereas human use will ordinarily be of single dose or of short duration.
Mutagenesis: Midazolam did not have mutagenic activity in Salmonella typhimurium (5 bacterial strains), Chinese hamster lung cells (V79), human lymphocytes, or in the micronucleus test in mice.
PRECAUTIONS: Midazolam does not protect against the increase in intracranial pressure or against the heart rate rise and/or blood pressure rise associated with endotracheal intubation under light general anaesthesia. The use of a narcotic premedicant is recommended for bronchoscopies. Administration of a muscle relaxant may sometimes be necessary to overcome Midazolam associated hiccoughs. As with other benzodiazepines Midazolam may have the potential to cause dependence.
Some published studies in children have observed cognitive deficits after repeated or prolonged exposures to anaesthetic/sedative agents early in life. These studies have substantial limitations, and it is not clear if the observed effects are due to the anaesthetic/sedation drug administration or other factors such as the surgery or underlying illness.

Risks from Concomitant Use with Opioids
Profound sedation, respiratory depression, coma, and death may result from the concomitant use of Domi Injection with opioids. Observational studies have demonstrated that concomitant use of opioids and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
If the decision is made to newly prescribe a benzodiazepine and an opioid together, prescribe the lowest effective dosages and minimum durations of concomitant use.
If the decision is made to prescribe a benzodiazepine in a patient already receiving an opioid, prescribe a lower initial dose of the benzodiazepine than indicated in the absence of an opioid, and titrate based on clinical response.
If the decision is made to prescribe an opioid in a patient already taking a benzodiazepine, prescribe a lower initial dose of the opioid, and titrate based on clinical response.
Follow patients closely for signs and symptoms of respiratory depression and sedation. Advise both patients and caregivers about the risks of respiratory depression and sedation when Domi Injection is used with opioids. Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of opioids (see Drug Interactions).

IV Midazolam has been associated with severe respiratory depression and respiratory arrest, especially when used for conscious sedation. In some cases, where this was not recognized promptly and treated effectively, death or hypoxic encephalopathy resulted. IV Midazolam should be used only in hospital or ambulatory care settings that provide for continuous monitoring of respiratory and cardiac functions. Assure immediate availability of resuscitative drugs, equipments, appropriate antidote and personnel trained in their use. Dosage of IV Midazolam must be individualized for each patient. Lower doses are usually required for elderly, debilitated or higher risk surgical patients. When Midazolam is administered intravenously for conscious sedation, it should be injected slowly (over at least 2 minutes); it should not be administered by rapid or single bolus IV injection because of respiratory depression and/or arrest, especially in elderly or debilitated patients. The initial dose may be as little as 1mg, but should not exceed 2.5mg in a normal healthy adult; administer over at least 2 minutes and allow additional 2 or more minutes to fully evaluate sedative effect. If further titration is necessary, use small increments to the appropriate level of sedation, allowing an additional 2 or more minutes after each increments to fully evaluate sedative effect. See Dosage and Administration for complete dosing information.

INTERACTION WITH OTHER MEDICAMENTS: Midazolam can enhance the central sedative effect of neuroleptics, tranquillisers, antidepressants, sleep-inducing drugs, analgesics and anaesthetics. This potentiation of effect can in certain cases be of advantage therapeutically.
Concomitant use of barbiturates, alcohol or other central nervous system depressants increases the risk of underventilation or apnoea and may contribute to a profound and/or prolonged drug effect. When Midazolam is used with a narcotic analgesic, the dosage of both agents should be reduced. Narcotic premedication also reduces the ventilatory response to carbon dioxide stimulation. The sedative effect of intravenous Midazolam is accentuated by premedication. Consequently, the dosage of Midazolam should be adjusted according to the type and amount of premedication administered. A moderate reduction in induction dosage requirements of thiopentone (about 15%) has been noted following use of intramuscular Midazolam for premedications. Simultaneous administration of cimetidine (but not ranitidine) has been reported to reduce clearance of Midazolam. The intravenous administration of Midazolam decreases the minimum alveolar concentration (MAC) of halothane required for general anaesthesia. This decrease correlates with the dose of Midazolam administered. The effects of Midazolam can be reversed by the benzodiazepine antagonist flumazenil.
There is potentially relevant interaction between Midazolam and compounds which inhibit certain hepatic enzymes (particularly cytochrome P450 III A). Therefore patients receiving compounds which inhibit P450 III A together with Midazolam should be monitored carefully for the first few hours after administration of Midazolam.

Opioids
Due to additive pharmacologic effect, the concomitant use of opioids with benzodiazepines increases the risk of respiratory depression, profound sedation, coma and death.
The concomitant use of opioids and benzodiazepines increases the risk of respiratory depression because of actions at different receptor sites in the central nervous system that control respiration. Opioids interact primarily at μ-receptors, and benzodiazepines interact at GABAA sites. When opioids and benzodiazepines are combined, the potential for benzodiazepines to significantly worsen opioid-related respiratory depression exists.
Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate (see ***Warnings and Precautions***).
Limit dosage and duration of concomitant use of benzodiazepines and opioids, and follow patients closely for respiratory depression and sedation.

USE IN PREGNANCY & LACTATION:
Use in Pregnancy: Midazolam crosses the placenta and other benzodiazepines given in the last weeks of pregnancy have resulted in neonatal CNS depression. Therefore, the risk benefit must be carefully considered when using Midazolam.
Teratological studies with Midazolam in a number of animal species have not shown association between administration of the drug and disturbances of foetal development, nor has clinical experience so far yielded any evidence of such an association.
Published animal studies of some anaesthetic/sedation drugs have reported adverse effects on brain development in early life and late pregnancy. These studies have demonstrated that anaesthetic and sedation drugs that block N-methyl-D-aspartate (NMDA) receptors and/or potentiate gamma-aminobutyric acid (GABA) activity during the period of rapid brain growth or synaptogenesis may result in neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis when used for longer than 3 hours. The clinical significance of these non-clinical findings is yet to be determined. However, based on comparisons across species, the window of vulnerability to these changes is believed to correlate with exposures in the third trimester through the first several months of life, but may extend out to approximately 3 years of age in humans.
Use in Lactation: Midazolam may pass into breast milk and caution should be exercised with its use in lactating mothers.

SIDE EFFECTS: Adverse Reactions: (see Warnings). Fluctuations in vital signs have been noted following parenteral administration of Midazolam and include respiratory depression (22.9% following IV administration and 10.8% of patients following I.M. administration) and apnoea (19% following IV administration), as well as variations in blood pressure and pulse rate. The common occurrences during anaesthesia and surgery are affected by the lightening or deepening of anaesthesia, instrumentation, intubation and use of concomitant drugs.
Administration of I.M. Midazolam to elderly and/or higher risk surgical patients has been associated with rare reports of death under circumstances compatible with cardiorespiratory depression. In most of these cases, the patients also received other central nervous system depressants capable of depressing respiration, especially narcotics (see also ***Dosage and Administration***).
The following additional adverse reactions were reported after intramuscular administration: headache (1.3%), local effects at intramuscular injection site: pain (3.7%), induration (0.5%), redness (0.5%), muscle stiffness (0.3%).
The following additional adverse reactions were reported subsequent to intravenous administration: hiccoughs (5.5%), nausea (3%), vomiting (2.9%), coughing (1.9%), oversedation (1%), drowsiness (1.3%), local effects at the IV site: tenderness (7%), pain during injection (6.2%), redness (3.8%), induration (1.9%), phlebitis (0.5%).
Other adverse experiences, mainly following IV injection and occurring at an incidence of less than 1%, are as follows: Respiratory: Laryngospasm, bronchospasm, dyspnea, hyperventilation, wheezing, shallow respirations, airway obstruction, tachypnea.
Cardiovascular: Bigeminy, premature ventricular contractions, tachycardia, nodal rhythm, cardiovascular collapse, vasovagal episode, cardiac arrest.
Gastrointestinal: Acid taste, excessive salivation, retching.
CNS/Neuromuscular: Anterograde amnesia, headache, euphoria, confusion, argumentativeness, nervousness, agitation, anxiety, grogginess, irritability, restlessness, emergence delirium or agitation, prolonged emergence from anaesthesia, dreaming during emergence, sleep disturbance, insomnia, nightmares, tonic/clonic movements, muscle tremor, involuntary movements, athetoid movements,

dizziness, ataxia, dysphoria, slurred speech, dysphonia, paraesthesia.
Ophthalmic: Blurred vision, diplopia, nystagmus, pinpoint pupils, cyclic movements of eyelids, difficulty in focusing.
Integumentary: Hives, hive-like elevation at injection site, swelling or feeling of burning, warmth or coldness at injection site, erythema, rash, pruritus.
Hypersensitivity: In isolated cases, generalized hypersensitivity including anaphylactic reactions and skin reactions have been reported.
Miscellaneous: Yawning, lethargy, chills, weakness, continued phonation, ears blocked, loss of balance, light-headedness, toothache, faint feeling, haematoma.

SYMPTOMS AND TREATMENT OF OVERDOSE: **Overdosage: Symptoms of overdosage:** The manifestations of Midazolam overdosage are similar to those observed with the other benzodiazepines, including sedation, somnolence, confusion, impaired coordination, diminished reflexes, coma and untoward effects on vital signs and cerebrovascular perfusion. Hepatic function should be monitored.
Treatment of overdosage: Treatment of Midazolam overdosage is the same as that followed for overdosage with other benzodiazepines. Respiration, pulse rate and blood pressure should be monitored and general supportive measures should be employed. Flumazenil can be used to reverse the effects of Midazolam. Intravenous fluid s should be administered and an adequate airway maintained. Hypotension may be combated by the judicious use of other accepted antihypotensive measures. There is no information as to whether peritoneal dialysis, forced diuresis or haemodialysis are of any value in the treatment of overdosage.

INCOMPATIBILITIES:
Midazolam solution for injection or infusion must not be diluted with 6% w/v dextran (with 0.9% sodium chloride) in glucose. Midazolam solution for injection or infusion must not be mixed with alkaline solutions for injection. Midazolam precipitates in solutions containing hydrogen carbonate. This medicinal product must not be diluted with other medicinal products except those mentioned in ***Recommended Dosage (Dilution and Admixture)*** section.

STORAGE CONDITIONS:
Store below 30ºC. Protect from light.
Admixtures of Midazolam Hydrochloride in compatible infusion solutions do not require protection from light for short term storage and administration.
Domi Injection when mixed with 500ml infusion fluids is chemically and physically stable for up to 24 hours at 30°C and up to 72 hours at 2 to 8°C.
KEEP OUT OF REACH OF CHILDREN. *JAUHKAN DARIPADA KANAK-KANAK.*

SHELF LIFE:
Please refer to outer package.

PACK SIZE:
3ml ampoule in box of 10's
5ml ampoule in box of 10's and 50's
1ml ampoule in box of 10's

PRODUCT REGISTRATION HOLDER & MANUFACTURER:
DUOPHARMA (M) SDN BHD
Lot 2599, Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.