Psychiatric disorders:
Rare: hallucinations, confusion, sleep disturbance, delirium, anxiety and nightmares. Psychic adverse reactions may occur following administration of tramadol which vary individually in intensity and nature (depending on personality and duration of treatment). These include changes in mood (usually elation, occasionally dysphoria), changes in activity (usually suppression, occasionally increase) and changes in cognitive and sensorial capacity (e.g. decision behaviour, perception disorders). Drug dependence may occur.
Symptoms of drug withdrawal syndrome, similar to those occurring during opiate withdrawal, may occur as follows: agitation, anxiety, nervousness, insomnia, hyperkinesia, tremor and gastrointestinal symptoms. Other symptoms that have very rarely been seen with tramadol discontinuation include: panic attacks, severe anxiety, hallucinations, paraesthesias, tinnitus and unusual CNS symptoms (i.e. confusion, delusions, depersonalisation, derealisation, paranoia).

Eye disorders:
Rare: miosis, mydriasis, blurred vision
Gastrointestinal disorders:
Very common: nausea
Common: vomiting, constipation, dry mouth
Uncommon: retching; gastrointestinal discomfort (a feeling of pressure in the stomach, bloating), diarrhoea

Skin and subcutaneous tissue disorders:
Common: hyperhidrosis
Uncommon: dermal reactions (e.g. pruritus, rash, urticaria)
Musculoskeletal and connective tissue disorders:
Rare: motorial weakness

Hepatobiliary disorders:
In a few isolated cases an increase in liver enzyme values has been reported in a temporal connection with the therapeutic use of tramadol.

Renal and urinary disorders:
Rare: micturition disorders (dysuria and urinary retention)

Immune system disorders:
Rare: allergic reactions (e.g. dyspnoea, bronchospasm, wheezing, angioneurotic oedema) and anaphylaxis

Metabolism and nutrition disorders:
Not known: hypoglycaemia

General disorders:
Common: fatigue

Postmarketing Experience:
Serotonin syndrome (See Warnings and Precautions)
Adrenal insufficiency (See Warnings and Precautions)
Androgen deficiency: Cases of androgen deficiency have occurred with chronic use of opioids. Chronic use of opioids may influence the hypothalamic pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date. Patients presenting with symptoms of androgen deficiency should undergo laboratory evaluation.
Infertility: Chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible.

Symptoms and Treatment of Overdose
Symptoms
In principle, on intoxication with tramadol symptoms similar to those of other centrally acting analgesics (opioids) are to be expected. These include in particular miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.
Treatment
The general emergency measures apply. Keep open the respiratory tract (aspiration), maintain respiration and circulation depending on the symptoms. The antidote for respiratory depression is naloxone. In animal experiments naloxone had no effect on convulsions. In such cases diazepam should be given intravenously.
In case of intoxication orally, gastrointestinal decontamination with activated charcoal or by gastric lavage is only recommended within 2 hours after tramadol intake. Gastrointestinal decontamination at a later time point may be useful in case of intoxication with exceptionally large quantities or prolonged release formulations. Tramadol is minimally eliminated from the serum by haemodialysis or haemofiltration. Therefore treatment of acute intoxication with Tramadol Hydrochloride capsules with haemodialysis or haemofiltration alone is not suitable for detoxification.

Effect on Ability to Drive and Use Machine
Even when taken according to instructions, tramadol may cause effects such as somnolence and dizziness and therefore may impair the reactions of drivers and machine operators. This applies particularly in conjunction with other psychotropic substances, particularly alcohol.
This medicine can impair cognitive function and can affect a patient's ability to drive safely. When prescribing this medicine, patients should be told:
• The medicine is likely to affect your ability to drive
• Do not drive until you know how the medicine affects you

Storage Condition
Store below 30°C, Protect from light and moisture.

Shelf Life
36 months

Manufacturer
MEDREICH LIMITED
Unit - 7, Survey No. 11, 12, 13, 14 and 15,
Poojaramanahalli Village,
Bangalore Rural District, IN-562114, INDIA.

Pack size
20 Capsules are packed in one Alu/PVC/PVDC blister.

Five such blisters packed in a carton (5 X 20's Capsules)

Product registration holder
Healol Pharmaceuticals Sdn. Bhd.,
No. 74-3, Jalan Wangsa Delima 6,
KLSC Wangsa Maju,
53300 Kuala Lumpur, Malaysia

Date of revision of the text
01/2024

1228065-V1

Package leaflet: Information for the patient

Unidol (Tramadol hydrochloride 50 mg Capsules)

Active Ingredient: Tramadol Hydrochloride
Excipients: Microcrystalline Cellulose (PH 101), Sodium Starch Glycolate, Colloidal Anhydrous Silica, Magnesium Stearate, Purified water and Hard Gelatin Capsule.

Product Description
Hard gelatin capsule shells of size '4' with yellow opaque cap and yellow opaque body marked as 'T50' with black ink on cap containing a white to off white powder.

Pharmacodynamics
ATC Code: N02AX02
Tramadol is a centrally acting opioid analgesic. It is a non-selective pure agonist at μ, δ, and κ opioid receptors with a higher affinity for the μ receptor. Other mechanisms which contribute to its analgesic effect are inhibition of neuronal reuptake of noradrenaline and enhancement of serotonin release.
Tramadol has an antitussive effect. In contrast to morphine, analgesic doses of tramadol over a wide range have no respiratory depressant effect. Also gastrointestinal motility is less affected. Effects on the cardiovascular system tend to be slight. The potency of tramadol is reported to be 1/10 (one tenth) to 1/6 (one sixth) that of morphine.

Pharmacokinetics
More than 90% of Tramadol Hydrochloride is absorbed after oral administration. The mean absolute bioavailability is approximately 70%, irrespective of the concomitant intake of food. The difference between absorbed and non-metabolised available tramadol is probably due to the low first-pass effect. The first-pass effect after oral administration is a maximum of 30%.
Tramadol has a high tissue affinity (V d,ß = 203 + 40 l). It has a plasma protein binding of about 20 %.
Following a single oral dose administration of tramadol 100 mg as capsules or Tablets to young healthy volunteers, plasma concentrations were detectable within approximately 15 to 45 minutes within a mean Cmax of 280 to 208mcg/L and Tmax of 1.6 to 2h.
Tramadol passes the blood-brain and placental barriers. Very small amounts of the substance and its O-desmethyl derivative are found in the breast-milk (0.1% and 0.02% respectively of the applied dose).
Elimination half-life t1/2,ß is approximately 6 h, irrespective of the mode of administration. In patients above 75 years of age it may be prolonged by a factor of approximately 1.4.
In humans tramadol is mainly metabolised by means of N- and Odemethylation and conjugation of the O-demethylation products with glucuronic acid. Only Odesmethyltramadol is pharmacologically active. There are considerable interindividual quantitative differences between the other metabolites. So far, eleven metabolites have been found in the urine. Animal experiments have shown that Odesmethyltramadol is more potent than the parent substance by the factor 2 - 4. Its half-life t1/2,ß (6 healthy volunteers) is 7.9 h (range 5.4 - 9.6 h) and is approximately that of tramadol.
The inhibition of one or both types of the isoenzymes CYP3A4 and CYP2D6 involved in the biotransformation of tramadol may affect the plasma concentration of tramadol or its active metabolite.
Tramadol and its metabolites are almost completely excreted via the kidneys. Cumulative urinary excretion is 90% of the total radioactivity of the administered dose. In cases of impaired hepatic and renal function the half-life may be slightly prolonged. In patients with cirrhosis of the liver, elimination half-lives of 13.3 + 4.9h (tramadol) and 18.5 + 9.4 h (O-desmethyltramadol), in an extreme case 22.3 h and 36h respectively, have been determined. In patients with renal insufficiency (creatinine clearance <5ml/min) the values were 11 + 3.2 h and 16.9 + 3 h, in an extreme case 19.5 h and 43.2 h respectively.
Tramadol has a linear pharmacokinetic profile within the therapeutic dosage range.
The relationship between serum concentrations and the analgesic effect is dose dependent, but varies considerably in isolated cases. A serum concentration of 100 - 300ng/ml is usually effective.

Indication
Treatment of moderate to severe pain.

Recommended Dosage:
The oral dosage should be adjusted according to the intensity of pain.
Adults and adolescents (12 years and older)
Unidol 50mg Capsule is not approved for use in patients below 12 years old.
Pediatric population:
The safety and efficacy of Unidol 50mg Capsule has not been studied in pediatric population. Therefore, use of Unidol 50mg Capsule is not recommended in patients under 12 years of age.
In general the daily dose:
1 to 2 capsules every 4 to 6 hours as needed, up to a maximum 8 capsules daily.
Dose Adjustment
Patients with liver and renal impairment: Creatinine clearance < 30 mL/minute: 50 – 100 mg every 12 hours, maximum 200 mg a day.
Patients with liver cirrhosis: 50 mg every 12 hours

Contraindications
Tramadol Hydrochloride capsules is contraindicated
- in hypersensitivity to the active substance or any of the Excipients
- in acute intoxication with alcohol, hypnotics, analgesics, opioids, or other psychotropic medicinal products,
- in patients who are receiving MAO inhibitors or who have taken them within the last 14 days,
- in patients with epilepsy not adequately controlled by treatment,
- For use in narcotic withdrawal treatment.
- Children younger than 18 years to treat pain after surgery to remove the tonsils and/or adenoids.
- Adolescents between 12 and 18 years who are obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of serious breathing problems.

Warnings and Precautions
Tramadol may only be used with particular caution in opioid-dependent patients, patients with head injury, shock, a reduced level of consciousness of uncertain origin, disorders of the respiratory centre or function, increased intracranial pressure.

In patients sensitive to opiates the product should only be used with caution.

Convulsions have been reported in patients receiving tramadol at the recommended dose levels. The risk may be increased when doses of tramadol exceed the recommended upper daily dose limit (400mg). In addition, tramadol may increase the seizure risk in patients taking other medicinal products that lowers the seizure threshold. Patients with epilepsy or those susceptible to seizures should be only treated with tramadol if there are compelling circumstances.
Care should be taken when treating patients with respiratory depression, or if concomitant CNS depressant drugs are being administered, or if the recommended dosage is significantly exceeded as the possibility of respiratory depression cannot be excluded in these situations.

CYP2D6 metabolism
Tramadol is metabolised by the liver enzyme CYP2D6. If a patient has a deficiency or is completely lacking this enzyme an adequate analgesic effect may not be obtained. Estimates indicate that up to 7% of the Caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is a risk of developing <side effects> of opioid toxicity even at commonly prescribed doses.
General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life threatening and very rarely fatal. Estimates of prevalence of ultra-rapid metabolisers in different populations are summarised below:

This section is continued overleaf

Colour
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Unit 7

MEDREICH LIMITED				Title: Art Work Approval Form			
Product	Unidol Capsules 50mg - S/L - English - PIL (SAP Descr.: UNIDOL 50MG CAPS PIL S/L ENGLISH-WA-HEAL)			Specification:	Printed on 40.5 (±3.5) GSM news print paper		
Customer	Healol Pharmaceuticals - Malaysia						
Reason for Issue	PIF No.: 1170PI2420029 New Product			Colours:	2 - Pantone Red 032 C & Black		
Related FG Codes	1307117	Pharmacode No.	1564	Dimensions:	440 x 190 mm (Open Size) 190 x 28 mm (Folded Size)		
Item Code	1228065-V1 (WA)	Blister Layout No.	EP 3015 - EP-3552 A 1711 6589R-1 - A 1810 7606	No. of Folds (only for PIL)	04	Artwork made to	100%
		Carton Layout No.	NA				
		PIL Layout No.	NA				
Verified By				Approved By			
PDC:		PDC:		Regulatory:		CQA:	

Population	Prevalence %
African/Ethiopia	29%
n African	3.4% to 6.5%
American Asian	1.2% to 2%
Caucasian	3.6% to 6.5%
Greek	6.0%
Hungarian	1.9%

Post-operative use in children

There have been reports in the published literature that tramadol given postoperatively in children after tonsillectomy and/or adenoidectomy for obstructive sleep apnoea, led to rare, but life threatening adverse events. Extreme caution should be exercised when tramadol is administered to children for post-operative pain relief and should be accompanied by close monitoring for symptoms of opioid toxicity including respiratory depression.

Children with compromised respiratory function

Tramadol is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of opioid toxicity.

Tolerance, psychic and physical dependence may develop, especially after long-term use. When a patient no longer requires therapy with tramadol, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal.

In patients with a tendency to drug abuse or dependence, treatment with tramadol should only be carried out for short periods under strict medical supervision.

Tramadol is not suitable as a substitute in opioid-dependent patients. Although it is an opioid agonist, tramadol cannot suppress morphine withdrawal symptoms.

Sleep-related breathing disorders

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

Adrenal insufficiency

Opioid analgesics may occasionally cause reversible adrenal insufficiency requiring monitoring and glucocorticoid replacement therapy. Symptoms of acute or chronic adrenal insufficiency may include e.g. severe abdominal pain, nausea and vomiting, low blood pressure, extreme fatigue, decreased appetite, and weight loss.

Paediatric population

The safety and efficacy of Unidol 50mg Capsule has not been studied in the paediatric population. Therefore, use of Unidol 50mg Capsule is not recommended in patients under 12 years of age.

Respiratory depression

Administer Unidol 50mg Capsule cautiously in patients at risk for respiratory depression, including patients with substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression, as in these patients, even therapeutic doses of Unidol 50mg Capsule may decrease respiratory drive to the point of apnea. In these patients, alternative nonopioid analgesics should be considered. When large doses of tramadol are administered with anaesthetic medications or alcohol, respiratory depression may result. Respiratory depression should be treated as an overdose. If naloxone is to be administered, use cautiously because it may precipitate seizures.

Cytochromes P450 (CYP) 2D6 Ultra-Rapid Metabolism

Some individuals may be CYP2D6 ultra-rapid metabolisers. These individuals convert tramadol more rapidly than other people into its more potent opioid metabolites O-desmethyltramadol (M1). This rapid conversion could result in higher than expected opioid-like side effects including life-threatening respiratory depression. The prevalence of this CYP2D6 phenotype varies widely and has been estimated at 0.5 to 1% in Chinese, Japanese and Hispanics, 1 to 10% in Caucasians, 3% in African Americans, and 16-28% in North Africans, Ethiopians, and Arabs. Data are not available for other ethnic groups.

Risks from Concomitant Use with Benzodiazepines

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of Unidol 50mg Capsule with benzodiazepines. 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 Unidol 50mg Capsule is used with benzodiazepines. Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine 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 benzodiazepines (See Drug Interactions).

Serotonin Syndrome with Concomitant Use of Serotonergic Drugs

Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concurrent use of Unidol 50mg Capsule with serotonergic drugs (See Interactions with Other Medicaments). This may occur within the recommended dosage range.

Serotonin syndrome symptoms may include mental-status changes (e.g. agitation, hallucinations, coma), autonomic instability (e.g. tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g. hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) and can be fatal (See Interactions with Other Medicaments). The onset of symptoms generally occurs within several hours to a few days of concomitant use, but may occur later than that. Discontinue Unidol 50mg Capsule if serotonin syndrome is suspected.

Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, decreased appetite, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement dosing of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

Sexual Function/Reproduction

Long term use of opioids may be associated with decreased sex hormone levels and symptoms such as low libido, erectile dysfunction, or infertility (See side effects, Post marketing Experience)

Interactions with Other Medicaments

Tramadol should not be combined with MAO inhibitors.

In patients treated with MAO inhibitors in the 14 days prior to the use of the opioid pethidine, life-threatening interactions on the central nervous system, respiratory and cardiovascular function have been observed. The same interactions with MAO inhibitors cannot be ruled out during treatment with Tramadol Hydrochloride Capsules.

Concomitant administration of tramadol with other centrally depressant medicinal products including alcohol may potentiate the CNS effects.

The results of pharmacokinetic studies have so far shown that on the concomitant or previous administration of cimetidine (enzyme inhibitor) clinically relevant interactions are unlikely to occur. Simultaneous or previous administration of carbamazepine (enzyme inducer) may reduce the analgesic effect and shorten the duration of action.

Tramadol can induce convulsions and increase the potential for selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, antipsychotics and other seizure threshold-lowering medicinal product (such as bupropion, mirtazapine, tehrahydrocannabinol) to cause convulsions.

Concomitant therapeutic use of tramadol and serotonergic drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors, tricyclic antidepressants and mirtazapine may cause serotonin toxicity. Serotonin syndrome is likely when one of the following is observed:

- Spontaneous clonus
- Inducible or ocular clonus with agitation or diaphoresis
- Tremor and hyperreflexia
- Hypertonia and body temperature >38ºC and inducible ocular clonus.

Withdrawal of the serotonergic drugs usually brings about a rapid improvement. Treatment depends on the type and severity of the symptoms. Caution should be exercised during concomitant treatment with tramadol and coumarin derivatives (e.g. warfarin) due to reports of increased INR with major bleeding and ecchymoses in some patients.

Other active substances known to inhibit CYP3A4, such as ketoconazole and erythromycin, might inhibit the metabolism of tramadol (N-demethylation) probably also the metabolism of the active O-demethylated metabolite. The clinical importance of such an interaction has not been studied.

In a limited number of studies the pre- or postoperative application of the antiemetic 5-HT3 antagonist ondansetron increased the requirement of tramadol in patients with postoperative pain.

Benzodiazepines:

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.

Serotonergic Drugs:

The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome. If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue Tramadol if serotonin syndrome is suspected. Examples of serotonergic drugs are selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonin neurotransmitter system (e.g. mirtazapine, trazodone, tramadol), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue) (See Warnings and Precautions).

Pregnancy and Breastfeeding

Pregnancy

Tramadol has been shown to cross the placenta. There are no adequate and well-controlled studies in pregnant women. Safe use in pregnancy has not been established. Unidol 50mg Capsule is not recommended for pregnant women.

Lactation

Approximately 0.1% of the maternal dose of tramadol is excreted in breast milk. In the immediate post-partum period, for maternal oral daily dosage up to 400 mg, this corresponds to a mean amount of tramadol ingested by breast-fed infants of 3% of the maternal weight-adjusted dosage. For this reason tramadol should not be used during lactation or alternatively, breastfeeding should be discontinued during treatment with tramadol. Discontinuation of breast-feeding is generally not necessary following a single dose of tramadol.

Fertility

Post marketing surveillance does not suggest an effect of tramadol on fertility. Animal studies did not show an effect of tramadol on fertility.

Adverse Effects/Undesirable Effects:

Respiratory depression (rare)

The most commonly reported adverse reactions are nausea and dizziness, both occurring in more than 10 % of patients.

The frequencies are defined as follows:
Very common: ≥1/10
Common: ≥1/100, <1/10
Uncommon: ≥1/1000, <1/100
Rare: ≥1/10 000, <1/1000
Very rare: <1/10 000
Not known: cannot be estimated from the available data

Cardiac disorders:
Uncommon: cardiovascular regulation (palpitation, tachycardia. These adverse reactions may occur especially on intravenous administration and in patients who are physically stressed.
Rare: bradycardia

Investigations:
Rare: increase in blood pressure

Vascular disorders:
Uncommon: cardiovascular regulation (postural hypotension or cardiovascular collapse). These adverse reactions may occur especially on intravenous administration and in patients who are physically stressed.

Metabolism and nutrition disorders:
Rare: changes in appetite
Not known: hypoglycaemia

Respiratory, thoracic and mediastinal disorders:
Rare: respiratory depression, dyspnoea
Unknown: hiccups
If the recommended doses are considerably exceeded and other centrally depressant substances are administered concomitantly, respiratory depression may occur.
Worsening of asthma has been reported, though a causal relationship has not been established.

Nervous system disorders:
Very common: dizziness
Common: headache, somnolence
Rare: paraesthesia, tremor, epileptiform convulsions, involuntary muscle contractions, abnormal coordination, syncope, speech disorders.
Convulsions occurred mainly after administration of high doses of tramadol or after concomitant treatment with medicinal products which can lower the seizure threshold .

This section is continued overleaf

Colour
Black
Pantone Red 032 C

Unit 7

MEDREICH LIMITED				Title: Art Work Approval Form			
Product	Unidol Capsules 50mg - S/L - English - PIL (SAP Descr.: UNIDOL 50MG CAPS PIL S/L ENGLISH-WA-HEAL)			Specification:	Printed on 40.5 (±3.5) GSM news print paper		
Customer	Healol Pharmaceuticals - Malaysia						
Reason for Issue	PIF No.: 1170PI2420029 New Product			Colours:	2 - Pantone Red 032 C & Black		
Related FG Codes	1307117	Pharmacode No.	1564	Dimensions:	440 x 190 mm (Open Size) 190 x 28 mm (Folded Size)		
Item Code	1228065-V1 (WA)	Blister Layout No.	EP 3015 - EP-3552 A 1711 6589R-1 - A 1810 7606	No. of Folds (only for PIL)	04	Artwork made to	100%
		Carton Layout No.	NA				
		PIL Layout No.	NA				
Verified By				Approved By			
PDC:	PDC:			Regulatory:	CQA:		