1. NAME OF MEDICINAL PRODUCT:

Temgesic® Injection 0.3mg/ml
Brand of buprenorphine hydrochloride

Indivior

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Buprenorphine hydrochloride 324 µg/ml, equivalent to 300 µg buprenorphine base.

3. PHARMACEUTICAL FORM:

Temgesic injection is a colourless, clear solution, essentially free from particles. Each ml of Temgesic Injection contains 0.324 mg buprenorphine hydrochloride equivalent to 0.3 mg buprenorphine base.

4. CLINICAL PARTICULARS:

It has been proposed that Temgesic exerts its analgesic effect via high affinity binding to the opiate receptors in the central nervous system. Temgesic is a partial agonist at one subclass of opiate receptors. *In vitro* and *in vivo* studies have shown that Temgesic has a high affinity for the (subclass and dissociates from this receptor slowly. It is believed that these qualities of receptor bindings contribute to the long duration of action and low level of physical dependence seen with Temgesic.

4.1 Therapeutic indication:

As a potent analgesic for use in moderate to severe pain.

4.2 Posology and method of administration:

Adults and children over 12 years old: 1 to 2 ml (300 to 600 micrograms) by IM or slow IV injection, every 6-8 hours or as required.

Temgesic injection may be employed in balanced anaesthetic techniques as a premedication at a dose of 300 micrograms intramuscularly or as an analgesic supplement at doses of 300-450 micrograms intravenously.

Children under 12 years:

Temgesic is suitable for use in children below 12 at a dose of 3 – 6 micrograms/kg of body weight every 6 to 8 hours in refractory cases up to 9 micrograms/kg may be administered.
There is no clinical experience in infants below the age of six months.

Elderly:

There is no indication that dosage needs to be modified for the elderly.

4.3 Contraindications:

Patients with impaired respiratory functions. Patients with impaired liver functions. Patients with concurrently given MAO inhibitors. Patients who are pregnant. Not to be given to patients who are known to be allergic to Temgesic or other opiates.

4.4 Special warnings and precautions for use:

Controlled human and animal studies indicate that buprenorphine has a substantially lower dependence liability than pure agonist analgesics. In patients abusing opioids in moderate doses, substitution with buprenorphine may prevent withdrawal symptoms. In man limited euphorigenic effects have been observed. This has resulted in some abuse of the product and cautions should be exercised when prescribing it to patients known to have or suspected of having problems with drug abuse.

There is evidence to indicate that therapeutic doses of buprenorphine do not reduce the analgesic efficacy of standard doses of an opioid agonist, and that when buprenorphine is employed within the normal range, standard doses of opioid agents may be administered before the effects of the former have ended without compromising analgesia. However, in individuals on high doses of opioids, buprenorphine may precipitate abstinence effects due to its properties as a partial agonist.

Temgesic may cause drowsiness which may be potentiated by other centrally-acting agents, including alcohol, tranquilisers, sedatives and hypnotics. Ambulant patients should be warned not to drive or operating machinery until they are certain they can tolerate Temgesic.

Temgesic occasionally causes significant respiratory depression and, as with other strong centrally-acting analgesics, care should be taken when treating patients with impaired respiratory function or patients who are receiving drugs which can cause respiratory depression. Although volunteer studies have indicated that opiate antagonists may not fully reverse the effects of Temgesic, clinical experience has shown that naloxone may be of benefit in reversing reduced respiratory rate. Respiratory stimulants such as Doxepram are also effective. The intensity and duration of action may be affected in patients with impaired liver function.

4.5 Interaction with other medicinal products and other forms of interaction:

Effects may be potentiated by other centrally acting drugs.

4.6 Pregnancy and lactation:

Temgesic is not recommended for use during pregnancy. Animal studies indicate that the amounts of buprenorphine excreted in milk are very low and in human use are unlikely to be of clinical significance to the baby. There is indirect evidence in animal studies to suggest that Temgesic may cause a reduction in milk flow during lactation. Although this occurred only at doses well in excess of the human dose, it should be borne in mind when treating lactating women.

4.7 Interference with laboratory tests:

Temgesic has no known effects on diagnostic laboratory tests.

4.8 Incompatibilities:

With MAO inhibitors.

4.9 Undesirable effects:

Drowsiness, or sleep from which the patient can easily be aroused, may occur particularly in the post-operative period. In common with other strong analgesics, nausea, vomiting, dizziness, sweating, and drowsiness have been reported, which may be more frequent in ambulant patients. Should nausea and vomiting occur, concurrent administration of an anti-emetic is advised. Hallucinations and other psychotomimetic effects have occurred although more rarely than with other agonist-antagonist. Elderly patients would be expected to be more susceptible to these effects. Hypotension leading to syncope may occur. Rashes, headache, urinary retention and blurring of vision have occasionally been reported. Rarely, a serious allergic reaction may occur following a single dose.

4.10 Overdose:

Temgesic has a wide safety margin and in clinical practice doses of buprenorphine well in excess of these recommended have been used without untoward effect. Supportive measures should be instituted and if appropriate, naloxone or respiratory stimulants can be used. The expected symptoms would be drowsiness, nausea and vomiting. Marked miosis may occur.

5. PHARMACOLOGICAL PROPERTIES:

Temgesic injection is a parenteral opiate analgesic approximately 30 times as potent as morphine sulphate. The onset of analgesic effect occurs 15 minutes after Intramuscular injection and persists up to 6 hours. Peak analgesic activity usually is observed at 1 hour. When used intravenously, the time to onset and peak affect are shortened.

The limits of sensitivity of available analytical methodology precluded demonstration of bioequivalence between intramuscular and intravenous routes of administration, in post-operative

patient pharmacokinetic studies have shown elimination half-lives ranging from 1.2-7.2 hours (mean 2.2 hours) after Intravenous administration of 0.3 mg buprenorphine. Buprenorphine, in common with morphine and other phenolic opiate analgesics, is metabolised by the liver, and its clearance is related to hepatic blood flow. Studies in patients anaesthetised with 0.5% halothane have shown that this anaesthetic decreases hepatic blood flow by about 30%. This would lead to a decrease in buprenorphine clearance with a consequent small increase in plasma levels of buprenorphine. As such changes are unimportant clinically and do not persist in the post-operative phase, dosage adjustments are not required. Temgesic may cause a decrease or rarely an increase in pulse rate and blood pressure in some patients.

A therapeutic dose of Temgesic (0.3 mg buprenorphine) can reduce the respiratory rate in an equivalent manner to an equal analgesic dose of morphine (10mg). One clinically study in normal volunteers indicated that the dose response curve for respiratory depression up to 1.2 mg was shallow. In another study in which Temgesic was administered in doses generally well in excess of those recommended there was no clinically significant alteration in respiratory frequency, depth and pattern, and in serial arterial blood gases.

The antagonist activity of buprenorphine becomes manifest at doses slightly above the recommended therapeutic range. Doses in the therapeutic range may produce severe respiratory depression in predisposed individuals (see Contraindications). Buprenorphine is an established drug substance which is well documented in the literature. From the toxicity studies in animals there is nothing to suggest that buprenorphine will be toxic in humans at doses far in excess of the therapeutic dosage level. No further data are available.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients

Dextrose
Hydrochloric acid
Water for injection

6.2 Shelflife:

60 months

6.3 Special precautions for storage:

Cool, dry place below 30°C, protect from light.

6.4 Nature and contents of container:

Temgesic Injection: Box of 5 ampoules. Temgesic Injection may be diluted with 5% Injection Dextrose BP or Injection Sodium Chloride BP.

Keep out of reach of children.

Further information can be obtained from the doctor or pharmacist.

Manufactured by Reckitt Benckiser Healthcare (UK) Ltd., Dansom Lane, Hull, HU8 7DS

For Indivior UK Limited

For adverse event reporting please contact:

Indivior UK Limited

+800-270-81901

PatientSafetyRoW@indivior.com

Market Authorisation Holder: Zuellig Pharma Pte Ltd

15 Changi North Way

#01-01

Singapore

498770

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