SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Temgesic 200 microgram Sublingual Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Buprenorphine hydrochloride 216µg/tablet, equivalent to 200µg buprenorphine base.

3 PHARMACEUTICAL FORM

Sublingual tablet

White to creamy white, circular, biconvex tablets, embossed on one side with "L".

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

As a strong analgesic for the relief of moderate to severe pain.

4.2 Posology and method of administration

Administration by the sublingual route.

Adults and children over 12:

1-2 tablets (200-400 micrograms) to be dissolved under the tongue every 6-8 hours or as required. The recommended starting dose for moderate to severe pain of the type typically presenting in general practice is 1 to 2 tablets, 8 hourly.

Elderly:

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

Children under 12 years:

Temgesic Sublingual is suitable for use in children under 12 as follows:

16 - 25 kg (35 - 55lb)	½ tablet
25 - 37.5 kg (55 - 82.5lb)	½-1 tablet
37.5 - 50 kg (82.5 - 110lb)	1-1½ tablets

The recommended dose should be administered every 6 to 8 hours.

Sublingual administration is not suitable for children under the age of six years.

Temgesic sublingual may be used in balanced anaesthetic techniques at a dose of 400 micrograms.

Special populations

Hepatic impairment:

The effects of hepatic impairment on the pharmacokinetics of buprenorphine were evaluated in a postmarketing study. Buprenorphine is extensively metabolised in the liver, and plasma levels were found to be higher for buprenorphine in patients with moderate and severe hepatic impairment compared to healthy subjects. Patients should be monitored for signs and symptoms of toxicity or overdose caused by increased levels of buprenorphine. Temgesic should be used with caution in patients with moderate to severe hepatic impairment (See section 5.2).

4.3 Contraindications

Not to be given to patients who are known to be allergic to Temgesic or other opiates.

Hypersensitivity to any of the constituents.

4.4 Special warnings and precautions for use

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 a reduced respiratory rate. Respiratory stimulants such as Doxapram are also effective. The intensity and duration of action may be affected in patients with impaired liver failure.

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 caution should be exercised when prescribing it to patients known to have, or suspected of having, problems with drug abuse.

Diversion:

Diversion of Temgesic has been reported. Diversion refers to the introduction of buprenorphine into the illicit market either by patients or by individuals who obtain the medicinal product through theft from patients or pharmacies. This diversion may lead to new addicts using buprenorphine as the primary drug of abuse, with the risks of overdose, spread of blood borne viral infections and respiratory depression.

Hepatic impairment:

The effects of hepatic impairment on the pharmacokinetics of buprenorphine were evaluated in a postmarketing study. Since buprenorphine is extensively metabolised, plasma levels were found to be elevated for buprenorphine in patients with moderate and severe hepatic impairment. Patients should be monitored for signs and symptoms of toxicity or overdose caused by increased

levels of buprenorphine. Temgesic sublingual tablets should be used with caution in patients with moderate to severe hepatic impairment (See section 5.2).

Athletes must be aware that this medicine may cause a positive reaction to 'anti-doping' tests.

4.5 Interaction with other medicinal products and other forms of interaction

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 therapeutic range, standard doses of opioid agonist 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 some drowsiness which may be potentiated by other centrally acting agents, including alcohol, tranquillisers, sedatives and hypnotics. Temgesic should be used with caution in patients receiving monoamine oxidase inhibitors, although animals studies have given no evidence of interactions.

Although interaction studies have not been performed, since this drug is metabolised by CYP3A4 (see section 5.2 pharmacokinetic properties), it is expected that gestodene, troleandomycin, ketoconazole, norfluoxetine, ritonavir, indinavir and saquinavir inhibit its metabolism. Alternatively, inducers of this enzyme such as phenobarbital, carbamazepine, phenytoin and rifampicin may reduce the levels of the drug. Since the magnitude of an inducing or inhibitory effect is unknown, such drug combinations should be avoided.

Temgesic has no known effects on diagnostic laboratory tests.

4.6 Fertility, 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 Effects on ability to drive and use machines

If you feel drowsy after taking these tablets do not use machines.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. 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
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - The medicine has been prescribed to treat a medical or dental problem and
  - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
  - It was not affecting your ability to drive safely

Details regarding the new driving offence concerning driving after drugs have been taken in Great Britain may be found here: https://www.gov.uk/drug-driving-law

4.8 Undesirable effects

Nausea, vomiting, dizziness, sweating and drowsiness have been reported and may be more frequent in ambulant patients. Hallucinations and other psychotomimetic effects have occurred although more rarely than with other agonists/antagonists. 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. Temgesic occasionally causes significant respiratory depression (see section 4.4 Special warnings and precautions for use).

Cases of bronchospasm, angioneurotic oedema and anaphylactic shock have also been reported.

During use of buprenorphine as substitution treatment the following adverse reactions have also been observed: hepatic necrosis and hepatitis.

4.9 Overdose

Supportive measures should be instituted and if appropriate Naloxone or respiratory stimulants can be used. The expected symptoms of overdosage would be drowsiness, nausea and vomiting; marked miosis may occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Buprenorphine is a μ (mu) opioid partial agonist and κ (kappa) antagonist. It is a strong analgesic of the partial agonist (mixed agonist/antagonist) class.

5.2 Pharmacokinetic properties

Absorption

When taken orally, buprenorphine undergoes first-pass hepatic metabolism with N-dealkylation and glucuroconjugation in the small intestine. The use of this medication by the oral route is therefore inappropriate.

Peak plasma concentrations are achieved 90 minutes after sublingual administration.

Distribution

The absorption of buprenorphine is followed by a rapid distribution phase and a half-life of 2 to 5 hours.

Metabolism and elimination

Buprenorphine is oxidatively metabolised by 14-N-dealkylation to N-desalkyl-buprenorphine (also known as norbuprenorphine) via cytochrome P450 CYP3A4 and by glucuroconjugation of the parent molecule and the dealkylated metabolite. Norbuprenorphine is a μ (mu) agonist with weak intrinsic activity.

Elimination of buprenorphine is bi- or tri- exponential, with a long terminal elimination phase of 20 to 25 hours, due in part to reabsorption of buprenorphine after intestinal hydrolysis of the conjugated derivative, and in part to the highly lipophilic nature of the molecule.

Buprenorphine is essentially eliminated in the faeces by biliary excretion of the glucuroconjugated metabolites (80%), the rest being eliminated in the urine.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, mannitol, maize starch, povidone K30, citric acid anhydrous, magnesium stearate, sodium citrate, purified water and alcohol (96%).

6.2 Incompatibilities

None stated.

6.3 Shelf life

3 years - Nylon/aluminium/uPVC blister strip.

3 years - HDPE bottle.

6.4 Special precautions for storage

Do not store above 30ºC. Store in the original package - Nylon/aluminium/ uPVC blister strip.

Do not store above 30ºC - HDPE bottle.

6.5 Nature and contents of container

Nylon/aluminium/uPVC blister strips of 10 tablets each, packed in cartons of 50 tablets.

HDPE bottle consisting of 50 tablets.

6.6 Special precautions for disposal

To be dissolved under the tongue and not to be chewed or swallowed.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 36699/0004

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10 DATE OF REVISION OF THE TEXT

18/05/2016