**Rebrikel (Buprenorphine) 5 µg/h, 10 µg/h, 20 µg/h Transdermal patch Prescribing Information. Prescribers should consult the SmPC before prescribing.**

**Presentation:** Each transdermal patch contains 5mg, 10mg, 20mg of buprenorphine releasing 5µg, 10µg, 20µg of buprenorphine per hour respectively.

**Indications:** Treatment of non-malignant pain of moderate intensity in adults when an opioid is necessary for obtaining adequate analgesia. Not suitable for treatment of acute pain.

**Dosage and administration:** Rebrikel should be administered every 7th day. Rebrikel 5 µg/h should be used as the initial dose. Titration: Dose may be adjusted every 3 days. Thereafter, 7-day dosing interval should be maintained. To increase the dose, a larger patch should replace the patch currently worn or a combination of patches should be applied in different places. Not recommended to use more than 2 patches at the same time regardless of strength. Conversion from opioids: Can be used as an alternative to treatment with other opioids.

Method of Administration: Apply to non-irritated, intact skin of the upper outer arm, upper chest, upper back or the side of the chest, but not to any parts of the skin with large scars. Apply immediately after removal from the sealed sachet. Press the patch firmly in place with the palm of the hand for approximately 30 seconds. The patch should be worn continuously for 7 days. The patch must not be divided or cut into pieces. *Duration of administration:* Do not prescribe for longer than absolutely necessary. If long-term pain treatment is required then careful and regular monitoring should be carried out. *Discontinuation*: Rebrikel is to be followed by other opioids. A subsequent opioid should not be administered within 24 hours after removal of the patch. *Patients with fever or exposed to external heat:* Advise patients to avoid exposing the application site to external heat sources. Fever may also increase absorption resulting in increased risk of opioid reactions.

**Special Populations:** *Paediatric population::* Safety and efficacy have not been established*. Elderly*: No dosage adjustment required. *Renal impairment:* No dosage adjustment required. *Hepatic impairment:* Use with caution and carefully monitor patients during treatment.

**Fertility, pregnancy and lactation:** *Pregnancy:* Rebrikel should not be used during pregnancy and in women of childbearing potential who are not using effective contraception. Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate. If prolonged use is required, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure appropriate treatment is available. Administration during labour may depress respiration in the neonate, therefore an antidote for the child should be readily available. Towards the end of pregnancy high doses of buprenorphine may induce respiratory depression in the neonate even after a short period of administration. *Breastfeeding*: Not recommended as buprenorphine may be secreted in breast milk and may cause respiratory depression in the infant. Should be used with caution during breast-feeding. *Fertility:* No human data available.

**Contraindications**: Patients with known hypersensitivity to buprenorphine or the excipients, Opioid dependent patients and for narcotic withdrawal treatment, conditions in which the respiratory centre and function are severely impaired or may become so, patients receiving MAOIs or have taken them within the last two weeks, patients suffering from myasthenia gravis or delirium tremens.

**Special warnings and precautions:** Use with caution in patients with; Respiratory depression, CNS depressants co-administration, serotonergic agents, psychological dependence, abuse profile and history of substance and/or alcohol abuse, sleep apnoea, acute alcohol intoxication, head injury, intracranial lesions or increased intracranial pressure, shock, a reduced level of consciousness of uncertain origin, severely impaired hepatic function, constipation.. Significant respiratory depression has been associated with buprenorphine, particularly by the intravenous route. A number of overdose deaths have occurred when addicts have intravenously abused buprenorphine, usually with benzodiazepines concomitantly. Additional overdose deaths due to ethanol and benzodiazepines in combination with buprenorphine have been reported., Concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. Not recommended for analgesia in the immediate post-operative period or in other situations characterised by a narrow therapeutic index or a rapidly varying analgesic requirement. Drug dependence, tolerance and potential for abuse: prolonged use may lead to drug dependence (addiction), even at therapeutic doses. Individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder are at increased risk. A comprehensive patient history should be taken before prescribing. Explain risks of developing tolerance to patients. Patients should be closely monitored for signs of tolerance, misuse, abuse or addiction. Overuse or misuse may result in overdose and/or death. Drug withdrawal syndrome: a withdrawal strategy for ending treatment with buprenorphine should be put in place prior to starting treatment. Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, taper the dose gradually to minimize symptoms of withdrawal. Tapering from a high dose may take weeks to months. Opioid drug withdrawal syndrome is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms include irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate. When withdrawal occurs, it's generally mild, begins after 2 days and may last up to 2 weeks. Sleep-related breathing disorders: Can cause sleep-related

beathing dioders including central sleep apnoea (CSA) and sleep-related hypoxemia. Skin reactions at application site: usually presented by a mild or moderate skin inflammation,and typical appearance may include erythema, oedema, pruritus, rash, small blisters (vesicles), and painful/burning sensation at the application site. Hyperalgesia: may be diagnosed if patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia is more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose. Endocrine System: May influence the hypothalamic-pituitary-adrenal or -gonadal axes. Rebrikel should not be used at higher doses than recommended.

**Drug Interactions:** CYP3A4 inhibitors, enzyme inducers (e.g. phenobarbital, carbamazepine, phenytoin and rifampicin), general anaesthetics (e.g. halothane), MAOIs (including patients who have received MAOIs within the previous 2 weeks), other opioid derivatives (analgesics and antitussives containing e.g. morphine, dextropropoxyphene, codeine, dextromethorphan or noscapine), antidepressants, sedative H1-receptor antagonists, alcohol, anxiolytics, neuroleptics, clonidine and related substances, benzodiazepines or related drugs.

**Effects on ability to drive/use machines**: May influence patient's ability to drive and use machines particularly in the beginning of treatment and in conjunction with other centrally acting substances including alcohol, tranquillisers, sedatives and hypnotics. Prescribers to give individual recommendations to patients. A general restriction is not necessary in cases where a stable dose is used. It is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988.

**Undesirable effects**: Anaphylactic reaction, anaphylactoid reaction, anorexia, confusion, depression, insomnia, nervousness, anxiety, hallucinations, psychotic disorder, depersonalization, drug dependence, headache, dizziness, somnolence, tremor, syncope, seizures, palpitations, tachycardia, angina pectoris, circulatory collapse, dyspnoea, respiratory depression, respiratory failure, constipation, nausea, vomiting, abdominal pain, diarrhoea, dyspepsia, dry mouth, dysphagia Ilius, diverticulitis, pruritus, erythema, rash, sweating, exanthema, dermatitis contact, , muscular weakness, urinary retention, erectile dysfunction, application site reaction, tiredness, asthenic conditions, peripheral oedema, drug withdrawal syndrome, drug withdrawal syndrome neonatal, drug tolerance. See SmPC for full list of adverse events.

P**ack size and UK list price:** Rebrikel 5 µg/h transdermal patch (PL 17780/0876) pack size:4 £5.25,

Rebrikel 10 µg/h transdermal patch (PL 17780/0874) pack size:4 £9.43,

Rebrikel 20 µg/h transdermal patch (PL 17780/0875) pack size:4 £17.19.

**Legal category**: POM

**Marketing Authorisation Holder**: Zentiva Pharma UK Limited, 12 New Fetter Lane, London, EC4A 1JP, UK

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**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Zentiva via email to PV-United-Kingdom@zentiva.com or via phone on 0800 090 2408.**