Opiodur 12µg/h, 25µg/h, 50µg/h, 75µg/h and 100µg/h Transdermal Patch (fentanyl) Prescribing Information. Prescribers should consult the SmPC before prescribing.

Presentation: Each transdermal patch contains 1.375mg, 2.75mg, 5.5mg, 8.25mg or 11.0mg of fentanyl, releasing 12.5µg, 25µg, 50µg, 75µg or 100µg of fentanyl per hour, respectively.

Indications: Opiodur is indicated in adults for the management of severe chronic pain that requires continuous long term opioid administration, and in children receiving opioid therapy from 2 years of age for the long-term management of severe chronic pain.

Dosage and administration: Prior to starting treatment, discuss strategy for ending treatment to minimise risk of addiction and drug withdrawal syndrome**.** Doses should be individualised based upon the status of the patient and should be assessed at regular intervals after application. The lowest effective dose should be used. *Initial dose selection*: should be based on the patient's current opioid use. It is recommended that Opiodur be used in patients who have demonstrated opioid tolerance. *Opioid-tolerant adult patients:* To convert opioid-tolerant patients from oral or parenteral opioids to Opiodur refer to the SmPC. *Opioid-naive adult patients*: Not recommended. *Dose titration and maintenance therapy for all patients*: The Opiodur patch should be replaced every 72 hours. The dose should be titrated individually on the basis of average daily use of supplement analgesics until a balance between analgesic efficacy and tolerability is attained. *Treatment duration and goals:* Before initiating treatment, a treatment strategy and a plan for end of treatment. *Treatment duration and goals:* Before initiating, a treatment strategy including treatment duration and treatment goals, and a plan for end of the treatment, should be agreed together with the patient, in accordance with pain management guidelines. *Discontinuation*: Replacement with other opioids should be gradual, starting at a low dose and increasing slowly. *Children aged 16 years and above*: Follow adult dosage. *Opioid-tolerant paediatric patients (ages 2 to 16 years)*: should be administered only to patients who are already receiving at least 30mg oral morphine equivalents per day. To convert paediatric patients from oral or parenteral opioids to Opiodur refer to the SmPC.

Method of Administration: Opiodur is for transdermal use and should be applied to non-irritated skin on a flat surface of the torso or upper arms. In young children, the upper back is the preferred location to minimize the potential of the child removing the patch. Should be applied immediately upon removal from the sealed package. May be worn continuously for 72 hours. A new patch should be applied to a different skin site after removal of the previous patch. Patients should be prompted to follow the instructions for proper application of the patch that are included in the patient information leaflet.

Special Populations: Paediatric population: should not be used in children <2yrs. Should not be administered to opioid-naive paediatric patients. Elderly: Data from intravenous studies with fentanyl suggests that elderly patients may have reduced clearance and a prolonged half-life and may be more sensitive to the active substance than younger patients. Observe elderly patients carefully for signs of fentanyl toxicity.

Fertility, pregnancy and lactation: Pregnancy: should not be used during pregnancy unless clearly necessary. Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate. Breastfeeding: should be discontinued during treatment and for at least 72 hours after the removal of the patch. Not recommended for use during childbirth. Fertility: No data available.

Contraindications: Hypersensitivity to the active substances or to any of the excipients. Contraindicated in patients with severe respiratory depression, acute or postoperative pain and opioid naïve patients.

Special warnings and precautions: Patients and their carers must be instructed that Opiodur contains an active substance in an amount that can be fatal, especially to a child. Therefore, they must keep all patches out of the sight and reach of children. Because of the risks, including fatal outcome, associated with accidental ingestion, misuse, and abuse, patients and their carers must be advised to keep Opiodur in a safe and secure place, not accessible by others. Use in *opioid-naive and not opioid-tolerant* patients has been associated with very rare cases of significant respiratory depression and/or fatality when used as initial opioid therapy, especially in patients with non-cancer pain. Some patients may experience *respiratory depression* and must be observed for these effects. Can cause sleep-related breathing disorders including central sleep apnoea and sleep related hypoxia. *Concomitant use of Opiodur and sedative medicines* such as benzodiazepines or related drugs, alcohol, or CNS depressant narcotic drugs, may result in sedation, respiratory depression, coma and death. Therefore, should be reserved for when alternative options are not possible. Patients should be followed closely for signs and symptoms of respiratory depression and sedation. Strongly recommended to inform patients and caregivers to be aware of these symptoms. May have more severe adverse effects in patients with *chronic obstructive or other pulmonary disease.* Repeated use may lead to *Opioid use disorder (OUD):* Abuse or intentional misuse may result in overdose and/or death. Monitor closely for signs of OUD. *Drug withdrawal syndrome* may occur upon abrupt cessation of therapy or dose reduction. Hyperalgesia may be diagnosed if the patient on long- term opioid therapy presents with increased pain . Use with caution in patients who have brain tumours and *central nervous system conditions* including increased intracranial pressure. Fentanyl may produce *cardiac disease* such as bradycardia and should therefore be administered with caution to patients with bradyarrhythmias. Opioids may cause *hypotension*, especially in patients with hypovolemia. Underlying symptomatic hypotension and/or hypovolaemia

should be corrected before treatment is initiated. Patients with *hepatic impairment* should be observed carefully for signs of fentanyl toxicity. Caution is advised in patients with *renal impairment* because fentanyl pharmacokinetics has not been evaluated in this patient population. Should only be considered if the benefits outweigh the risks. Fentanyl concentrations may increase if the skin temperature increases. Therefore, patients with *fever* should be monitored as there is a potential for temperature-dependent increases in fentanyl released from the system resulting in possible overdose and death. All patients should be advised to avoid exposing the application site to direct *external heat sources.* Caution is advised for co-administration with medicinal products that affect the serotonergic neurotransmitter systems. If *serotonin syndrome* is suspected, treatment should be discontinued.

Drug Interactions: Concomitant use with *CYP3A4 inhibitors* may result in an increase in fentanyl plasma concentrations, which could increase or prolong both the therapeutic and adverse effects and may cause serious respiratory depression. Concomitant use with *CYP3A4 inducers* may result in decrease in fentanyl plasma concentrations and a decreased therapeutic effect. *Accidental transfer* of a fentanyl patch to the skin of a non-patch wearer (particularly a child), while sharing a bed or being in close physical contact with a patch wearer, may result in an opioid overdose for the non-patch wearer. Opioids increase the tone and decrease the propulsive contractions of the smooth muscle of the *gastrointestinal tract*. Non-epileptic (myo)clonic reactions can occur in *patients with myasthenia gravis*. Concomitant use of *mixed opioid agonists/antagonists* such as buprenorphine, nalbuphine or pentazocine is not recommended. When *opioid induced hyperalgesia* is suspected, the dose of opioid should be reduced or tapered off. Concomitant use of *centrally acting medicinal products and alcohol* may result in respiratory depression, hypoventilation, hypotension and profound sedation, coma or death. Not recommended for use in patients who require the concomitant administration of *Monoamine Oxidase Inhibitors (MAOI)*. Coadministration of fentanyl with *serotonergic medicinal products* may increase the risk of serotonin syndrome. Use with caution. Concomitant use of buprenorphine, nalbuphine or pentazocine is not recommended.

Effects on ability to drive/use machines: May impair mental and/or physical ability required for the performance of potentially hazardous tasks such as driving or operating machinery. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988.

Undesirable effects: Somnolence, dizziness, headache, nausea, vomiting, constipation, hypersensitivity, anorexia, insomnia, depression, anxiety, confusional state, hallucination, tremor, paraesthesia, vertigo, palpitations, tachycardia, hypertension, dyspnoea, diarrhoea, dry mouth, abdominal pain, abdominal pain upper, dyspepsia, hyperhidrosis, pruritus, rash, erythema, muscle spasms, urinary retention, fatigue, oedema peripheral, asthenia, malaise, feeling cold, convulsion (including clonic convulsions and grand mal convulsion), loss of consciousness, bradycardia, cyanosis, respiratory depression, respiratory distress, ileus, erectile dysfunction, drug withdrawal syndrome, apnoea, hypoventilation, anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, delirium, drug dependence, serotonin syndrome, drug tolerance. See SmPC for full list of adverse events.

Pack size and UK list price:
Opiodur 12µg/h (PL 17780/0944) pack size: 5, £5.64
Opiodur 25µg/h (PL 17780/0945) pack size: 5, £8.07
Opiodur 50µg/h (PL 17780/0946) pack size: 5, £15.09
Opiodur 75µg/h (PL 17780/0947) pack size: 5, £21.05
Opiodur 100µg/h (PL 17780/0948) pack size: 5, £25.94

Legal category: POM

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

Date of Preparation: 24 Aug 2023 **Ref:** 000602946

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.