SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fentanyl 50 micrograms/ml solution for injection/infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml contains 50 micrograms of Fentanyl as Fentanyl citrate

Each 2 ml ampoule contains 100 micrograms of Fentanyl as Fentanyl citrate.

Each 10 ml ampoule contains 500 micrograms of Fentanyl as Fentanyl citrate.

For Fentanyl Injection 2 ml ampoules: This medicine contains less than 1 mmol sodium (23 mg) per 2 ml ampoule, that is to say essentially 'sodium-free'.

For Fentanyl Injection 10 ml ampoule: This medicine contains less than 1 mmol sodium (23 mg) per 10 ml ampoule, that is to say essentially 'sodium-free'

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection/infusion

A clear, colourless solution for injection/infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Fentanyl is an opioid analgesic used:

a. In low doses to provide analgesia during short surgical procedures.

b. In high doses as an analgesic/respiratory depressant in patients requiring assisted ventilation.

c. In combination with a neuroleptic in the technique of neuroleptanalgesia.

d. In the treatment of severe pain, such as the pain of myocardial infarction.

4.2 Posology and method of administration

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with fentanyl citrate in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4).

Route of administration

Intravenous administration either as a bolus or by infusion.

Intramuscular administration.

Fentanyl should be given only in an environment where the airway can be controlled and by personnel who can control the airway (see section 4.4 Special warnings and precautions).

To avoid bradycardia, it is recommended to administer a small intravenous dose of an anti-cholinergic just before anaesthetic induction.

It is recommended to wear gloves while opening the ampoule (see section 6.6 Special precautions for disposal and other handling).

Posology

Fentanyl Injection , by the intravenous route, can be administered to both adults and children.

The dose of Fentanyl Injection should be individualised according to age, body weight, physical status, underlying pathological condition, use of other drugs and type of surgery and anaesthesia. Adults

The usual dosage regimen in adults is as follows:

Doses in excess of 200 mcg are for use in anaesthesia only. As a premedicant, 1-2 ml Fentanyl Injection may be given intramuscularly 45 minutes before induction of anaesthesia.

Initial		Supplemental
Spontaneous Respiration	50-200 mcg	50 mcg

Assisted Ventilation	300-3500 mcg	100-200 mcg

After intravenous administration in unpremedicated adult patients, 2 ml Fentanyl Injection may be expected to provide sufficient analgesia for 10-20 minutes in surgical procedures involving low pain intensity. 10 ml Fentanyl Injection injected as a bolus gives analgesia lasting about one hour. The analgesia produced is sufficient for surgery involving moderately painful procedures. Giving a dose of 50 mcg/kg Fentanyl Injection will provide intense analgesia for some four to six hours, for intensely stimulating surgery.

Fentanyl may also be given as an infusion. In ventilated patients, a loading dose of fentanyl may be given as a fast infusion of approximately 1 mcg/kg/min for the first 10 minutes followed by an infusion of approximately 0.1 mcg/kg/min.

Alternatively the loading dose of Fentanyl may be given as a bolus. Infusion rates should be titrated to individual patient response; lower infusion rates may be adequate. Unless it is planned to ventilate post-operatively, the infusion should be terminated at about 40 minutes before the end of surgery.

Lower infusion rates, e.g. 0.05-0.08 mcg/kg/minute are necessary if spontaneous ventilation is to be maintained. Higher infusion rates (up to 3 mcg/kg/minute) have been used in cardiac surgery.

Fentanyl is chemically incompatible with the induction agents thiopentone and methohexitone because of wide differences in pH.

Paediatric population

Children aged 12 to 17 years old: Follow adult dosage.

Children aged 2 to 11 years old: The usual dosage regimen in children is as follows:

Age		Initial	Supplemental
Spontaneous Respiration	2-11 yrs	1-3 mcg/kg	1-1.25 mcg/kg
Assisted Ventilation	2-11 yrs	1-3 mcg/kg	1-1.25 mcg/kg

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 or other opioids.

Respiratory depression, obstructive airways disease.

Concurrent administration with monoamine oxidase inhibitors, or within 2 weeks of their discontinuation.

4.4 Special warnings and precautions for use

Warnings:

Tolerance and Opioid use disorder (abuse and dependence)

Tolerance, physical dependence, and psychological dependence may develop upon repeated administration of opioids

Repeated use of opioids may lead to Opioid use disorder (OUD). Abuse or intentional misuse of opioids may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or a family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patientsonly use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction.

The clinical need for analgesic treatment should be reviewed regularly.

<u>Drug withdrawal syndrome</u>

Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with fentanyl.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Hyperalgesia

Hyperalgesia may be diagnosed if the 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 tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

Following intravenous administration of fentanyl, a transient fall in blood pressure may occur, especially in hypovolaemic patients. Appropriate measures to maintain a stable arterial pressure should be taken.

Respiratory Depression

As with all potent opioids, profound analgesia is accompanied by marked respiratory depression, which may persist into or recur in the early postoperative period. Care should be taken after large doses or infusions of fentanyl to ensure

that adequate spontaneous breathing has been established and maintained before discharging the patient from the recovery area.

Significant respiratory depression will occur following the administration of fentanyl in doses in excess of 200 mcg. This, and the other pharmacological effects of fentanyl, can be reversed by specific opioid antagonists, but additional doses may be necessary because the respiratory depression may last longer than the duration of action of the opioid antagonist.

Resuscitation equipment and opioid antagonists should be readily available.

Hyperventilation during anaesthesia may alter the patient’s response to CO2, thus affecting respiration postoperatively.

Administration in labour may cause respiratory depression in the new born infant.

Cardiac disease

Bradycardia, and possibly cardiac arrest, can occur if the patient has received an insufficient amount of anticholinergic, or when fentanyl is combined with nonvagolytic muscle relaxants. Bradycardia can be antagonised by atropine.

Muscle rigidity

Muscular rigidity (morphine-like effect) may occur. Rigidity, which may also involve the thoracic muscles, can be avoided by the following measures:

- slow IV injection (usually sufficient for lower doses);
- premedication with benzodiazepines;
- use of muscle relaxants.

Non-epileptic (myo)clonic movements can occur.

Precautions:

Fentanyl should be given only in an environment where the airway can be controlled and by personnel who can control the airway.

Special dosing conditions

The use of rapid bolus injections of opioids should be avoided in patients with compromised intracerebral compliance; in such patients the transient decrease in the mean arterial pressure has occasionally been accompanied by a transient reduction of the cerebral perfusion pressure.

It is recommended to reduce dosage in the elderly and debilitated patients. In uncontrolled hypothyroidism, pulmonary disease, decreased respiratory reserve, alcoholism and hepatic or renal impairment the dosage should be titrated with care and prolonged post-operative monitoring is required.

Patients on chronic opioid therapy or with a history of opioid abuse may require higher doses.

Myasthenia gravis

In patients with myasthenia gravis, careful consideration should be applied in the use of certain anticholinergic agents and neuromuscular-blocking pharmaceutical agents prior to, and during, the administration of a general anaesthetic regimen which includes administering intravenous fentanyl.

Interaction with neuroleptics

If fentanyl is administered with a neuroleptic, the user should be familiar with the special properties of each drug, particularly the difference in duration of action. When such a combination is used, there is a higher incidence of hypotension. Neuroleptics can induce extrapyramidal symptoms that can be controlled with anti-Parkinson agents.

Bile duct

As with other opioids, due to the anticholinergic effects, administration of fentanyl may lead to increases of bile duct pressure and, in isolated cases, spasms of the Sphincter of Oddi might be observed.

Serotonin Syndrome

Caution is advised when fentanyl is coadministered with drugs that affect the serotonergic neurotransmitter systems.

The development of a potentially life-threatening serotonin syndrome may occur with the concomitant use of serotonergic drugs such as Selective Serotonin Re-uptake Inhibitors (SSRIs) and Serotonin Norepinephrine Re-uptake Inhibitors (SNRIs), and with drugs which impair metabolism of serotonin (including Monoamine OxidaseInhibitors [MAOIs]). This may occur within the recommended dose.

Serotonin syndrome may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperoreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea).

If serotonin syndrome is suspected, rapid discontinuation of fentanyl should be considered.

Risk from concomitant use of Central Nervous System (CNS) depressants, especially benzodiazepines or related drugs

Concomitant use of fentanyl and CNS depressants especially benzodiazepines or related drugs in spontaneous breathing patients, may increase the risk of profound sedation, respiratory depression, coma and death. If a decision is made to administer fentanyl concomitantly with a CNS depressant, especially a benzodiazepine or a related drug, the lowest effective dose of both drugs should be administered, for the shortest period of concomitant use. Patients should be carefully monitored for signs and symptoms of respiratory depression and profound sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see Interactions).

Paediatric population

Techniques that involve analgesia in a spontaneously breathing child should only be used as part of an anaesthetic technique, or given as part of a sedation / analgesia

technique, with experienced personnel in an environment that can manage sudden chest wall rigidity requiring intubation, or apnoea requiring airway support.

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For Fentanyl Injection 10 ml ampoules: This medicine contains less than 1 mmol sodium (23 mg) per 10 ml ampoule, that is to say essentially 'sodium-free'.

To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Effect of other drugs on fentanyl

Central Nervous System (CNS) depressants

The use of opioid premedication, barbiturates, benzodiazepines or related drugs, neuroleptics, general anaesthetics, gabapentinoids (gabapentin and pregabalin), and other non-selective CNS depressants (e.g. alcohol) may enhance or prolong the respiratory depression of fentanyl.

When patients have received other CNS-depressants, the dose of fentanyl required may be less than usual. Concomitant use with fentanyl in spontaneously breathing patients may increase the risk of respiratory depression, profound sedation, coma, and death (see warnings and precautions).

Cytochrome P450 3A4 (CYP3A4) inhibitors

Fentanyl, a high clearance drug, is rapidly and extensively metabolised mainly by CYP3A4. When fentanyl is used, the concomitant use of a CYP3A4 inhibitor may result in a decrease in fentanyl clearance. With single-dose fentanyl administration, the period of risk for respiratory depression may be prolonged, which may require special patient care and longer observation. With multiple-dose fentanyl administration, the risk for acute and/or delayed respiratory depression may be increased, and a dose reduction of fentanyl may be required to avoid accumulation of fentanyl. Oral ritonavir (a potent CYP3A4 inhibitor) reduced the clearance of a single intravenous fentanyl dose by two thirds, although peak plasma concentrations of fentanyl were not affected. However, itraconazole (another potent CYP3A4 inhibitor) at 200 mg/day given orally for 4 days had no significant effect on the pharmacokinetics of a single intravenous fentanyl dose. Co-administration of other potent or less potent CYP3A4 inhibitors, such as voriconazole or fluconazole, and fentanyl may also result in an increased and/or prolonged exposure to fentanyl.

Bradycardia and possibly cardiac arrest can occur when fentanyl is combined with non vagolytic muscle relaxants.

Serotonergic Drugs

Coadministration of fentanyl with a serotonergic agent, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) or a Monoamine Oxidase Inhibitor (MAOI), may increase the risk of serotonin syndrome, a potentially life-threatening condition (see section 4.3 Contraindications).

Effect of fentanyl on other drugs

Following the administration of fentanyl, the dose of other CNS depressant drugs should be reduced. This is particularly important after surgery, because profound analgesia is accompanied by marked respiratory depression, which can persist or recur in the postoperative period. Administration of a CNS depressant, such as a benzodiazepine or related drugs, during this period may disproportionally increase the risk for respiratory depression (see warnings and precautions).

Plasma concentrations of etomidate increased considerably (by a factor 2-3) when combined with fentanyl. The total plasma clearance and volume of distribution of etomidate is decreased by a factor of 2 to 3 without a change in half-life when administered with fentanyl.

Simultaneous administration of fentanyl and intravenous midazolam results in an increase in the terminal plasma half-life and a reduction in the plasma clearance of midazolam. When these drugs are co-administered with fentanyl their dose may need to be reduced.

4.6 Fertility, pregnancy and lactation

Pregnancy

Fentanyl can cross the placenta in early pregnancy. Studies in animals have shown some reproductive toxicity (see Section 5.3, Preclinical safety data). Administration during childbirth (including Caesarean section) is not recommended because fentanyl crosses the placenta and may suppress spontaneous respiration in the newborn period. If fentanyl is administered, assisted ventilation equipment must be immediately available for the mother and infant if required. An opioid antagonist for the child must always be available. Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.

If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast-feeding

Administration to nursing women is not recommended as fentanyl may be secreted in breast milk and may cause respiratory depression in the infant. The risk/benefit of breast-feeding following fentanyl administration should be considered.

Fertility

There are no clinical data on the effects of fentanyl on male or female fertility. In animal studies, some tests on rats showed reduced female fertility at maternal toxic doses (see section 5.3 Preclinical safety data).

4.7 Effects on ability to drive and use machines

Where early discharge is envisaged, patients should be advised not to drive or operate machinery for at least 24 hours following administration.

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.

4.8 Undesirable effects

The safety of fentanyl IV was evaluated in 376 subjects who participated in 20 clinical trials evaluating fentanyl IV as an anaesthetic. These subjects took at least 1 dose of fentanyl IV and provided safety data. Based on pooled safety data from these clinical trials, the most commonly reported (≥5% incidence) Adverse Reactions were (with % incidence): nausea (26.1); vomiting (18.6); muscle rigidity (10.4); hypotension (8.8); hypertension (8.8); bradycardia (6.1); and sedation (5.3).

Including the above-mentioned adverse reactions, Table 1 displays adverse reactions that have been reported with the use of fentanyl IV from either clinical trials or postmarketing experience.

The displayed frequency categories use the following convention: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data).

Table 1: Adverse Reactions

System Organs Class	Adverse Reactions			
	Frequency Category			
	Very Common (≥1/10)	**Common (≥1/100 to <1/10**	**Uncommon (≥1/1000 to <1/100)**	**Not known**
Immune System Disorders				Hypersensitivity (such as anaphylactic shock, anaphylactic reaction, urticaria)
Psychiatric Disorders		Agitation	Euphoric mood	Delirium Drug dependence (see section 4.4)
Nervous System Disorders	Muscle rigidity (which may also involve the thoracic muscle)	Dyskinesia; Sedation; Dizziness	Headache	Convulsions; Loss of consciousness; Myoclonus
Eye Disorders		Visual disturbance		
Cardiac Disorders		Bradycardia; Tachycardia; Arrhythmia		Cardiac arrest
Vascular Disorders		Hypotension; Hypertension; Venous pain	Phlebitis; Blood pressure fluctuation	
Respiratory, Thoracic and Mediastinal Disorders		Laryngospasm; Bronchospasm; Apnoea	Hyperventilation; Hiccups	Respiratory depression
Gastrointestinal Disorders	Nausea; Vomiting		Dysphagia	
Skin and Subcutaneous Tissue Disorders		Allergic dermatitis		Pruritus
General Disorders and Administration Site Conditions			Chills; Hypothermia Drug withdrawal syndrome	Drug withdrawal syndrome (see section 4.4)
Injury, Poisoning and Procedural		Postoperative confusion	Airway complication of anaesthesia	

Complications				

When a neuroleptic is used with fentanyl, the following adverse reactions may be observed: chills and/or shivering, restlessness, postoperative hallucinatory episodes and extrapyramidal symptoms (see Section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the yellow card Scheme Website:www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

Symptoms and signs:

The manifestations of fentanyl overdosage are generally an extension of its pharmacological action. Depending on the individual sensitivity, the clinical picture is determined primarily by the degree of respiratory depression, which varies from bradypnoea to apnoea. Toxic leukoencephalopathy has been observed with fentanyl overdose.

Treatment:

Hypoventilation or apnoea: O_2 administration, assisted or controlled respiration.

Respiratory depression: Specific opioid antagonist.

This does not preclude the use of immediate countermeasures.

The respiratory depression may last longer than the effect of the antagonist; additional doses of the latter may therefore be required.

Muscular rigidity: Intravenous neuromuscular blocking agent to facilitate assisted or controlled respiration.

The patient should be carefully observed; body warmth and adequate fluid intake should be maintained. If hypotension is severe or if it persists, the possibility of hypovolaemia should be considered and, if present, it should be controlled with appropriate parenteral fluid administration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetic general, opioid anaesthetic, ATC code: N01AH01

Fentanyl is a synthetic opiate with a clinical potency of 50 to 100 times that of morphine. Its onset of action is rapid and its duration of action is short. In man, a single IV dose of 0.5-1 mg/70 kg body weight immediately produces a pronounced state of surgical analgesia, respiratory depression, bradycardia and other typical morphine-like effects. The duration of action of the peak effects is about 30 minutes. All potent morphine-like drugs produce relief from pain, ventilatory depression, emesis, constipation, physical dependence, certain vagal effects and varying degrees of sedation. Fentanyl, however, differs from morphine not only by its short duration of action but also by its lack of emetic effect and minimal hypotensive activity in animals.

5.2 Pharmacokinetic properties

Some pharmacokinetic parameters for fentanyl are as follows:

Urinary excretion = 8%

Bound in plasma = 80%

Clearance (ml/min/kg) = 13±2

Volume of distribution (litres/kg) = 4.0±0.4

Estimates of terminal half-life range from 141 to 853 minutes.

Renal impairment

Data obtained from a study administering IV fentanyl in patients undergoing renal transplantation suggest that the clearance of fentanyl may be reduced in this patient population. If patients with renal impairment receive fentanyl, they should be observed carefully for signs of fentanyl toxicity and the dose reduced if necessary (see section 4.2 Posology and method of administration).

Obese Patients

An increase in clearance of fentanyl is observed with increased body weight. In patients with a BMI >30, clearance of fentanyl increases by approximately 10% per 10 kg increase of the fat free mass (lean body mass).

5.3 Preclinical safety data

In vitro fentanyl showed, like other opioid analgesics, mutagenic effects in a mammalian cell culture assay, only at cytotoxic concentrations and along with metabolic activation. Fentanyl showed no evidence of mutagenicity when tested in in vivo rodent studies and bacterial assays. In a two-year rat bioassay, fentanyl was not carcinogenic.

Some tests on female rats showed reduced fertility as well as embryo mortality. These findings were related to maternal toxicity and not a direct effect of the drug on the developing embryo. There was no evidence of teratogenic effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Hydroxide (for pH adjustment)

Water for injections

6.2 Incompatibilities

The product is chemically incompatible with the induction agents thiopentone and methohexitone because of the wide differences in pH.

6.3 Shelf life

24 months

Chemical and physical in-use stability of the medicinal product in 0.9% sodium chloride and 5% Glucose has been demonstrated for 24 hours at 15°C-25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Type I, colourless glass ampoules

Pack size: packs of 10 of 2 ml ampoules; packs of 5 of 10 ml ampoules.

Not all pack sizes maybe marketed.

6.6 Special precautions for disposal

Wear gloves while opening ampoule.

Accidental dermal exposure should be treated by rinsing the affected area with water. Avoid usage of soap, alcohol, and other cleaning materials that may cause chemical or physical abrasions to the skin.

Store as a CD.

7 MARKETING AUTHORISATION HOLDER

ELC Group s.r.o.
Pobřežní 394/12, Karlin,
186 00 Prague 8,
Czech Republic

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 41947/0044

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14/08/2024

10 DATE OF REVISION OF THE TEXT

14/08/2024