Summary of Product Characteristics
GEMCITABINE FOR INJECTION
(Gemcitabine 1000 mg/vial, Powder for Solution for Infusion)

1. Name of the medicinal product

Gemcitabine for Injection 1000 mg/vial

Gemcitabine 1000 mg Powder for Solution for Infusion

2. Qualitative and quantitative composition

Each vial contains gemcitabine hydrochloride equivalent to 1000 mg of gemcitabine.

After reconstitution, the solution contains 38 mg/ml of gemcitabine.

Excipient with known effect
Each 1000 mg vial contains 17.5 mg (less than 1 mmol) of sodium, that is to say essentially 'sodium-free'.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for solution for infusion.

White to off-white plug or powder.

4. Clinical particulars

4.1 Therapeutic indications

- Gemcitabine is indicated for the treatment of locally advanced or metastatic bladder cancer, in combination with cisplatin.
- Gemcitabine is indicated for the treatment of patients with locally advanced or metastatic adenocarcinoma of the pancreas.
- Gemcitabine, in combination with cisplatin, is indicated as first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC). Gemcitabine monotherapy can be considered in elderly patients or those with performance status 2.
- Gemcitabine is indicated, in combination with carboplatin, for the treatment of patients with locally advanced or metastatic epithelial ovarian carcinoma who have relapsed following a recurrence-free interval of at least 6 months after platinum-based first-line therapy.
- Gemcitabine, in combination with paclitaxel, is indicated for the treatment of patients with unresectable, locally recurrent or metastatic breast cancer who have relapsed following adjuvant/neoadjuvant chemotherapy. Prior chemotherapy should have included an anthracycline unless clinically contraindicated.

4.2 Posology and method of administration

Gemcitabine should only be prescribed by a physician qualified in the use of anti-cancer chemotherapy.

Posology

Bladder cancer (combination use)

The recommended dose of gemcitabine is 1,000 mg/m², given by 30-minute infusion on Days 1, 8 and 15 of each 28-day cycle, in combination with cisplatin. Cisplatin is given at a recommended dose of 70 mg/m² on Day 1 following gemcitabine, or on Day 2 of each 28-day cycle. This cycle is then repeated.

Pancreatic cancer

The recommended dose of gemcitabine is 1,000 mg/m², given by 30-minute intravenous infusion once weekly for up to 7 weeks, followed by a week of rest. Subsequent cycles consist of infusions once weekly for 3 consecutive weeks out of every 4 weeks.

Non-small cell lung cancer

Monotherapy: the recommended dose is 1,000 mg/m², given by 30-minute intravenous infusion once weekly for 3 weeks, followed by a 1-week rest period; this 4-week cycle is then repeated. Combination use: the recommended dose is 1,250 mg/m², given as a 30-minute intravenous infusion on Days 1 and 8 of a 21-day cycle. Cisplatin has been used at doses between 75 and 100 mg/m² once every 3 weeks.

Breast cancer (combination use)

Paclitaxel 175 mg/m² is administered on Day 1 over approximately 3 hours as an intravenous infusion, followed by gemcitabine 1,250 mg/m² as a 30-minute intravenous infusion on Days 1 and 8 of each 21-day cycle. Patients should have an absolute granulocyte count of at least 1,500 ($\times 10^6$/l) prior to initiation of the gemcitabine plus paclitaxel combination.

Ovarian cancer (combination use)

Gemcitabine 1,000 mg/m² is administered on Days 1 and 8 of each 21-day cycle as a 30-minute intravenous infusion. After gemcitabine, carboplatin is given on Day 1 at a target area under the curve (AUC) of 4.0 mg/ml·min.

Monitoring for toxicity and dose modification due to toxicity

Dose modification due to non-haematological toxicity

Periodic physical examination and checks of renal and hepatic function should be made to detect non-haematological toxicity. In general, for severe (Grade 3 or 4) non-haematological toxicity, except nausea/vomiting, therapy with gemcitabine should be withheld or decreased depending on the judgement of the treating physician, until the toxicity has resolved. For cisplatin, carboplatin and paclitaxel dose adjustment in combination therapy, refer to the corresponding Summary of Product Characteristics.

Dose modification due to haematological toxicity – initiation of a cycle

For all indications, the patient must be monitored before each dose for platelet and granulocyte counts. Patients should have an absolute granulocyte count of at least 1,500 (× 10^6/l) and a platelet count of 100,000 (× 10^6/l) prior to the initiation of a cycle.

Dose modification due to haematological toxicity – within a cycle

Bladder cancer, NSCLC and pancreatic cancer (monotherapy or in combination with cisplatin)

Absolute granulocyte count (× 10^6/l)	**Platelet count (× 10^6/l)**	**Percentage of standard dose of gemcitabine (%)**
> 1,000 and	> 100,000	100
500–1,000 or	50,000–100,000	75
< 500 or	< 50,000	Omit dose *

* Treatment omitted will not be reinstated within a cycle before the absolute granulocyte count reaches at least 500 (× 10^6/l) and the platelet count reaches 50,000 (× 10^6/l).

Breast cancer (in combination with paclitaxel)

Absolute granulocyte count (× 10^6/l)	**Platelet count (× 10^6/l)**	**Percentage of standard dose of gemcitabine (%)**
≥ 1,200 and	> 75,000	100
1,000 – < 1,200 or	50,000–75,000	75
700 – < 1,000 and	≥ 50,000	50
< 700 or	< 50,000	Omit dose *

* Treatment omitted will not be reinstated within a cycle. Treatment will start on Day 1 of the next cycle once the absolute granulocyte count reaches at least 1,500 (× 10^6/l) and the platelet count reaches 100,000 (× 10^6/l).

Ovarian cancer (in combination with carboplatin)

Absolute granulocyte count (× 10^6/l)	**Platelet count (× 10^6/l)**	**Percentage of standard dose of gemcitabine (%)**
> 1,500 and	≥ 100,000	100
1,000–1,500 or	75,000–100,000	50
< 1,000 or	< 75,000	Omit dose *

* Treatment omitted will not be reinstated within a cycle. Treatment will start on Day 1 of the next cycle once the absolute granulocyte count reaches at least 1,500 (× 10^6/l) and the platelet count reaches 100,000 (× 10^6/l).

Dose modification due to haematological toxicity in subsequent cycles (all indications)

The gemcitabine dose should be reduced to 75% of the original cycle-initiation dose in the case of any of the following haematological toxicities: absolute granulocyte count < 500 × 10^6/l for more than 5 days; absolute granulocyte count < 100 × 10^6/l for more than 3 days; febrile neutropenia; platelets < 25,000 × 10^6/l; or a cycle delay of more than 1 week due to toxicity.

Special populations

Renal or hepatic impairment

Gemcitabine should be used with caution in patients with hepatic or renal insufficiency, as there is insufficient information from clinical studies to allow clear dose recommendations for these populations (see sections 4.4 and 5.2).

Elderly (over 65 years)
Gemcitabine has been well tolerated in patients over the age of 65. There is no evidence that dose adjustments, other than those already recommended for all patients, are necessary in the elderly (see section 5.2).

Paediatric population (under 18 years)
Gemcitabine is not recommended for use in children under 18 years of age, owing to insufficient data on safety and efficacy.

Method of administration
Gemcitabine is for intravenous infusion. It is tolerated well during infusion and may be administered on an ambulatory basis. If extravasation occurs, the infusion should generally be stopped immediately and restarted in another blood vessel; the patient should be monitored carefully after administration. For instructions on reconstitution before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Breast-feeding (see section 4.6).

4.4 Special warnings and precautions for use

Prolongation of the infusion time and increased dosing frequency have been shown to increase toxicity.

Haematological toxicity
Gemcitabine can suppress bone-marrow function, manifested as leucopenia, thrombocytopenia and anaemia. Patients should be monitored before each dose for platelet, leucocyte and granulocyte counts, and suspension or modification of therapy considered when drug-induced bone-marrow depression is detected (see section 4.2). Myelosuppression is usually short-lived and rarely results in discontinuation, but peripheral blood counts may continue to deteriorate after gemcitabine has been stopped. Treatment should be started with caution in patients with impaired bone-marrow function, and the risk of cumulative bone-marrow suppression must be considered when gemcitabine is given with other chemotherapy.

Hepatic and renal impairment
Gemcitabine should be used with caution in patients with hepatic or renal impairment, as there is insufficient information from clinical studies to allow clear dose recommendations. Administration in patients with concurrent liver metastases or a pre-existing history of hepatitis, alcoholism or liver cirrhosis may lead to exacerbation of the underlying hepatic impairment. Laboratory evaluation

of renal and hepatic function (including virological tests) should be performed periodically.

Concomitant radiotherapy

Concomitant radiotherapy (given together or ≤ 7 days apart) has been associated with toxicity (see section 4.5).

Live vaccinations

Yellow fever vaccine and other live attenuated vaccines are not recommended in patients treated with gemcitabine (see section 4.5).

Posterior reversible encephalopathy syndrome (PRES)

PRES, with potentially severe consequences, has been reported in patients receiving gemcitabine alone or in combination. Acute hypertension and seizure activity were reported in most affected patients, but headache, lethargy, confusion and blindness may also occur; diagnosis is optimally confirmed by MRI. PRES was typically reversible with appropriate supportive measures. Gemcitabine should be permanently discontinued, and supportive measures (including blood-pressure control and anti-seizure therapy) implemented, if PRES develops.

Cardiovascular

Owing to the risk of cardiac and/or vascular disorders, particular caution must be exercised in patients with a history of cardiovascular events.

Capillary leak syndrome

Capillary leak syndrome has been reported with gemcitabine alone or in combination; it is usually treatable if recognised early, but fatal cases have occurred. Features include generalised oedema, weight gain, hypoalbuminaemia, severe hypotension, acute renal impairment and pulmonary oedema. Gemcitabine should be discontinued and supportive measures implemented if it develops.

Pulmonary

Pulmonary effects, sometimes severe (such as pulmonary oedema, interstitial pneumonitis or adult respiratory distress syndrome), have been reported. If such effects develop, discontinuation of gemcitabine should be considered; early supportive care may help ameliorate the condition.

Haemolytic uraemic syndrome

Clinical findings consistent with haemolytic uraemic syndrome (HUS), a potentially life-threatening disorder, have rarely been reported. Gemcitabine should be discontinued at the first evidence of microangiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, or elevation of serum bilirubin, creatinine, blood urea nitrogen or LDH. Renal failure may not be reversible on discontinuation, and dialysis may be required.

Fertility

In fertility studies, gemcitabine caused hypospermatogenesis in male mice (see section 5.3). Men being treated with gemcitabine are advised not to father a child during and up to 6 months after treatment, and to seek advice on cryoconservation of sperm before treatment because of the possibility of infertility (see section 4.6).

Sodium

This medicinal product contains 17.5 mg (less than 1 mmol) of sodium per 1000 mg vial, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No specific interaction studies have been performed (see section 5.2).

Radiotherapy

Gemcitabine has radiosensitising activity. When given concurrently (together or ≤ 7 days apart) with therapeutic radiation, severe and potentially life-threatening toxicity (particularly mucositis, oesophagitis and pneumonitis) has been observed, and the optimum regimen for safe concurrent administration has not been established for all tumour types. When given more than 7 days before or after radiation, no enhanced toxicity has been observed other than radiation recall; gemcitabine may be started after the acute effects of radiation have resolved, or at least one week after radiation. Radiation injury has been reported on targeted tissues (e.g. oesophagitis, colitis and pneumonitis) with both concurrent and non-concurrent use.

Live vaccines

Yellow fever and other live attenuated vaccines are not recommended, owing to the risk of systemic, possibly fatal, disease, particularly in immunosuppressed patients.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data on the use of gemcitabine in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). Based on animal data and the mechanism of action, gemcitabine should not be used during pregnancy unless clearly necessary. Women should be advised not to become pregnant during treatment and to inform their physician immediately if this occurs.

Breast-feeding

It is not known whether gemcitabine is excreted in human milk, and adverse effects on the breast-fed child cannot be excluded. Breast-feeding must be discontinued during gemcitabine therapy.

Fertility

In fertility studies, gemcitabine caused hypospermatogenesis in male mice. Men being treated with gemcitabine are advised not to father a child during and up to

6 months after treatment, and to seek advice on cryoconservation of sperm before treatment because of the possibility of infertility.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, gemcitabine has been reported to cause mild to moderate somnolence, especially in combination with alcohol. Patients should be cautioned against driving or operating machinery until it is established that they do not become somnolent.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions include nausea with or without vomiting and raised liver transaminases (AST/ALT) and alkaline phosphatase (in approximately 60% of patients); proteinuria and haematuria (approximately 50%); dyspnoea (10–40%, highest in lung cancer patients); and allergic skin rash (approximately 25%), associated with itching in about 10% of patients. Dose-limiting adverse reactions are reductions in thrombocyte, leucocyte and granulocyte counts. The frequency and severity of adverse reactions are affected by the dose, infusion rate and intervals between doses.

Tabulated list of adverse reactions

Frequencies are defined as: 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 data).

System Organ Class	Frequency	Undesirable effect
Infections and infestations	Common	Infections
	Not known	Sepsis
Blood and lymphatic system disorders	Very common	Leucopenia (neutropenia Grade 3 = 19.3%; Grade 4 = 6%); thrombocytopenia; anaemia. Bone-marrow suppression is usually mild to moderate and mostly affects the granulocyte count (see section 4.2)
	Common	Febrile neutropenia
	Very rare	Thrombocytosis; thrombotic microangiopathy
Immune system disorders	Very rare	Anaphylactoid reaction
Metabolism and nutrition disorders	Common	Anorexia
Nervous system disorders	Common	Headache, insomnia, somnolence
	Uncommon	Cerebrovascular accident
	Very rare	Posterior reversible encephalopathy syndrome (see section 4.4)
Cardiac disorders	Uncommon	Arrhythmias, predominantly supraventricular in nature; heart failure
	Rare	Myocardial infarction

System Organ Class	Frequency	Undesirable effect
Vascular disorders	Rare	Clinical signs of peripheral vasculitis and gangrene; hypotension
	Very rare	Capillary leak syndrome (see section 4.4)
Respiratory, thoracic and mediastinal disorders	Very common	Dyspnoea (usually mild and passing rapidly without treatment)
	Common	Cough; rhinitis
	Uncommon	Interstitial pneumonitis (see section 4.4); bronchospasm (usually mild and transient, but may require parenteral treatment)
	Rare	Pulmonary oedema; adult respiratory distress syndrome (see section 4.4)
Gastrointestinal disorders	Very common	Vomiting; nausea
	Common	Diarrhoea; stomatitis and ulceration of the mouth; constipation
	Very rare	Ischaemic colitis
Hepatobiliary disorders	Very common	Elevation of liver transaminases (AST and ALT) and alkaline phosphatase
	Common	Increased bilirubin
	Uncommon	Serious hepatotoxicity, including liver failure and death
	Rare	Increased gamma-glutamyltransferase (GGT)
Skin and subcutaneous tissue disorders	Very common	Allergic skin rash, frequently associated with pruritus; alopecia
	Common	Itching; sweating
	Rare	Severe skin reactions, including desquamation and bullous skin eruptions; ulceration; vesicle and sore formation; scaling
	Very rare	Toxic epidermal necrolysis; Stevens-Johnson syndrome
	Not known	Pseudocellulitis
Musculoskeletal and connective tissue disorders	Common	Back pain; myalgia
Renal and urinary disorders	Very common	Haematuria; mild proteinuria
	Uncommon	Renal failure (see section 4.4); haemolytic uraemic syndrome (see section 4.4)
General disorders and administration site conditions	Very common	Influenza-like symptoms (most commonly fever, headache, chills, myalgia, asthenia and anorexia; cough, rhinitis, malaise, perspiration and sleeping difficulties have also been reported); oedema / peripheral oedema, including facial oedema (usually reversible after stopping treatment)
	Common	Fever; asthenia; chills
	Rare	Injection site reactions (mainly mild in nature)

System Organ Class	Frequency	Undesirable effect
Injury, poisoning and procedural complications	Rare	Radiation toxicity (see section 4.5); radiation recall

Combination use

The frequency of Grade 3 and 4 haematological toxicities, particularly neutropenia, increases when gemcitabine is used in combination (for example with paclitaxel in breast cancer, or with platinum agents in bladder and ovarian cancer), although this is not associated with an increased incidence of infections or haemorrhagic events. Fatigue and febrile neutropenia occur more frequently in combination with paclitaxel; fatigue, which is not associated with anaemia, usually resolves after the first cycle.

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 to the National Regulatory Authority.

4.9 Overdose

There is no known antidote for overdose of gemcitabine. Doses as high as 5,700 mg/m² have been administered by intravenous infusion over 30 minutes every 2 weeks with clinically acceptable toxicity. In the event of suspected overdose, the patient should be monitored with appropriate blood counts and should receive supportive therapy as necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antineoplastic agents, pyrimidine analogues. ATC code: L01BC05.

Mechanism of action

Gemcitabine (dFdC) is a pyrimidine antimetabolite that is metabolised intracellularly by nucleoside kinase to the active diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides. Its cytotoxic effect is due to inhibition of DNA synthesis by two mechanisms: dFdCDP inhibits ribonucleotide reductase, reducing the concentration of deoxynucleotides (in particular dCTP) required for DNA synthesis; and dFdCTP competes with dCTP for incorporation into DNA. The reduced intracellular dCTP concentration potentiates the incorporation of dFdCTP into DNA (self-potentiation). After incorporation, one additional nucleotide is added to the growing DNA strand, resulting in essentially complete inhibition of further DNA synthesis (masked chain termination) and induction of apoptosis. The action of gemcitabine is phase-specific, primarily killing cells undergoing DNA synthesis (S-phase) and, under certain circumstances, blocking progression at the G1/S-phase boundary.

Clinical efficacy and safety

Efficacy has been demonstrated in randomised phase III studies. In advanced or metastatic bladder cancer, gemcitabine plus cisplatin gave median survival, time to progression and response rates comparable to MVAC, with a better toxicity profile. In advanced pancreatic cancer, gemcitabine gave a significantly higher clinical-benefit response rate than 5-fluorouracil (23.8% vs 4.8%), with prolonged median survival (5.7 vs 4.4 months). In NSCLC, gemcitabine plus cisplatin significantly improved response rate, time to progression and median survival versus cisplatin alone. In relapsed ovarian carcinoma, gemcitabine plus carboplatin significantly prolonged time to progression versus carboplatin (8.6 vs 5.8 months). In metastatic breast cancer, gemcitabine plus paclitaxel significantly prolonged time to progression (6.14 vs 3.98 months) and overall survival (18.6 vs 15.8 months) versus paclitaxel.

5.2 Pharmacokinetic properties

The pharmacokinetics of gemcitabine were examined in 353 patients over doses ranging from 500 to 2,592 mg/m² infused over 0.4 to 1.2 hours.

Absorption and peak concentrations

Peak plasma concentrations (within 5 minutes of the end of infusion) were 3.2 to 45.5 micrograms/ml. Following 1,000 mg/m² over 30 minutes, plasma concentrations of the parent compound exceeded 5 micrograms/ml for about 30 minutes after the end of infusion and 0.4 micrograms/ml for a further hour.

Distribution

The volume of distribution of the central compartment was 12.4 l/m² for women and 17.5 l/m² for men; that of the peripheral compartment was 47.4 l/m². Plasma protein binding is considered negligible.

Biotransformation

Gemcitabine is rapidly metabolised by cytidine deaminase in the liver, kidney, blood and other tissues. Intracellular metabolism produces the mono-, di- and triphosphates, of which dFdCDP and dFdCTP are active. The primary inactive metabolite, 2'-deoxy-2',2'-difluorouridine (dFdU), is found in plasma and urine.

Elimination

The elimination half-life ranged from 42 to 94 minutes depending on age and gender, with elimination virtually complete within 5 to 11 hours of the start of infusion; gemcitabine does not accumulate when administered once weekly. Systemic clearance ranged from 29.2 to 92.2 l/h/m² (about 25% lower in women, and decreasing with age). Less than 10% is excreted as unchanged drug in the urine; during the week following administration, 92 to 98% of the dose is recovered, 99% in the urine (mainly as dFdU) and about 1% in the faeces.

Special populations

Mild to moderate renal insufficiency (GFR 30 to 80 ml/min) has no consistent, significant effect on gemcitabine pharmacokinetics. Combination therapy with paclitaxel or carboplatin did not alter gemcitabine pharmacokinetics.

5.3 Preclinical safety data

In repeat-dose studies of up to 6 months in mice and dogs, the principal finding was schedule- and dose-dependent, reversible haematopoietic suppression. Gemcitabine is mutagenic in an in vitro mutation test and an in vivo bone-marrow micronucleus test; long-term carcinogenicity studies have not been performed. In fertility studies, gemcitabine caused reversible hypospermatogenesis in male mice, with no effect detected on female fertility. Animal studies have shown reproductive toxicity, including birth defects and other effects on embryo-foetal development, gestation and perinatal and postnatal development.

6. Pharmaceutical particulars

6.1 List of excipients

- Mannitol (E421)
- Sodium acetate (E262)
- Hydrochloric acid (E507) (for pH adjustment)
- Sodium hydroxide (E524) (for pH adjustment)

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Unopened vial

2 years.

Reconstituted solution

Chemical and physical in-use stability has been demonstrated for 24 hours at 30°C. From a microbiological point of view, the product should be used immediately; if not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not exceed 24 hours at room temperature, unless reconstitution has taken place in controlled and validated aseptic conditions. Reconstituted solutions should not be refrigerated, as crystallisation may occur.

6.4 Special precautions for storage

Unopened vial: store at not more than 30°C. For storage conditions of the reconstituted medicinal product, see section 6.3.

6.5 Nature and contents of container

Type I flint glass vial, stoppered with a grey butyl rubber stopper and sealed with an aluminium seal with a polypropylene flip-off cap. Each pack contains 1 vial.

6.6 Special precautions for disposal and other handling

Handling

The normal safety precautions for cytotoxic agents must be observed when preparing and disposing of the infusion solution. Preparation should be carried out in a safety cabinet, and protective gowns and gloves should be worn; if no safety cabinet is available, the equipment should be supplemented with a mask and protective glasses. If the preparation contacts the eyes it may cause serious irritation; the eyes should be rinsed immediately and thoroughly with water, and a doctor consulted if irritation persists. If the solution is spilled on the skin, rinse thoroughly with water.

Reconstitution

The only approved diluent for reconstitution is sodium chloride 9 mg/ml (0.9%) solution for injection, without preservative. Owing to solubility considerations, the maximum concentration on reconstitution is 40 mg/ml; reconstitution above 40 mg/ml may result in incomplete dissolution and should be avoided. Using aseptic technique, add 25 ml of sterile sodium chloride 9 mg/ml (0.9%) solution for injection, without preservative, to the 1000 mg vial; the total volume after reconstitution is 26.3 ml, yielding a gemcitabine concentration of 38 mg/ml (allowing for the displacement volume of the lyophilised powder). Shake to dissolve. Further dilution with sterile sodium chloride 9 mg/ml (0.9%) solution for injection, without preservative, may be performed. The reconstituted solution is clear and colourless to light straw-coloured. Parenteral products should be inspected visually for particulate matter and discolouration before administration; if particulate matter is observed, do not administer.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

National Pharmacy Limited

P.O. Box 17843-00500, Old Mombasa Road, Behind Nice and Lovely, Colchester Park Godown No. 11, Nairobi, Kenya.

Manufacturer

Biozenta Lifescience Pvt. Ltd.

Khasra No. 59, 60 & 61, Bela Bathri, Haroli, Una, Himachal Pradesh 174301, India.

8. Marketing Authorisation Number

CTD12647

9. Date of first authorisation / renewal of the authorisation

03.07.2026

10. Date of revision of the text

03.07.2026