OXAPLIN 5 mg/ml

Concentrate Solution for Infusion

Name and strength of active ingredient
Oxaliplatin 5 mg/ml

Dosage form
Injection

Product Description
A clear colourless solution in a clear glass vial. When examined under suitable conditions of visibility it should be practically free from particles.

Description of diluted preparation: Clear colourless solution free from visible particulate matter

Pharmacodynamic properties
Pharmacotherapeutic group: other antineoplastic agents, platinum compounds
ATC code: L01XA 03
Oxaliplatin is an antineoplastic active substance belonging to a new class of platinum-based compounds in which the platinum atom is complexed with 1,2-diaminocyclohexane ("DACH") and an oxalate group.
Oxaliplatin is a single enantiomer, (*SP*-4-2)-[(1*R*,2*R*)-Cyclohexane-1,2-diamine-k*N*, k*N'*] [ethanedioato(2-)-kO^1, kO^2] platinum.
Oxaliplatin exhibits a wide spectrum of both *in vitro* cytotoxicity and *in vivo* antitumour activity in a variety of tumour model systems including human colorectal cancer models. Oxaliplatin also demonstrates *in vitro* and *in vivo* activity in various cisplatin resistant models.
A synergistic cytotoxic action has been observed in combination with 5-fluorouracil both *in vitro*and *in vivo*.
Studies on the mechanism of action of oxaliplatin, although not completely elucidated, show that the aqua-derivatives resulting from the biotransformation of oxaliplatin, interact with DNA to form both inter and intra-strand cross-links, resulting in the disruption of DNA synthesis leading to cytotoxic and antitumour effects.
Pharmacokinetic properties
The pharmacokinetics of individual active compounds have not been determined. The pharmacokinetics of ultrafiltrable platinum, representing a mixture of all unbound, active and inactive platinum species, following a two-hour infusion of oxaliplatin at 130 mg /m² every three weeks for 1 to 5 cycles and oxaliplatin at 85 mg/m² every two weeks for 1 to 3 cycles are as follows:
Summary of Platinum Pharmacokinetic Parameter Estimates in Ultrafiltrate Following Multiple Doses of Oxaliplatin at 85 mg/m² Every Two Weeks or at 130 mg/m² Every Three Weeks

Dose	C_{max} µg/mL	AUC_{0-48} µg.h/mL	AUC µg.h/mL	$t_{1/2}\alpha$ h	$t_{1/2}\beta$ h	$t_{1/2}\gamma$ h	V_{ss} L	CL L/h
85 mg/m²	0.814	4.19	4.68	0.43	16.8	391	440	17.4
Mean SD	0.193	0.647	1.40	0.35	5.74	406	199	6.35
130 mg/m²	1.21	8.20	11.9	0.28	16.3	273	582	10.1
Mean SD	0.10	2.40	4.60	0.06	2.90	19.0	261	3.07

Mean AUC_{0-48}, and C_{max} values were determined on Cycle 3 (85 mg/m²) or cycle 5 (130 mg/m²).
Mean AUC, V_{ss} and CL values were determined on Cycle 1.
C_{max}, AUC, AUC_{0-48}, V_{ss} and CL values were determined by non-compartmental analysis.
$t_{1/2}\alpha$, $t_{1/2}\beta$, and $t_{1/2}\gamma$, were determined by compartmental analysis (Cycles 1-3 combined).
At the end of a 2-hour infusion, 15% of the administered platinum is present in the systemic circulation, the remaining 85% being rapidly distributed into tissues or eliminated in the urine. Irreversible binding to red blood cells and plasma, results in half-lives in these matrices that are close to the natural turnover of red blood cells and serum albumin. No accumulation was observed in plasma ultrafiltrate following 85 mg/m² every two weeks or 130mg/m² every three weeks and steady state was attained by cycle one in this matrix. Inter- and intra-subject variability is generally low.
Biotransformation *in vitro* is considered to be the result of non-enzymatic degradation and there is no evidence of cytochrome P450-mediated metabolism of the diaminocyclohexane (DACH) ring. Oxaliplatin undergoes extensive biotransformation in patients, and no intact drug was detectable in plasma ultrafiltrate at the end of a 2h-infusion. Several cytotoxic biotransformation products including the monochloro-, dichloro- and diaquo-DACH platinum species have been identified in the systemic circulation together with a number of inactive conjugates at later time points.
Platinum is predominantly excreted in urine, with clearance mainly in the 48 hours following administration.
By day 5, approximately 54% of the total dose was recovered in the urine and < 3% in the faeces.
The effect of renal impairment on the disposition of oxaliplatin was studied in patients with varying degrees of renal function. Oxaliplatin was administered at a dose of 85 mg/m² in the control group with a normal renal function (CLcr > 80 ml/min, n=12) and in patients with mild (CLcr = 50 to 80 ml/min, n=13) and moderate (CLcr = 30 to 49 ml/min, n=11) renal impairment, and at a dose of 65mg/m² in patients with severe renal impairment (CLcr < 30 ml/min, n=5). Median exposure was 9, 4, 6, and 3 cycles, respectively, and PK data at cycle 1 were obtained in 11, 13, 10, and 4 patients respectively.
There was an increase in plasma ultrafiltrate (PUF) platinum AUC, AUC/dose and a decrease in total and renal CL and Vss with increasing renal impairment especially in the (small) group of patients with severe renal impairment: point estimate (90% CI) of estimated mean ratios by renal status versus normal renal function for AUC/dose were 1.36 (1.08, 1.71), 2.34 (1.82, 3.01) and 4.81 (3.49, 6.64) for patients with mild and moderate and in severe renal failure respectively.
Elimination of oxaliplatin is significantly correlated with the creatinine clearance. Total PUF platinum CL was respectively 0.74 (0.59, 0.92), 0.43 (0.33, 0.55) and 0.21 (0.15, 0.29) and for Vss respectively 0.52 (0.41, 0.65), 0.73 (0.59, 0.91) and 0.27 (0.20, 0.36) for patients with mild, moderate and severe renal failure respectively. Total body clearance of PUF platinum was therefore reduced by respectively 26% in mild, 57% in moderate, and 79% in severe renal impairment compared to patients with normal function.
Renal clearance of PUF platinum was reduced in patients with impaired renal function by 30% in mild, 65% in moderate, and 84% in severe renal impairment compared to patients with normal function.
There was an increase in beta half life of PUF platinum with increasing degree of renal impairment mainly in the severe group. Despite the small number of patients with severe renal dysfunction, these data are of concern in patients in severe renal failure and should be taken into account when prescribing oxaliplatin in patients with renal impairment
Indication
Oxaliplatin in combination with 5-fluorouracil (5-FU) and folinic acid (FA) is indicated for:
- Adjuvant treatment of stage III (Duke's C) colon cancer after complete resection of primary tumor.
- Treatment of metastatic colorectal cancer.

Recommended Dose
FOR ADULTS ONLY
The recommended dose for oxaliplatin in adjuvant setting is 85 mg/m² intravenously repeated every two weeks for 12 cycles (6 months).
The recommended dose for oxaliplatin in treatment of metastatic colorectal cancer is 85 mg/m² intravenously repeated every 2 weeks.
Dosage given should be adjusted according to tolerability.
Oxaliplatin should always be administered before fluoropyrimidines – i.e. 5-fluorouracil.
Oxaliplatin is administered as a 2- to 6-hour intravenous infusion in 250 to 500 ml of 5% glucose solution to give a concentration between 0.2 mg/ml and 0.70 mg/ml; 0.70 mg/ml is the highest concentration in clinical practice for an oxaliplatin dose of 85 mg/m².
Oxaliplatin was mainly used in combination with continuous infusion 5-fluorouracil based regimens. For the two-weekly treatment schedule 5-fluorouracil regimens combining bolus and continuous infusion were used.
Special Populations
- Renal impairment:
Oxaliplatin must not be administered in patients with severe renal impairment. In patients with mild to moderate renal impairment, the recommended dose of oxaliplatin is 85 mg/m².
- Hepatic insufficiency:
In a phase I study including patients with several levels of hepatic impairment, frequency and severity of hepato-biliary disorders appeared to be related to progressive disease and impaired liver function tests at baseline. No specific dose adjustment for patients with abnormal liver function tests was performed during clinical development.
- Elderly patients:
No increase in severe toxicities was observed when oxaliplatin was used as a single agent or in combination with 5-fluorouracil in patients over the age of 65. In consequence no specific dose adaptation is required for elderly patients.
- Paediatric patients:
There is no relevant indication for use of oxaliplatin in children. The effectiveness of oxaliplatin single agent in the paediatric populations with solid tumors has not been established.

Route of Administration
Method of administration
Oxaliplatin is administered by intravenous infusion.
The administration of oxaliplatin does not require hyperhydration.
Oxaliplatin diluted in 250 to 500 ml of 5% glucose solution to give a concentration not less than 0.2 mg/ml must be infused via a central venous line or peripheral vein over 2 to 6 hours. Oxaliplatin infusion must always precede the administration of 5-fluorouracil.
In the event of extravasation, administration must be discontinued immediately.
Instructions for use:
Oxaliplatin must be diluted before use. Only 5% glucose diluent is to be used to dilute the concentrate for solution for infusion product.
Direction for dilution:
Special precautions for administration
- DO NOT use injection equipment containing aluminium.
- DO NOT administer undiluted.
- Only 5% glucose solution is to be used as a diluent. DO NOT dilute for infusion with sodium chloride or chloride containing solutions.
- DO NOT mix with any other medicinal products in the same infusion bag or administer simultaneously by the same infusion line.
- DO NOT mix with alkaline drugs or solutions, in particular 5-fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of others drugs. Alkaline drugs or solutions will adversely affect the stability of oxaliplatin.

Instruction for use with folinic acid (as calcium folinate or disodium folinate)
Oxaliplatin 85mg/m² IV infusion in 250 to 500 ml of 5% glucose solution is given at the same time as folinic acid intravenous infusion in 5% glucose solution, over 2 to 6 hours, using a Y-line placed immediately before the site of infusion.
These two medicinal products should not be combined in the same infusion bag. Folinic acid must not contain trometamol as an excipient and must only be diluted using isotonic 5% glucose solution, never in alkaline solutions or sodium chloride or chloride containing solutions.
Instruction for use with 5 fluorouracil
Oxaliplatin should always be administered before fluoropyrimidines – i.e. before 5-fluorouracil. After oxaliplatin administration, flush the line and then administer 5-fluorouracil.
USE ONLY the recommended solvents.
Preparation of the infusion solution
Withdraw the required amount of concentrate from the vial(s) and then dilute with 250 ml to 500 ml of a 5% glucose solution to give an oxaliplatin concentration between 0.2 mg/ml and 2 mg/ml; concentration range for which the physico-chemical stability of oxaliplatin has been demonstrated.
Administer by Intravenous infusion.
Inspect visually prior to use. Only clear solutions without particles should be used.
The medicinal product is for single use only. Any unused infusion solution should be discarded.
NEVER use sodium chloride or chloride containing solutions for dilution.
The compatibility of Oxaliplatin solution for infusion has been tested with representative, PVC-based, administration sets.
Infusion of the solution
The administration of oxaliplatin does not require prehydration.
Oxaliplatin diluted in 250 to 500 ml of a 5% glucose solution to give a concentration not less than 0.2 mg/ml must be infused either by peripheral vein or central venous line over 2 to 6 hours. When oxaliplatin is administered with 5-fluorouracil, the oxaliplatin infusion must precede the administration of 5-fluorouracil.
Disposal
Remnants of the medicinal product as well as all materials that have been used for dilution and administration must be destroyed according to hospital standard procedures applicable to cytotoxic agents and in accordance with local requirements related to the disposal of hazardous waste.
Contraindication
Oxaliplatin is contraindicated in patients who
- have a known history of hypersensitivity to oxaliplatin.
- are breast feeding.
- have myelosuppression prior to starting first course, as evidenced by baseline neutrophils <$2x10^9$/l and/or platelet count of <$100x10^9$/l.
- have a peripheral sensitive neuropathy with functional impairment prior to first course.
- have a severely impaired renal function (creatinine clearance less than 30 ml/min)

Warnings & Precautions
Oxaliplatin should only be used in specialised departments of oncology and should be administered under the supervision of an experienced oncologist.
Renal impairment
Patients with mild to moderate renal impairment should be closely monitored for adverse reactions and the dose adjusted according to toxicity.
Hypersensitivity reactions
Special surveillance should be ensured for patients with a history of allergic manifestations to other products containing platinum. In case of anaphylactic manifestations the infusion should be interrupted immediately and an appropriate symptomatic treatment started. Re-administration of oxaliplatin to such patients is contra-indicated. Cross reactions, sometimes fatal, have been reported with all platinum compounds.
In case of oxaliplatin extravasation, the infusion must be stopped immediately and usual local symptomatic treatment initiated.
Neurological Symptoms
Neurological toxicity of oxaliplatin should be carefully monitored, especially if co-administered with other medicinal products with specific neurological toxicity. A neurological examination should be performed before each administration and periodically thereafter.
For patients who develop acute laryngopharyngeal dysaesthesia, during or within the hours following the 2-hour infusion, the next oxaliplatin infusion should be administered over 6 hours.
Peripheral neuropathy
If neurological symptoms (paraesthesia, dysaesthesia) occur, the following recommended oxaliplatin dosage adjustment should be based on the duration and severity of these symptoms:
- If symptoms last longer than seven days and are troublesome, the subsequent oxaliplatin dose should be reduced from 85 to 65 mg/m² (metastatic setting) or 75 mg/m² (adjuvant setting).
- If paraesthesia without functional impairment persists until the next cycle, the subsequent oxaliplatin dose should be reduced from 85 to 65 mg/m² (metastatic setting) or 75 mg/m² (adjuvant setting).
- If paraesthesia with functional impairment persists until the next cycle, oxaliplatin should be discontinued.
- If these symptoms improve following discontinuation of oxaliplatin therapy, resumption of therapy may be considered.

Patients should be informed of the possibility of persistent symptoms of peripheral sensory neuropathy after the end of the treatment. Localized moderate paresthesias or paresthesias that may interfere with functional activities can persist after up to 3 years following treatment cessation in the adjuvant setting.
Reversible Posterior Leukoencephalopathy Syndrome (RPLS)
Cases of Reversible Posterior Leukoencephalopathy Syndrome (RPLS also known as PRES, Posterior Reversible Encephalopathy Syndrome) have been reported in patients receiving oxaliplatin in combination chemotherapy. RPLS is a rare, reversible, rapidly evolving neurological condition, which can include seizure, hypertension, headache, confusion, blindness, and other visual and neurological disturbances. Diagnosis of RPLS is based upon confirmation by brain imaging, preferably MRI (Magnetic Resonance Imaging)
Nausea, vomiting, diarrhoea, dehydration and haematological changes
Gastrointestinal toxicity, which manifests as nausea and vomiting, warrants prophylactic and/or therapeutic anti-emetic therapy.

Dehydration, paralytic ileus, intestinal obstruction, hypokalemia, metabolic acidosis and renal impairment may be caused by severe diarrhoea/emesis particularly when combining oxaliplatin with 5-fluorouracil.

If haematological toxicity occurs (neutrophils < $1.5x10^9$/l or platelets < $50x10^9$/l), administration of the next course of therapy should be postponed until haemotological values return to acceptable levels. A full blood count with white cell differential should be performed prior to start of therapy and before each subsequent course.

Patients must be adequately informed of the risk of diarrhoea/emesis, mucositis/stomatitis and neutropenia after oxaliplatin and 5-fluorouracil administration so that they can urgently contact their treating physician for appropriate management.

If mucositis/stomatitis occurs with or without neutropenia, the next treatment should be delayed until recovery from mucositis/stomatitis to grade 1 or less and/or until the neutrophil count is ≥ 1.5×10^9/l. For oxaliplatin combined with 5-fluorouracil (with or without folinic acid), the usual dose adjustments for 5-fluorouracil associated toxicities should apply.

If grade 4 diarrhoea, grade 3-4 neutropenia (neutrophils < $1.0x10^9$/l), grade 3-4 thrombocytopenia (platelets < $50x10^9$/l) occur, the dose of oxaliplatin should be reduced from 85 to 65 mg/m² (metastatic setting) or 75 mg/m² (adjuvant setting), in addition to any 5-fluorouracil dose reductions required.

Pulmonary

In the case of unexplained respiratory symptoms such as non-productive cough, dyspnoea, crackles or radiological pulmonary infiltrates, oxaliplatin should be discontinued until further pulmonary investigations exclude an interstitial lung disease.

Hepatic

In case of abnormal liver function test results or portal hypertension which does not obviously result from liver metastases, very rare cases of drug-induced hepatic vascular disorders should be considered.

Fertility

Genotoxic effects were observed with oxaliplatin in the preclinical studies. Therefore male patients treated with oxaliplatin are advised not to father a child during and up to 6 months after treatment and to seek advice on conservation of sperm prior to treatment because oxaliplatin may have an anti-fertility effect which could be irreversible.

Women should not become pregnant during treatment with oxaliplatin and should use an effective method of contraception

Interaction with other medicaments

In patients who have received a single dose of 85 mg/m² of oxaliplatin, immediately before administration of 5-fluorouracil, no change in the level of exposure to 5-fluorouracil has been observed. *In vitro*, no significant displacement of oxaliplatin binding to plasma proteins has been observed with the following agents: erythromycin, salicylates, granisetron, paclitaxel, and sodium valproate.

Pregnancy and Lactation

To date there is no available information on safety of use in pregnant women. In animal studies, reproductive toxicity was observed. Consequently, oxaliplatin is not recommended during pregnancy and in women of childbearing potential not using contraceptive measures.

The use of oxaliplatin should only be considered after suitably appraising the patient of the risk to the foetus and with the patient's consent.

Appropriate contraceptive measures must be taken during and after cessation of therapy during 4 months for women and 6 months for men.

Excretion in breast milk has not been studied. Breast-feeding is contra-indicated during oxaliplatin therapy.

Oxaliplatin may have an anti-fertility effect (see section **Warnings & Precautions**).

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, oxaliplatin treatment resulting in an increased risk of dizziness, nausea and vomiting, and other neurologic symptoms that affect gait and balance may lead to a minor or moderate influence on the ability to drive and use machines.

Vision abnormalities, in particular transient vision loss (reversible following therapy discontinuation), may affect patients' ability to drive and use machines. Therefore, patients should be warned of the potential effect of these events on the ability to drive or use machines.

Side effects/Adverse Reactions

The most frequent adverse events of oxaliplatin in combination with 5-fluorouracil/folinic acid (5-FU/FA) were gastrointestinal (diarrhea, nausea, vomiting and mucositis), haematological (neutropenia, thrombocytopenia) and neurological (acute and dose cumulative peripheral sensory neurophathy). Overall, these adverse events were more frequent and severe with oxaliplatin and 5-FU/FA combination than with 5-FU/FA alone.

MedDRA Organ system classes	Very common	Common	Uncommon	Rare
Investigations	- Hepatic enzyme increase - Blood alkaline phosphatase increase - Blood bilirubin increase - Blood lactate dehydrogenase increase - Weight increase (adjuvant setting)	- Blood creatinine increase - Weight decrease (metastatic setting)		
Blood and lymphatic system disorders	- Anaemia - Neutropenia - Thrombocytopenia - Leukopenia - Lymphopenia	- Febrile neutopenia		- Immunoallergic thrombocytopenia **-** Haemolytic anaemia
Nervous system disorders	- Peripheral sensory neuropathy ***- Sensory disturbance*** - Dysgeusia - Headache	***- Dizziness*** - Motor neuritis - Meningism		- Dysarthria - Reversible Posterior Leukoencepha-lopathy syndrome (RPLS, or PRES)
Eye disorders		***- Conjunctivitis*** - Visual disturbance		**-** Visual acuity reduced transiently - Visual field disturbances - Optic neuritis - Transient vision loss, reversible following therapy discontinuation
Ear and labyrinth disorders			- Ototoxicity	- Deafness
Respiratory, thoracic and mediastinal disorders	**-** Dyspnoea - Cough - Epistaxis	- Hiccups - Pulmonary embolism		- Interstitial lung disease, sometimes fatal **-** Pulmonary fibrosis
Gastrointestinal disorders	***- Nausea*** - Diarrhoea ***- Vomiting*** ***- Stomatitis/ Mucositis*** ***- Abdominal pain*** - Constipation	***- Dyspepsia*** ***-Gastroesophageal reflux*** - Gastrointestinal hemorrhage - Rectal haemorrhage	**-** Ileus **-** Intestinal obstruction	- Colitis including clostridium difficile diarrhea - Pancreatitis
Renal and urinary disorders		-Haematuria - Dysuria - Micturition frequency abnormal		
Skin and subcutaneous tissue disorders	**-** Skin disorder - Alopecia	- Skin exfoliation (i.e. Hand & Foot syndrome) - Rash erythematous - Rash - Hyperhidrosis - Nail disorder		
Musculoskeletal and connective tissue disorders	- Back pain	***- Arthralgia*** - Bone pain		
Metabolism and nutrition disorders	- Anorexia - Hyperglycaemia - Hypokalaemia - Hypernatraemia	***- Dehydration***	**-** Metabolic acidosis	
Infections and infestations	**-** Infection	- Rhinitis - Upper respiratory tract infection ***- Neutropenic sepsis***		
Vascular disorders		***- Haemorrhage*** ***- Flushing*** ***- Deep vein thrombosis*** - Hypertension		
General disorders and administration site conditions	- Fatigue - Fever++ - Asthenia - Pain - Injection site reaction+++			
Immune system disorders	**-** *Allergy/ allergic reaction+*			
Psychiatric disorders		***- Depression*** ***- Insomnia***	**-** Nervous-ness	

\+ Very common allergies/allergic reactions, occurring mainly during infusion, sometimes fatal. Common allergic reactions include skin rash, particularly urticaria, conjunctivitis, and rhinitis. Common anaphylactic or anaphylactoid reactions, include bronchospasm, angioedema, hypotension, sensation of chest pain and anaphylactic shock.

++ Very common fever, rigors (tremors), either from infection (with or without febrile neutropenia) or possibly from immunological mechanism.

+++ Injection site reactions including local pain, redness, swelling and thrombosis have been reported. Extravasation may also result in local pain and inflammation which may be severe and lead to complications including necrosis, especially when oxaliplatin is infused through a peripheral vein. Dehydration, paralytic ileus, intestinal obstruction, hypokalemia, metabolic acidosis and renal impairment may be caused by severe diarrhoea/emesis particularly when combining oxaliplatin with 5 fluorouracil (5 FU).

Hepato-biliary disorders

Very rare (< 1/10,000):

Liver sinusoidal obstruction syndrome, also known as veno-occlusive disease of liver, or pathological manifestations related to such liver disorder, including peliosis hepatis, nodular regenerative hyperplasia, perisinusoidal fibrosis. Clinical manifestations may be portal hypertension and/or increased transaminases.

Renal and urinary disorders

Very rare (< 1/10,000):

Acute tubular necrosis, acute interstitial nephritis and acute renal failure.

Signs & Symptoms of overdose and Treatment

There is no known antidote to oxaliplatin. In cases of overdose, exacerbation of adverse events can be expected. Monitoring of haematological parameters should be initiated and symptomatic treatment given.

Incompatibilities

The diluted medicinal product should not be mixed with other medications in the same infusion bag or infusion line. Under instructions for use described in section **Direction for dilution** can be co-administered with folinic acid (FA) via a Y-line.

- DO NOT mix with alkaline medicinal products or solutions, in particular 5-fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of other drugs. Alkaline drugs or solutions will adversely affect the stability of oxaliplatin.
- DO NOT dilute oxaliplatin with saline or other solutions containing chloride ions (including calcium, potassium or sodium chloride).
- DO NOT mix with other medicinal products in the same infusion bag or infusion line (see section **Direction for dilution** for instructions concerning simultaneous administration with folinic acid).
- DO NOT use injection equipment containing aluminium

Storage Conditions

Keep out of the reach and sight of children. Keep the vial in the outer carton in order to protect from light. Store below 30°C. Do not freeze.

After dilution in 5% glucose, chemical and physical in-use stability has been demonstrated for 48 hours at 2°C to 8°C and for 24 hours at 25°C.

From a microbiological point of view, this infusion preparation 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°C to 8°C unless dilution has taken place in controlled and validated aseptic conditions.

Inspect visually prior to use. Only clear solutions without particles should be used.

The medicinal product is for single use only. Any unused concentrate should be discarded.

Shelf life

24 months.

Dosage Forms and Packaging Available

Oxaliplatin Injection 5 mg/ml available in 10 ml vial & 20 ml vial and is packed as 1 vial per carton.

Manufactured by:

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