PRESCRIBING INFORMATION:
For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

ACCORD PEMETREXED

(Pemetrexed for Injection 100 mg/vial & 500 mg/vial)

1. NAME:

Accord Pemetrexed 100 mg powder for concentrate for solution for infusion.
Accord Pemetrexed 500 mg powder for concentrate for solution for infusion.

2. NAME AND STRENGTH OF ACTIVE SUBSTANCE(S):

Pemetrexed disodium (Hemipentahydrate) eq. to Pemetrexed; 100 mg or 500 mg
After reconstitution, each vial contains 25 mg/ml of pemetrexed.

3. DESCRIPTION:

Powder for concentrate for solution for infusion.

White to either light yellow or greenish yellow lyophilized powder.

After reconstitution / dilution: A colorless to yellow or green–yellow colored solution free from visible particulate matter.

4. PHARMACOLOGICAL PROPERTIES:

Pharmacotherapeutic group: Folic acid analogues. ATC code: L01BA04.

Accord Pemetrexed is a multi-targeted anti-cancer antifolate agent that exerts its action by disrupting crucial folate dependent metabolic processes essential for cell replication.

Pemetrexed behaves as a multi-targeted antifolate by inhibiting thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT), which are key folate dependent enzymes for the de novo biosynthesis of thymidine and purine nucleotides. Pemetrexed is transported into cells by both the reduced folate carrier and membrane folate binding protein transport systems. Once in the cell, pemetrexed is rapidly and efficiently converted to polyglutamate forms by the enzyme folylpolyglutamate synthetase.

The polyglutamate forms are retained in cells and are even more potent inhibitors of TS and GARFT. Polyglutamation is a time- and concentration-dependent process that occurs in tumour cells and, to a lesser extent, in normal tissues. Polyglutamated metabolites have an increased intracellular half-life resulting in prolonged drug action in malignant cells.

Pharmacokinetic properties

Pemetrexed has a steady-state volume of distribution of 9 L/m^2. Binding is not notably affected by varying degrees of renal impairment. Pemetrexed undergoes limited hepatic metabolism. Pemetrexed is primarily eliminated in the urine, with 70% to 90% of the administered dose being recovered unchanged in urine within the first 24 hours following administration. Pemetrexed total systemic clearance is 91.8mL/min and the elimination half-life from plasma is 3.5 hours in patients with normal renal function (creatinine clearance of 90ml/min). Pemetrexed total systemic exposure (AUC) and maximum plasma concentration increase proportionally with dose. The pharmacokinetics of pemetrexed are consistent over multiple treatment cycles.

The pharmacokinetic properties of pemetrexed are not influenced by concurrent administered cisplatin. Oral folic acid and intramuscular vitamin B_{12} supplementation do not affect the pharmacokinetics of pemetrexed.

5. INDICATION:

Malignant pleural mesothelioma:

Accord Pemetrexed in combination with cisplatin is indicated for the treatment of chemotherapy naive patients with unresectable malignant pleural mesothelioma.

Non-small cell lung cancer:

Accord Pemetrexed in combination with cisplatin is indicated for the first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology.

Accord Pemetrexed is indicated as monotherapy for the maintenance treatment of locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum- based chemotherapy.

Accord Pemetrexed is indicated as monotherapy for the second-line treatment of patients with locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology.

6. RECOMMENDED DOSE:

Posology

Accord Pemetrexed must only be administered under the supervision of a physician qualified in the use of anti-cancer chemotherapy.

Accord Pemetrexed in combination with cisplatin

The recommended dose of Accord Pemetrexed is 500 mg/m^2 of body surface area (BSA) administered as an intravenous infusion over 10 minutes on the first day of each 21-day cycle. The recommended dose of cisplatin is 75 mg/m^2 BSA infused over two hours approximately 30 minutes after completion of the pemetrexed infusion on the first day of each 21-day cycle.

Patients must receive adequate anti-emetic treatment and appropriate hydration prior to and/or after receiving cisplatin.

Accord Pemetrexed as single agent

In patients treated for non-small cell lung cancer after prior chemotherapy, the recommended dose of Accord Pemetrexed is 500 mg/m^2 BSA administered as an intravenous infusion over 10 minutes on the first day of each 21-day cycle.

Pre-medication Regimen

To reduce the incidence and severity of skin reactions, a corticosteroid should be given the day prior to, on the day of, and the day after pemetrexed administration. The corticosteroid should be equivalent to 4 mg of dexamethasone administered orally twice a day.

To reduce toxicity, patients treated with pemetrexed must also receive vitamin supplementation.

Patients must take oral folic acid or a multivitamin containing folic acid (350 to 1,000 micrograms) on a daily basis. At least five doses of folic acid must be taken during the seven days preceding the first dose of pemetrexed, and dosing must continue during the full course of therapy and for 21 days after the last dose of pemetrexed. Patients must also receive an intramuscular injection of vitamin B_{12} (1,000 micrograms) in the week preceding the first dose of pemetrexed and once every three cycles thereafter. Subsequent vitamin B_{12} injections may be given on the same day as pemetrexed.

Monitoring

Patients receiving pemetrexed should be monitored before each dose with a complete blood count, including a differential white cell count (WCC) and platelet count. Prior to each chemotherapy administration, blood chemistry tests should be collected to evaluate renal and hepatic function. Before the start of any cycle of chemotherapy, patients are required to have the following: absolute neutrophil count (ANC) should be ≥ 1,500 cells/mm^3 and platelets should be ≥ 100,000 cells/mm^3.

Creatinine clearance should be ≥ 45ml/min.

The total bilirubin should be ≤ 1.5-times upper limit of normal. Alkaline phosphatase (AP), aspartate aminotransferase (AST or SGOT), and alanine aminotransferase (ALT or SGPT)

should be ≤ 3-times upper limit of normal. Alkaline phosphatase, AST, and ALT ≤ 5-times upper limit of normal is acceptable if liver has tumour involvement.

Dose Adjustments

Dose adjustments at the start of a subsequent cycle should be based on nadir haematologic counts or maximum nonhaematologic toxicity from the preceding cycle of therapy. Treatment may be delayed to allow sufficient time for recovery. Upon recovery, patients should be re-treated using the guidelines in Tables 1, 2, and 3, which are applicable for Accord Pemetrexed used as a single agent or in combination with cisplatin.

Table 1. Dose Modification Table for Accord Pemetrexed (as Single Agent or in Combination) and Cisplatin -Haematologic Toxicities

Nadir ANC < 500/mm^3 and nadir platelets ≥ 50,000/mm^3	75% of previous dose (both Accord Pemetrexed and cisplatin)
Nadir platelets < 50,000/mm^3 regardless of nadir ANC	75% of previous dose (both Accord Pemetrexed and cisplatin)
Nadir platelets < 50,000/mm^3 with bleedinga, regardless of nadir ANC	50% of previous dose (both Accord Pemetrexed and cisplatin)

[a] These criteria meet the National Cancer Institute Common Toxicity Criteria (CTC v2.0; NCI 1998) definition of ≥ CTC Grade 2 bleeding.

If patients develop non-haematologic toxicities ≥ Grade 3 (excluding neurotoxicity), Accord Pemetrexed should be withheld until resolution to less than or equal to the patient's pre-therapy value. Treatment should be resumed according to the guidelines in Table 2.

Table 2. Dose Modification Table for Accord Pemetrexed (as Single Agent or in Combination) and Cisplatin - Non-Haematologic Toxicities[ab]

	Dose of Accord Pemetrexed (mg/m^2)	Dose for Cisplatin (mg/m^2)
Any Grade 3 or 4 toxicities except mucositis	75% of previous dose	75% of previous dose
Any diarrhoea requiring hospitalization (irrespective of grade) or Grade 3 or 4 diarrhoea	75% of previous dose	75% of previous dose
Grade 3 or 4 mucositis	50% of previous dose	100% of previous dose

[a] National Cancer Institute Common Toxicity Criteria (CTC v2.0; NCI 1998)
[b] Excluding neurotoxicity

In the event of neurotoxicity, the recommended dose adjustment for Accord Pemetrexed and cisplatin is documented in Table 3. Patients should discontinue therapy if Grade 3 or 4 neurotoxicity is observed.

Table 3. Dose Modification Table for Accord Pemetrexed (as Single Agent or in Combination) and Cisplatin -Neurotoxicity

CTC[a] Grade	Dose of Accord Pemetrexed (mg/m^2)	Dose for Cisplatin (mg/m^2)
0-1	100% of previous dose	100% of previous dose
2	100% of previous dose	50% of previous dose

[a] National Cancer Institute Common Toxicity Criteria (CTC v2.0; NCI 1998)

Treatment with Accord Pemetrexed should be discontinued if a patient experiences any haematologic or non-haematologic Grade 3 or 4 toxicity after 2 dose reductions or immediately if Grade 3 or 4 neurotoxicity is observed.

Elderly: In clinical studies, there has been no indication that patients 65 years of age or older are at increased risk of adverse events compared to patients younger than 65 years old. No dose reductions other than those recommended for all patients are necessary.

Paediatric population: There is no relevant use of Accord Pemetrexed in the paediatric population in malignant pleural mesothelioma and non-small cell lung cancer.

Patients with renal impairment (standard Cock croft and Gault formula or glomerular filtration rate measured Tc99m DPTA serum clearance method): Pemetrexed is primarily eliminated unchanged by renal excretion. In clinical studies, patients with creatinine clearance of ≥ 45ml/min required no dose adjustments other than those recommended for all patients. There are insufficient data on the use of pemetrexed in patients with creatinine clearance below 45ml/min; therefore, the use of pemetrexed is not recommended.

Patients with hepatic impairment: No relationships between AST (SGOT), ALT (SGPT), or total bilirubin and pemetrexed pharmacokinetics were identified. However, patients with hepatic impairment, such as bilirubin > 1.5-times the upper limit of normal and/or aminotransferase > 3.0-times the upper limit of normal (hepatic metastases absent) or > 5.0-times the upper limit of normal (hepatic metastases present), have not been specifically studied.

7. ROUTE OF ADMINISTRATION

For precautions to be taken before handling or administering Pemetrexed, see section 15. Pemetrexed should be administered as an intravenous infusion over 10 minutes on the first day of each 21-day cycle. For instructions on reconstitution and dilution of Pemetrexed Accord before administration, see section 15.

8. CONTRAINDICATION:

- Hypersensitivity to the active substance or to any of the excipients.
- Breast-feeding.
- Concomitant yellow fever vaccine.

9. WARNINGS & PRECAUTION

Pemetrexed can suppress bone marrow function as manifested by neutropenia, thrombocytopenia, and anaemia (or pancytopenia). Myelosuppression is usually the dose- limiting toxicity. Patients should be monitored for myelosuppression during therapy and pemetrexed should not be given to patients until absolute neutrophil count (ANC) returns to ≥ 1,500 cells/mm^3 and platelet count returns to ≥ 100,000 cells/mm^3. Dose reductions for subsequent cycles are based on nadir ANC, platelet count, and maximum non- haematologic toxicity seen from the previous cycle.

Less toxicity and reduction in Grade 3/4 haematologic and non-haematologic toxicities, such as neutropenia, febrile neutropenia, and infection with Grade 3/4 neutropenia, were reported when pre-treatment with folic acid and vitamin B_{12} was administered. Therefore, all patients treated with pemetrexed must be instructed to take folic acid and vitamin B_{12} as a prophylactic measure to reduce treatment-related toxicity.

Skin reactions have been reported in patients not pre-treated with a corticosteroid. Pre- treatment with dexamethasone (or equivalent) can reduce the incidence and severity of skin reactions.

Patients with mild to moderate renal insufficiency (creatinine clearance from 45 to 79ml/min) should avoid taking nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, and aspirin (>1.3g daily) for 2 days before, on the day of, and 2 days following pemetrexed administration.

In patients with mild to moderate renal insufficiency eligible for pemetrexed therapy, NSAIDs with long elimination halflives should be interrupted for at least 5 days prior to, on the day of, and at least 2 days following pemetrexed administration.

Serious renal events, including acute renal failure, have been reported with pemetrexed alone or in association with other chemotherapeutic agents. Many of the patients in whom these occurred had underlying risk factors for the development of renal events, including dehydration or pre-existing hypertension or diabetes.

The effect of third-space fluid, such as pleural effusion or ascites, on pemetrexed is not fully defined. A Phase 2 study of pemetrexed in 31 solid tumour patients with stable third- space fluid demonstrated no difference in pemetrexed dose normalised plasma concentrations or clearance compared to patients without third-space fluid collections. Thus, drainage of third-space fluid collection prior to pemetrexed treatment should be considered, but may not be necessary.

Due to the gastrointestinal toxicity of pemetrexed given in combination with cisplatin, severe dehydration has been observed. Therefore, patients should receive adequate anti- emetic treatment and appropriate hydration prior to and/or after receiving treatment.

Serious cardiovascular events, including myocardial infarction and cerebrovascular events, have been uncommonly reported during clinical studies with pemetrexed, usually when given in combination with another cytotoxic agent. Most of the patients in whom these events have been observed had pre-existing cardiovascular risk factors.

Immuno-depressed status is common in cancer patients. As a result, concomitant use of live attenuated vaccines is not recommended.

Pemetrexed can have genetically damaging effects. Sexually mature males are advised not to father a child during the treatment and up to 6 months thereafter. Contraceptive measures or abstinence are recommended. Owing to the possibility of pemetrexed treatment causing irreversible infertility, men are advised to seek counselling on sperm storage before starting treatment.

Women of childbearing potential must use effective contraception during treatment with pemetrexed.

Cases of radiation pneumonitis have been reported in patients treated with radiation either prior, during, or subsequent to their pemetrexed therapy. Particular attention should be paid to these patients, and caution exercised with use of other radiosensitising agents.

Cases of radiation recall have been reported in patients who received radiotherapy weeks or years previously.

This medicinal product contains sodium. To be taken into consideration by patients on a controlled sodium diet.

10. INTERACTION WITH OTHER MEDICAMENTS

Pemetrexed is mainly eliminated unchanged renally by tubular secretion and to a lesser extent by glomerular filtration. Concomitant administration of nephrotoxic drugs (e.g., aminoglycoside, loop diuretics, platinum compounds, cyclosporin) could potentially result in delayed clearance of pemetrexed. This combination should be used with caution. If necessary, creatinine clearance should be closely monitored.

Concomitant administration of substances that are also tubularly secreted (e.g., probenecid, penicillin) could potentially result in delayed clearance of pemetrexed. Caution should be made when these drugs are combined with pemetrexed. If necessary, creatinine clearance should be closely monitored.

In patients with normal renal function (creatinine clearance ≥ 80ml/min), high doses of non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen > 1600 mg/day) and aspirin at higher doses (≥ 1.3 g daily) may decrease pemetrexed elimination and, consequently, increase the occurrence of pemetrexed adverse events. Therefore, caution should be made when administering higher doses of NSAIDs or aspirin, concurrently with pemetrexed to patients with normal function (creatinine clearance ≥ 80 ml/min).

In patients with mild to moderate renal insufficiency (creatinine clearance from 45 to 79ml/min), the concomitant administration of pemetrexed with NSAIDs (e.g., ibuprofen) or aspirin at higher doses should be avoided for 2 days before, on the day of, and 2 days following pemetrexed administration.

In the absence of data regarding potential interaction with NSAIDs having longer half-lives such as piroxicam or rofecoxib, the concomitant administration with pemetrexed in patients with mild to moderate renal insufficiency should be interrupted for at least 5 days prior to, on the day of, and at least 2 days following pemetrexed administration. If concomitant administration of NSAIDs is necessary, patients should be monitored closely for toxicity, especially myelosuppression and gastrointestinal toxicity.

Pemetrexed undergoes limited hepatic metabolism. Results from in vitro studies with human liver microsomes indicated that pemetrexed would not be predicted to cause clinically significant inhibition of the metabolic clearance of drugs metabolised by CYP3A, CYP2D6, CYP2C9, and CYP1A2.

Interactions Common to all Cytotoxics

Due to the increased thrombotic risk in patients with cancer, the use of anticoagulation treatment is frequent. The high intra-individual variability of the coagulation status during diseases and the possibility of interaction between oral anticoagulants and anti-cancer chemotherapy require increased frequency of INR (International Normalised Ratio) monitoring, if it is decided to treat the patient with oral anticoagulants.

Concomitant Use Contraindicated

Yellow fever vaccine: Risk of fatal generalised vaccinale disease.

Concomitant Use Not Recommended
Live attenuated vaccines (except yellow fever, for which concomitant use is contraindicated): Risk of systemic, possibly fatal, disease. The risk is increased in subjects who are already immunosuppressed by their underlying disease. Use an inactivated vaccine where it exists (poliomyelitis).

11. FERTILITY, PREGNANCY AND LACTATION:

Contraception in males and females

Women of childbearing potential must use effective contraception during treatment with pemetrexed. Pemetrexed can have genetically damaging effects. Sexually mature males are advised not to father a child during the treatment, and up to 6 months thereafter. Contraceptive measures or abstinence are recommended.

Pregnancy

There are no data from the use of pemetrexed in pregnant women; but pemetrexed, like other anti-metabolites, is suspected to cause serious birth defects when administered during pregnancy. Animal studies have shown reproductive toxicity. Pemetrexed should not be used during pregnancy unless clearly necessary, after a careful consideration of the needs of the mother and the risk for the foetus.

Breast-feeding

It is not known whether pemetrexed is excreted in human milk, and adverse reactions on the suckling child cannot be excluded. Breast-feeding must be discontinued during pemetrexed therapy.

Fertility

Owing to the possibility of pemetrexed treatment causing irreversible infertility, men are advised to seek counselling on sperm storage before starting treatment.

12. SIDE EFFECTS/ADVERSE REACTIONS:

Summary of the safety profile

The most commonly reported undesirable effects related to pemetrexed, whether used as monotherapy or in combination, are bone marrow suppression manifested as anaemia, neutropenia, leucopenia, thrombocytopenia; and gastrointestinal toxicities, manifested as anorexia, nausea, vomiting, diarrhoea, constipation, pharyngitis, mucositis, and stomatitis. Other undesirable effects include renal toxicities, increased aminotransferases, alopecia, fatigue, dehydration, rash, infection/sepsis and neuropathy. Rarely seen events include Stevens-Johnson syndrome and Toxic epidermal necrolysis.

Tabulated list of adverse reactions

System organ class	Event*
Blood and lymphatic system disorders	Haemoglobin decreased
	Leucocytes decreased
	Neutrophils decreased
Nervous system disorders	Neuropathy -sensory
Gastrointestinal disorders	Nausea
	Anorexia
	Vomiting
	Mucositis/ Stomatitis
Hepatobiliary disorders	ALT (SGPT) elevation
	AST (SGOT) elevation
Skin and subcutaneous tissue disorders	Rash/desquamation
General disorders and administration site conditions	Fatigue
	Pain
	Oedema
Renal disorders	Renal disorders**
Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; CTCAE = Common Terminology Criteria for Adverse Event; NCI = National Cancer Institute; SGOT = serum glutamic oxaloacetic aminotransferase; SGPT = serum glutamic pyruvic amino transferase.	
*Refer to NCI CTCAE Criteria (Version 3.0; NCI 2003) for each grade of toxicity. The reporting rates shown are according to CTCAE version 3.0. ** Combined term includes increased serum/blood creatinine, decreased glomerular filtration rate, renal failure and renal/genitourinary - other.	

Serious cardiovascular and cerebrovascular events, including myocardial infarction, angina pectoris, cerebrovascular accident, and transient ischaemic attack, have been uncommonly reported during clinical studies with pemetrexed, usually when given in combination with another cytotoxic agent. Most of the patients in whom these events have been observed had pre-existing cardiovascular risk factors.

Rare cases of hepatitis, potentially serious, have been reported during clinical studies with pemetrexed.

Pancytopenia has been uncommonly reported during clinical trials with pemetrexed.

Uncommon cases of oedema have been reported in patients treated with pemetrexed.

Oesophagitis/ radiation oesophagitis has been uncommonly reported during clinical trials with pemetrexed.

Sepsis, sometimes fatal, has been commonly reported during clinical trials with pemetrexed.

13. 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, it has been reported that pemetrexed may cause fatigue. Therefore, patients should be cautioned against driving or operating machines if this event occurs.

14. OVERDOSE AND TREATMENT:

Reported symptoms of overdose include neutropenia, anaemia, thrombocytopenia, mucositis, sensory polyneuropathy, and rash. Anticipated complications of overdose include bone marrow suppression as manifested by neutropenia, thrombocytopenia, and anaemia. In addition, infection with or without fever, diarrhoea, and/or mucositis may be seen. In the event of suspected overdose, patients should be monitored with blood counts and should receive supportive therapy as necessary. The use of calcium folinate/folinic acid in the management of pemetrexed overdose should be considered.

14. INCOMPATIBILITIES:

Pemetrexed is physically incompatible with diluents containing calcium, including lactated Ringer's injection and Ringer's injection. In the absence of other compatibility studies this medicinal product must not be mixed with other medicinal products.

15. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:

- Use aseptic technique during the reconstitution and further dilution of Pemetrexed for intravenous infusion administration.

- Calculate the dose and the number of Accord Pemetrexed vials needed. Each vial contains an excess of Pemetrexed to facilitate delivery of label amount.

- Reconstitute 100 mg vials with 4.2 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, without preservative, resulting in a solution containing 25 mg/ml Pemetrexed.

Reconstitute 500 mg vials with 20 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, without preservative, resulting in a solution containing 25 mg/mL Pemetrexed.

Gently swirl each vial until the powder is completely dissolved. The resulting solution is clear and ranges in colour from colourless to yellow or green-yellow without adversely affecting product quality. The pH of the reconstituted solution is between 6.6 and 7.8. **Further dilution is required**.

- The appropriate volume of reconstituted Pemetrexed solution must be further diluted to 100 ml with sodium chloride 9 mg/mL (0.9%) solution for injection, without preservative, and administered as an intravenous infusion over 10 minutes.

- Pemetrexed infusion solutions prepared as directed above are compatible with polyvinyl chloride- and polyolefin- lined administration sets and infusion bags.

- Parenteral medicinal products must be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.

- Pemetrexed solutions are for single use only. Any unused medicinal product or waste material must be disposed of in accordance with local requirements.

Preparation and administration precautions:

As with other potentially toxic anti-cancer agents, care should be exercised in the handling and preparation of pemetrexed infusion solutions. The use of gloves is recommended. If a pemetrexed solution contacts the skin, wash the skin immediately and thoroughly with soap and water. If pemetrexed solutions contact the mucous membranes, flush thoroughly with water. Pemetrexed is not a vesicant. There is not a specific antidote for extravasation of pemetrexed. There have been few reported cases of pemetrexed extravasation, which were not assessed as serious by the investigator. Extravasation should be managed by local standard practice as with other non- vesicants.

16. STORAGE CONDITIONS:

Unopened vial:
Store below 30°C.
Keep out of the sight and reach of the children.

For storage conditions of the reconstituted solution for infusion, see section **Shelf life**.

17. DOSAGE FORMS AND PACKAGING AVAILABLE:

Powder for concentrate for solution for infusion.

Accord Pemetrexed 100 is available in 10 mL clear tubular flat glass vial with aluminum flip off plain lavender seal. Each vial is packed in a separate carton.

Accord Pemetrexed 500 is available in 50 mL clear tubular glass vial with aluminum flip off royal blue seal. Each vial is packed in a separate carton.

18. SHELF LIFE:

Unopened vial: 3 years

Reconstituted and infusion solutions

When prepared as directed, reconstituted and infusion solutions of Accord Pemetrexed contain no antimicrobial preservatives. Chemical and physical in-use stability of reconstituted and infusion solutions of pemetrexed were demonstrated for 24 hours at refrigerated temperature. 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 not be longer than 24 hours at 2 °C to 8 °C.

19. NAME AND ADDRESS OF MANUFACTURER:

INTAS PHARMACEUTICALS LIMITED.
Plot No. 5, 6 & 7, Pharmez, Near Village Matoda,
Tal – Sanand City: Matoda,
Dist: Ahmedabad, Gujarat, India

20: DATE OF REVISION OF PACKAGE INSERT:

August, 2017

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