LEUSTATIN™ Injection

Blanco

NAME OF THE MEDICINAL PRODUCT

LEUSTATIN™ Injection

International Nonproprietary Name

cladribine

QUALITATIVE AND QUANTITATIVE COMPOSITION

LEUSTATIN (cladribine) Injection is a synthetic antineoplastic agent for continuous intravenous infusion. LEUSTATIN Injection is available in single-use vials containing 10 mg (1 mg/mL) of cladribine, a chlorinated purine nucleoside analog.

For excipients see List of Excipients.

PHARMACEUTICAL FORM

LEUSTATIN Injection is a clear, colorless, sterile, preservative-free, isotonic solution. The solution has a pH range of 5.5 to 8.0

CLINICAL PARTICULARS

Therapeutic Indications

LEUSTATIN Injection is indicated for the treatment of hairy cell leukemia.

Posology and Method of Administration

Posology

The recommended treatment for hairy cell leukemia is a single course of LEUSTATIN Injection 0.09 mg/kg/day (3.6 mg/m2/day) given by continuous

intravenous infusion for 7 consecutive days. Deviations from this dosage regimen are not advised. If the patient does not respond to the initial course of LEUSTATIN Injection for hairy cell leukemia, it is unlikely that they will benefit from additional courses. However, limited experience indicates that additional courses may be beneficial in patients who relapse after an initial response to LEUSTATIN Injection.

Method of Administration

LEUSTATIN Injection must be diluted prior to intravenous administration. Since the product does not contain an anti-microbial preservative or bacteriostatic agent, aseptic technique and proper environmental precautions must be observed when preparing a solution of LEUSTATIN Injection. For full details concerning the preparation of an infusion solution **see Instructions for Use/Handling**.

Should the drug accidentally be given extravenously, local tissue damage is unlikely. If extravasation occurs, the administration should be stopped immediately and restarted in another vein. Other recommended local measures include elevating the arm and applying an ice pack to reduce swelling.

See also: **Safety Experience Following Intravenous or Subcutaneous Administration in Patients with Multiple Sclerosis.**

Contraindications

LEUSTATIN Injection is contraindicated in patients hypersensitive to cladribine or the other components of this product.

Special Warnings and Special Precautions for Use

LEUSTATIN Injection is a potent antineoplastic agent with potentially toxic side effects. It should be administered under the supervision of a qualified physician experienced in the use of antineoplastic therapy.

Patients with active infections should be treated for these underlying conditions prior to receiving LEUSTATIN Injection therapy. Patients who are or become Coombs' positive should be monitored carefully for potential hemolysis.

Allopurinol and adequate hydration should be considered for patients with initially high WBC, to alleviate potential tumor lysis syndrome side effects of therapy.

Patients should be monitored closely for infections. Those presenting with herpes infections should be treated with acyclovir.

Bone Marrow Suppression:

Suppression of bone marrow function, including neutropenia, anemia, and thrombocytopenia, should be anticipated. This is usually reversible and appears to be dose dependent. The myelosuppressive effects of LEUSTATIN

Injection are most notable during the first month following treatment. Careful hematologic monitoring, especially during the first 4 to 8 weeks after treatment with LEUSTATIN Injection is recommended. Proceed carefully in patients with severe bone marrow impairment of any etiology since further suppression of bone marrow function should be anticipated.

During the first two weeks after treatment initiation, mean platelet count, absolute neutrophil count (ANC), and hemoglobin concentration declined and then subsequently increased with normalization of mean counts by day 15, week 5, and week 8, respectively. The myelosuppressive effects of LEUSTATIN Injection were most notable during the first month following treatment. Careful hematological monitoring, especially during the first 4 to 8 weeks after treatment with LEUSTATIN Injection, is recommended. (See Laboratory Tests and UNDESIRABLE EFFECTS).

Neurotoxicity

Serious neurological toxicity (including irreversible paraparesis and quadraparesis) has been reported in patients who received LEUSTATIN Injection by continuous infusion at high doses (4 to 9 times the recommended dose for hairy cell leukemia). Neurological toxicity appears to demonstrate a dose

relationship; however severe, neurological toxicities have rarely been reported with the recommended dose. Physicians should consider delaying or discontinuing therapy if neurotoxicity occurs.

Fever/Infection

In clinical trials, fever was associated with the use of LEUSTATIN Injection in approximately 72% (89/124) of patients. Most febrile episodes occurred during the first month and were not associated with documented infection.

Since the majority of fevers occurred in neutropenic patients, patients should be closely monitored during the first month of treatment and empiric antibiotics should be initiated as clinically indicated. Febrile events should be investigated with appropriate clinical diagnostic tests. Practitioners should carefully evaluate the risks and benefits of administering this drug to patients with active infections. Since fever may be accompanied by increased fluid loss, patients should be kept well hydrated (See UNDESIRABLE EFFECTS).

Rare cases of tumor lysis syndrome have been reported in patients treated with cladribine with other hematologic malignancies having a high tumor burden.

Effect on Renal and Hepatic Function

Acute renal insufficiency has developed in some patients receiving high doses of

LEUSTATIN Injection. As there are inadequate data on dosing patients with renal or hepatic insufficiency, caution is advised when administering the drug to such patients. As with other potent chemotherapeutic agents, monitoring of renal and hepatic function should be performed as clinically indicated, especially in patients with underlying kidney or liver dysfunction. Physicians should consider delaying or discontinuing therapy if neurotoxicity or renal toxicity occurs. (See Effects of High Doses and UNDESIRABLE EFFECTS).

Laboratory Tests

During and following treatment, the patient's hematologic profile should be monitored regularly to determine the degree of hematopoietic suppression. In the clinical studies, following reversible decline in all cell counts, the mean platelet count reached 100 x 109/L by day 15, the mean absolute neutrophil count reached 1500 x 106/L by week 5 and the mean hemoglobin reached 12 g/dL by week 8.

Carcinogenesis/Mutagenesis

No animal carcinogenicity studies have been conducted with cladribine. However, its carcinogenic potential cannot be excluded owing to the demonstrated genotoxicity of cladribine. In mammalian cells in culture, cladribine causes an imbalance of intracellular deoxyribonu-

cleotide triphosphate pools. This imbalance results in the inhibition of DNA synthesis and DNA repair synthesis, yielding DNA strand breaks and subsequently cell death. Inhibition of thymidine incorporation into human lymphoblastic cells was 90% at concentrations of 0.3 mM. Cladribine was also incorporated into the DNA of these cells. Cladribine induced chromosomal effects when tested in both an in vivo bone marrow micronucleus assay in mice and an in vitro assay using CHOWBL cells. Cladribine was not mutagenic to bacteria and did not induce unscheduled DNA synthesis in primary rat hepatocyte cultures.

Impairment of Fertility

When administered intravenously to cynomolgus monkeys, LEUSTATIN Injection suppressed rapidly generating cells, including testicular cells. The effect on human fertility is unknown.

Pediatric Use

Safety and effectiveness in children have not been established. In a Phase I study of 1–21 year old patients with leukemia, LEUSTATIN Injection was given by continuous intravenous infusion in doses ranging from 3 to 10.7 mg/m2/day for 5 days (one-half to twice the recommended dose for hairy cell leukemia). The dose-limiting toxicity was severe myelosuppression with

profound neutropenia and thrombocytopenia. At the highest dose, 3 of 7 patients developed irreversible myelosuppression and fatal systemic bacterial or fungal infections. No toxicities unique to pediatric patients were noted.

Interaction with Other Medicaments and Other Forms of Interaction

Caution should be exercised if LEUSTATIN Injection is administered following or in conjunction with other drugs known to cause myelosuppression. Following administration of LEUSTATIN Injection, caution should be exercised before administering other immunosuppressive or myelosuppressive therapy. (See Bone Marrow Suppression).

Pregnancy and Lactation

LEUSTATIN Injection should not be given during pregnancy. If LEUSTATIN Injection is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

There are no adequate and well controlled studies in pregnant women. Women of childbearing age should be advised to avoid becoming pregnant. LEUSTATIN Injection is teratogenic in mice and rabbits.

It is not known whether this drug passes into human milk. LEUSTATIN Injection should not be given to a nursing mother.

Effects on Ability to Drive and Use

Machines

Given the patient's underlying medical condition, caution should be exercised when a patient is performing activities requiring substantial physical well-being while using LEUSTATIN Injection.

Undesirable Effects

Clinical Trial Experience

Overview:

The following safety data are based on 124 patients with hairy cell leukemia who were enrolled in the pivotal studies. In the first month, severe neutropenia was noted in 70% of patients and infection in 31% of patients. Fever was noted in 72% of patients. Other adverse experiences reported frequently during the first 14 days after initiating treatment included: fatigue (49%), nausea (29%), rash (31%), headache (23%) and decreased appetite (23%). Most non-hematologic adverse experiences were mild to moderate in severity.

During the first 14 days, adverse events reported by more than 5% but less than 20% of patients included (listed by body system):

Body as a Whole: Chills (13%), Asthenia (11%), Diaphoresis (11%), Malaise (8%), runk Pain (7%)

Gastrointestinal: Vomiting (14%), Constipation (14%), Diarrhea (12%), Abdominal Pain (8%), Flatulence (7%)

Hemic/Lymphatic: Purpura (12%),

Petechiae (9%) (See Bone Marrow Suppression)

Nervous System: Dizziness (13%), Insomnia (8%), Anxiety (7%)

Cardiovascular System: Edema (8%), Tachycardia (8%), Heart Murmur (7%)

Respiratory System: Abnormal Breath Sounds (14%), Cough (12%), Abnormal Chest Sounds (12%), Shortness of Breath (7%)

Skin/Subcutaneous Tissue: Injection site reactions (15%), Pruritus (9%), Pain (9%), Erythema (8%)

Injection site reactions (i.e. redness, swelling, pain), thrombosis and phlebitis appear usually to be related to the infusion procedure and/or indwelling catheter, rather than to the medication or the vehicle. The majority of rashes were mild and occurred in patients who were receiving or had recently been treated with other medications (e.g. allopurinol or antibiotics) known to cause rash.

Musculoskeletal System:

Myalgia (8%), Arthralgia (7%)

Bone Marrow Suppression:

Myelosuppression was frequently observed during the first month after starting treatment with LEUSTATIN Injection. Neu tropenia (ANC less than 500x106/L) was noted in 69% of patients, compared with 25% in whom it was present initially. Severe anemia

(hemoglobin less than 8.5 g/dL) occurred in 41% of patients, compared with 12% initially and thrombocytopenia (platelets less than 20 x 109/L) occurred in 15% of patients compared to 5% in whom it was noted initially. Forty three percent (43%) of patients received transfusions with RBCs and 13% received transfusions with platelets during month 1. Treatment with cladribine is associated with prolonged depression of CD4 lymphocyte counts and transient suppression of CD8 lymphocyte counts. In a follow-up of 78 of the 124 patients enrolled in the clinical trials, prior to treatment the CD4 count was 766/µl. The mean lowest CD4 count nadir, which occurred 4 to 6 months following treatment was 272/µl. Fifteen months after treatment the mean CD4 count remained below 500/µl. Although CD8 counts decreased initially, increasing counts were observed by 9 months. The clinical significance of the prolonged CD4 lymphopenia is unclear. Prolonged bone marrow hypocellularity (<35%) was observed. It is not known whether the hypocellularity is the result of disease related marrow fibrosis or LEUSTATIN Injection toxicity.

Fever/Infection:

Fever was a frequently observed adverse event during the first month of

study. Serious, including fatal, infections (e.g. septicemia, pneumonia) were reported in 7% of all patients. During the second month, the overall rate of documented infection was 8%; these infections were mild to moderate and no severe systemic infections were seen. After the third month, the monthly incidence of infection was either less than or equal to that of the months immediately preceding LEUSTATIN Injection therapy.

Safety Experience Following Intravenous or Subcutaneous Administration in Patients with Multiple Sclerosis

While the use of cladribine cannot be recommended in indications other than hairy cell leukemia [or chronic lymphocytic leukemia], nor can subcutaneous administration be recommended, data are available from the following investigations which were designed to evaluate the potential efficacy of the drug in the treatment of multiple sclerosis.

In two studies which employed the intravenous route, cladribine was infused in doses ranging from 0.087 to 0.1 mg/kg/day for seven days, with this regimen being repeated for a total of 4 to 6 months. Cumulative doses achieved thus ranged from 2.8 to 3.65 mg/kg. Additionally, in three studies which utilized the subcutaneous

route, cladribine was administered in doses ranging from 0.07 to 0.14 mg/kg/day for 5 days, with this regimen being repeated for a total of 2 to 6 months. Cumulative total doses administered thus ranged from 0.7 to 2.1 mg/kg. The safety profile established based on these trials reflects the drug's expected lymphocytotoxic and bone marrow-suppressing effects and is consistent with the safety profile attributable to the intravenous route of administration in the currently recommended indications of HCL and CLL.

In these trials, most of the frequently reported adverse events, including serious adverse events, were events typically associated with the underlying disease. Most occurred with comparable frequency in placebo- and cladribine-treated subjects. Inflammation and/or pain at the injection site were seen with subcutaneous injection of the study drug. Subjects treated with cladribine had a higher incidence of upper respiratory tract infection, purpura, hypertonia, and muscle weakness than did subjects treated with placebo, with the inter-group difference in the incidence of muscle weakness due primarily to results obtained by a single investigator. With the exception of a higher incidence of thrombocytopenia after re-treatment

(8%) compared to initial treatment (4%), there were no notable differences in the adverse events profile associated with an initial cladribine treatment versus re-treatment among the 78 subjects who received more than one course of cladribine treatment.

Less common, but clinically important adverse events, included those associated with myelosuppression and compromised immune function (pneumonia, aplastic anemia, pancytopenia, thrombocytopenia, herpes simplex, and herpes zoster infections) and these occurred either exclusively or with increased incidence and severity in subjects who received a cumulative cladribine dose of 2.8 mg/kg or higher, particularly when the total dose was administered in an interval as short as four months.

Post-marketing Experience:

The following additional adverse events have been reported since the drug became commercially available. These adverse events have been reported primarily in patients who received multiple courses of LEUSTATIN Injection:

Hematologic: bone marrow suppression with prolonged pancytopenia, including some reports of aplastic anemia; hemolytic anemia, which was reported in patients with lymphoid

malignancies, occurring within the first few weeks following treatment; hypereosinophilia. Rare cases of myelodysplastic syndrome have been reported.
Hepatic: reversible, generally mild, increases in bilirubin and transaminases.
Nervous System: neurological toxicity; however severe neurotoxicity has rarely been reported following treatment with standard cladribine dosing regimens.
Respiratory System: pulmonary interstitial infiltrates, in most cases an infectious etiology was identified.
Skin/Subcutaneous: urticaria.
Opportunistic infections have occurred in the acute phase of treatment due to the immunosuppression mediated by LEUSTATIN Injection.

Overdose:
In a Phase I study with 31 patients in which LEUSTATIN Injection was administered at high doses (4 to 9 times that recommended for hairy cell leukemia) for 7–14 days in conjunction with cyclophosphamide and total body irradiation as preparation for bone marrow transplantation, acute nephrotoxicity, delayed onset neurotoxicity, severe bone marrow suppression with neutropenia, anemia, and thrombocytopenia and gastrointestinal symptoms were reported.
Six patients (19%) developed manifestations of acute renal dysfunction/

insufficiency (e.g. acidosis, anuria, elevated serum creatinine, etc.) within 7 to 13 days after starting treatment with LEUSTATIN Injection, 5 of the affected patients required dialysis. Renal insufficiency was reversible in 2 of these patients. Evidence of tubular damage was noted at autopsy in 2 (of 4) patients whose renal function had not recovered at the time of death. Several of these patients had also been treated with other medications having known nephrotoxic potential.

Eleven patients (35%) experienced delayed onset neurological toxicity. In the majority, this was characterized by progressive irreversible motor weakness, of the upper and/or lower extremities (paraparesis/ quadraparesis), noted 35 to 84 days after starting high dose therapy. Axonal peripheral polyneuropathy was observed in a dose escalation study at the highest dose levels (approximately 4 times the recommended dose for hairy cell leukemia) in patients not receiving cyclophosphamide or total irradiation.

There is no known specific antidote. It is not known whether the drug can be removed by dialysis or hemofiltration. Treatment of overdosage consists of discontinuation of LEUSTATIN Injection, careful observation and appropriate supportive measures.

PHARMACOLOGICAL PROPERTIES

The chemical name for cladribine is 2-chloro-6-amino-9-(2-deoxy-ß-D-erythropentofuranosyl)purine (also commonly known as 2-chloro-2′-deoxy-ß-D-adenosine or 2-CdA).

Pharmacodynamic Properties

LEUSTATIN Injection, a purine nucleoside analogue, is a synthetic antineoplastic agent.

Cellular Resistance and Sensitivity: The selective toxicity of cladribine (2-CdA) towards certain normal and malignant lymphocyte and monocyte populations is based on the relative activities of deoxycytidine kinase and deoxynucleotidase.

Cladribine passively crosses the cell membrane. In cells with a high ratio of deoxycytidine kinase to deoxynucleotidase, it is phosphorylated by deoxycytidine inase to 2-chloro-2′-deoxy-ß-D-adenosine monophosphate (2-CdAMP). Since 2-CdA is resistant to deamination by adenosine deaminase and there is little deoxynucleotidase in lymphocytes and monocytes, 2-CdAMP accumulates intracellularly and is subsequently converted into the active triphosphate deoxynucleotide,2-chloro-2′-deoxy-ß-D-adenosine triphosphate (2-CdATP). It is postulated that cells with high deoxycytidine kinase and low deoxynucleotidase activities will be

selectively killed by cladribine as toxic deoxynucleotides accumulate intracellularly. Cells containing high concentrations of deoxynucleotides are unable to properly repair single-strand DNA breaks. The broken ends of DNA activate the enzyme poly (ADP-ribose) polymerase resulting in NAD and ATP depletion and disruption of cellular metabolism. There is evidence, also, that 2-CdATP is incorporated into the DNA of dividing cells, resulting in impairment of DNA synthesis. LEUSTATIN Injection can be distinguished from other chemotherapeutic agents affecting purine metabolism in that it is cytotoxic to both actively dividing and quiescent lymphocytes and monocytes, inhibiting both DNA synthesis and repair.

Pharmacokinetic Properties

In one study of 17 patients with hairy cell leukemia and normal renal function, the mean steady-state serum cladribine concentration was estimated to be approximately 5.7 ng/mL with a systemic clearance of approximately 663.5 mL/h/kg when LEUSTATIN Injection was given by continuous infusion at 0.09 mg/kg/d over 7 days.

Plasma concentrations are reported to decline multi-exponentially after intravenous infusions with terminal half-lives ranging from approximately 3–22 hours.

In general, the apparent volume of distribution of cladribine is very large (mean approximately 9 L/kg), indicating an extensive distribution of cladribine in body tissues. The mean half-life of cladribine in leukemic cells has been reported to be 23 hours.

There is little information available on the metabolism or route of excretion of cladribine in man. An average of 18% of the administered dose has been reported to be excreted in the urine of patients with solid tumors during a 5-day continuous intravenous infusion of 3.5 -8.1 mg/m2/day of LEUSTATIN. The effect of renal and hepatic impairment on the elimination of cladribine has not been investigated in humans.

Cladribine penetrates into cerebrospinal fluid. One report indicates that concentrations are approximately 25% of those in plasma.

Cladribine is bound approximately 20% to plasma proteins.

Subcutaneous Dosing

In clinical pharmacology studies conducted on oncology patients, cladribine was shown to be 100% bioavailable when administered subcutaneously.

Cladribine accumulates minimally after a daily subcutaneous dose of 0.14 mg/kg for 5 days and the disposition kinetics of cladribine remain

unchanged after multiple daily subcutaneous dosing. The mean Cmax observed on Days 1 and 5 were 57.0 and 62.3 ng/mL, respectively. The corresponding mean tmax were 0.80 and 0.86 hours. The half-life observed on Day 5 was 13.1 hours.

These studies also demonstrated bioequivalence with regard to area under the plasma concentration-time curve following subcutaneous administration of two formulations/dose strengths of cladribine (1 and 5 mg/mL).

PHARMACEUTICAL PARTICULARS

List of Excipients

Each 1 ml of LEUSTATIN Injection contains 9.0 mg (0.15 mEq) of sodium chloride. Phosphoric acid and/or dibasic sodium phosphate have been added to adjust the pH.

Incompatibilities

Since limited compatibility data are available, adherence to the recommended diluents and infusion systems is advised. Solutions containing LEUSTATIN Injection should not be mixed with other intravenous drugs or additives or infused simultaneously via a common intravenous line, since compatibility testing has not been performed.

If the same intravenous line is used for sequential infusion of several different drugs, the line should be flushed with a compatible diluent before and after infusion of LEUSTATIN Injection (See: INSTRUCTIONS FOR USE/HANDLING). The use of 5% dextrose as a diluent is not recommended because of increased degradation of cladribine.

Shelf Life

Observe expiry date on the outer pack.

Special Precautions for Storage

Store refrigerated 2° to 8°C (36° to 46°F). Protect from light during storage.

Keep out of reach of children.

Nature and Contents of Container

LEUSTATIN Injection is supplied as a sterile, preservative-free, isotonic solution containing 10 mg (1 mg/mL) of cladribine (as 10 mL) in a 20 mL single-use, flint glass vial.

Instructions for Use/Handling

LEUSTATIN Injection for intravenous application must be diluted with the designated diluent prior to administration. Since the drug product does not contain any anti-microbial preservative or bacteriostatic agent, aseptic technique and proper environmental precautions must be observed when preparing of a solution of LEUSTATIN Injection.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. A precipitate may occur during the exposure of LEUSTATIN Injection to low temperatures; it may be resolubilized by allowing the solution to warm naturally to room temperature and by shaking vigorously. DO NOT HEAT OR MICROWAVE. Care must be taken to assure the sterility of prepared solutions. Once diluted, solutions of LEUSTATIN Injection should be administered promptly or stored in the refrigerator (2° to 8°C) for no more than 8 hours prior to the start of administration. Vials of LEUSTATIN Injection are for single-use only. Any unused portion should be discarded in an appropriate manner.

The potential hazards associated with cytotoxic agents are well established and proper precautions should be taken when handling, preparing, and administering LEUSTATIN Injection. The use of disposable gloves and protective garments is recommended. If LEUSTATIN Injection contacts the skin or mucous membranes, wash the surface concerned immediately with copious amounts of water. Several guidelines on this subject have been published.

Preparation of a Single Daily Dose for

intravenous application: Add the calculated dose (0.09 mg/kg or 0.09 mL/kg) of LEUSTATIN Injection to an infusion bag containing 100 mL to 500 mL of 0.9% Sodium Chloride Injection, Ph Eur. Infuse continuously over 24 hours. Repeat daily for a total of 7 consecutive days. The use of 5% dextrose as a diluent is not recommended because of increased degradation of cladribine. Admixtures of LEUSTATIN Injection are chemically and physically stable for at least 24 hours at room temperature under normal room fluorescent light in most commonly available PVC infusion containers.

Preparation of a 7-day Infusion: The 7-day infusion solution should only be prepared with bacteriostatic 0.9% sodium chloride injection, USP (0.9% benzyl alcohol preserved). In order to minimize the risk of microbial contamination, both LEUSTATIN Injection and the diluent should be passed through a sterile 0.22µ disposable hydrophilic syringe filter as each solution is being introduced into the infusion reservoir. First add the calculated dose of LEUSTATIN Injection (7 days x 0.09 mg/kg or mL/kg) to the infusion reservoir through the sterile filter. Then add a calculated amount of bacteriostatic 0.9% sodium chloride injection, USP

(0.9% benzyl alcohol preserved) also through the filter to bring the total volume of the solution to 100 mL. After completing solution preparation, clamp off the line, disconnect and discard the filter. Aseptically aspirate air bubbles from the reservoir as necessary using the syringe and a dry second sterile filter or a sterile vent filter assembly. Reclamp the line and discard the syringe and filter assembly. Infuse continuously over 7 days. Solutions prepared with bacteriostatic sodium chloride injection for individuals weighing more than 85 kg may have reduced preservative effectiveness due to greater dilution of the benzyl alcohol preservative. Admixtures for the 7-day infusion have demonstrated acceptable chemical and physical stability for at least 7 days in SIMS Deltec MEDICATION CASSETTES™ Reservoir.

MANUFACTURED BY
See outer carton.

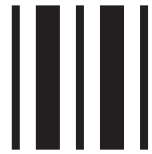
DATE OF REVISION OF THE TEXT
November 2005

day
able
r at
CA-

Back

Cover Back - outside

INT - 27612D



CILAG SCHAFFHAUSEN
T&D Prepress
Tel. Inge Vermeiren: +32 14606915 - Fax CPM: +32 14605157

BOOKLET Leustatin
Article Number : **27612D**
Dimensions : BRO 2609A (105x65)
Pointsize : 7,5pt
File Name : 27612D.indd (MAC)

Market : INT
Sickcode : 41
Operator : KEI

L A B

Black

Date : 1. 06-12-2005
2.
3.
4.
5.