

## DISCUSSION

<b>Name of the Finished Pharmaceutical Product:</b>	Lamivudine 150mg and Stavudine 40mg Tablet
<b>Manufacturer of PreQualified Product:</b>	Strides Arcolab Limited India
<b>Active Pharmaceutical Ingredient(s) (API):</b>	Lamivudine Stavudine
<b>International Nonproprietary Name:</b>	Lamivudine Stavudine
<b>Pharmaco-therapeutic group (ATC Code):</b>	Nucleoside and nucleotide reverse transcriptase inhibitors, combinations. ATC code: J05AF30.
<b>Therapeutic indication:</b>	Lamivudine 150mg and Stavudine 40mg Tablet is indicated for the treatment of HIV infection.

### 1. Introduction

Lamivudine 150mg and Stavudine 40mg Tablet is a prescription medicine used in combination with other antiretroviral drugs to treat adults and children who are infected with HIV (human immunodeficiency virus), the virus that causes AIDS.

Lamivudine is a synthetic nucleoside analogue. Intra-cellularly, lamivudine is phosphorylated to its active 5'-triphosphate metabolite, lamivudine triphosphate (L-TP). The principle mode of action of L-TP is the inhibition of HIV-1 reverse transcriptase (RT) via DNA chain termination after incorporation of the nucleoside analogue into viral DNA.

Stavudine a nucleoside analogue of thymidine, inhibits the replication of HIV in human cells in vitro.

### 2. Assessment of Quality

The assessment was done according to SOP 20 of the WHO Prequalification program.

#### Composition

The product contains 40 mg stavudine and 150 mg lamivudine. The product is presented as light pink to pink colored, circular, flat, bevel-edged tablets with LS 40 engraved on one side and plain on the other. The tablets also contain the following ingredients: microcrystalline cellulose, colloidal anhydrous silica, croscarmellose sodium, colour iron oxide red, povidone and magnesium stearate.

#### Method of preparation

The development of the final composition has been described. Critical process variables were

optimized during the pharmaceutical R&D stage.

The manufacturing process for Stavudine 40mg and Lamivudine 150mg Tablet is a conventional wet granulation followed by compression and packaging. Appropriate in-process controls have been set to ensure batch-to-batch reproducibility. Validation data presented on three pilot scale batches demonstrate the consistency of the process and the quality of the product. The applicant has committed to submit validation data for the first three commercial batches.

### **Control of starting materials**

Lamivudine is official in the USP and its quality is therefore considered as well established.

A monograph for stavudine was not included in any major pharmacopoeia by the time of submission / assessment of the dossier. The stavudine specifications as set by the FPP manufacturer were judged to be acceptable.

All excipients are official in major international pharmacopoeias and are commonly used in the manufacture of tablets.

### **Control testing of the finished medicinal product**

The release and shelf-life specifications are in line with the requirements of major internationally used pharmacopoeias and guidelines for tablets. The test methods have been adequately validated.

### **Stability**

#### Lamivudine

24 month real-time data ( $25 \pm 2^{\circ}\text{C}/60 \pm 5\% \text{RH}$ ) were submitted for three Lamivudine batches. All results remained within specifications. The data show neither visible variability nor trend over time. The submitted stability studies support a two (2) year retest period, on condition that lamivudine API is stored in well-closed, light resistant containers, at a temperature not exceeding  $25^{\circ}\text{C}$ .

#### Stavudine

Stability studies have been conducted on three batches stored at  $25 \pm 2^{\circ}\text{C}/60 \pm 5\% \text{RH}$  (24 months) and  $40 \pm 2^{\circ}\text{C}/75 \pm 5\% \text{RH}$  (6 months). Stability data did not show variability or a change over the time so statistical analysis was not required. A re-test period of 24 months was allowed for stavudine when stored at  $25^{\circ}\text{C}$  in a well-closed container.

#### Lamivudine 150mg and Stavudine 40mg

18-month long-term ( $25 \pm 2^{\circ}\text{C}/60 \pm 5\% \text{RH}$ ), 18 month intermediate ( $30 \pm 2^{\circ}\text{C}/65 \pm 5\% \text{RH}$ ) and 6-months accelerated ( $40 \pm 2^{\circ}\text{C}/75 \pm 5\% \text{RH}$ ) stability data have been submitted for three pilot scale batches. The accelerated stability data for all the three batches showed a distinct drop of dissolution rate for stavudine after six months at all storage conditions but the results remained within specification. The statistical analysis of the pooled dissolution data and the statistical analysis of the assay values of the single batches under long-term conditions ( $25 \pm 2^{\circ}\text{C}/60 \pm 5\% \text{RH}$ ) supported the conclusion that the product will be stable for 24 month.

### **Conclusions**

With additional information still to be provided, it is concluded that the data submitted ensure acceptable quality of Lamivudine 150mg and Stavudine 40mg Tablet when stored at a temperature not exceeding  $25^{\circ}\text{C}$ .

### **3. Assessment of Bio-Equivalence**

The following bioequivalence study has been performed in 2003 according to internationally accepted guidelines.

A randomized, open label, two treatment, two period, single dose, crossover bioequivalence study on Lamivudine 150 mg + Stavudine 40 mg tablets (Strides Arcolab Ltd., India) comparing with individual capsules of Zerit 40 mg (manufactured by Bristol-Myers Squibb Co., France), and Epivir 150 mg tablets (manufactured by GlaxoSmithKline, Greenford Middlesex, UK) in 24 healthy, adult, male subjects under fasting conditions (study number 213/03).

The objective of the study was to compare the bioavailability of the stated combinational product manufactured by Strides Arcolab Ltd., India (test drug) with the same dose of individual tablets of each respective compound (two individual formulations given as reference) and to assess bioequivalence. The comparison was performed as a single centre, open label, randomized, crossover study in healthy male subjects. Each subject was assigned to receive each of the following two treatments in a randomized fashion:

Treatment T: Test – Stavudine 40 mg + Lamivudine 150 mg tablets Batch No. ZEP3001  
 Treatment R: Reference – Zerit 40 mg capsules + Epivir 150 mg tablets  
 (stavudine 40 mg + lamivudine 150 mg)  
 Batch Nos. 0196 and BO 86631

A seven day wash-out period was observed between administration of test and reference. Serial blood samples (1 pre-dose sample and 19 samples within 36 h post dose) were taken during each study period to obtain bioavailability characteristics AUC,  $C_{max}$  and  $t_{max}$  for bioequivalence evaluation. Drug concentrations for stavudine and lamivudine in plasma were analyzed using a validated LC-MS/MS method. Limits of quantification were stated to be 0.0201 µg/ml for stavudine and 0.0198 µg/ml for lamivudine.

The study was performed with 26 participants, data generated from a total of 24 subjects were utilized for analysis to establish pharmacokinetic parameters and assess bioequivalence.

Geometric means ( $AUC$ ,  $C_{max}$ ) and arithmetic means ( $t_{max}$ ) for stavudine and lamivudine as well as statistical results are summarised in the following tables:

### Lamivudine

Pharmacokinetic Parameter	Test formulation (T) geom. means (CV%)	Reference (R) geom. means (CV%)	log-transformed parameters	
			Ratio of least square means T/R (%)	Conventional 90% CI (Parametric)
$t_{max}$ (h) *)	1.168 (0.717)	1.047 (0.416)	-	-
$C_{max}$ (µg/ml)	1.842 (26.13)	1.761 (35.34)	109.07	94.32 – 126.12
$AUC_{0-t}$ (µg.h/ml)	7.614 (23.40)	7.518 (27.99)	103.33	94.35 – 113.16
$AUC_{0-\infty}$ (µg.h/ml)	7.756 (23.11)	7.673 (27.51)	102.96	94.21 – 112.51

\* arithm. mean (SD)

### Stavudine

Pharmacokinetic Parameter	Test formulation (T) geom. means (CV%)	Reference (R) geom. means (CV%)	log-transformed parameters	
			Ratio of least square means T/R (%)	Conventional 90% CI (Parametric)
$t_{max}$ (h) *	0.933 (1.142)	0.633 (0.223)	-	-
$C_{max}$ (µg/ml)	1.199 (32.44)	1.130 (26.62)	104.45	94.77 – 115.11
$AUC_{0-t}$ (µg.h/ml)	2.562 (27.16)	2.503 (23.61)	101.96	92.42 – 112.48
$AUC_{0-\infty}$ (µg.h/ml)	2.646 (26.56)	2.621 (23.73)	100.57	91.27 – 110.82

\* arrithm. mean (SD)

The results of the study show that preset acceptance limits of 80 -125 % are met by both AUC and  $C_{max}$  values regarding stavudine and lamivudine. Accordingly, the test product Lamivudine 150mg and Stavudine 40mg Tablet meets the criteria for bioequivalence with regard to rate and extent of absorption and is therefore bioequivalent to the reference, administered as individual formulations (40 mg stavudine and 150 mg lamivudine).

## 4. Summary of Product Safety and Efficacy

### 1. Introduction

#### Background

Lamivudine 150mg and Stavudine 40mg Tablet is a prescription medicine used in combination with other antiretroviral drugs to treat adults and children who are infected with HIV (human immunodeficiency virus), the virus that causes AIDS.

Lamivudine is a synthetic nucleoside analogue. Intra-cellularly, lamivudine is phosphorylated to its active 5'-triphosphate metabolite, lamivudine triphosphate (L-TP). Stavudine a nucleoside analogue of thymidine, inhibits the replication of HIV in human cells in vitro.

Lamivudine 150mg and Stavudine 40mg Tablet are available for oral administration in strengths of lamivudine 150mg and stavudine40 mg.

#### Product Design

The development strategy for Lamivudine 150mg and Stavudine 40mg Tablet was concentrated on compatibility of the active ingredients lamivudine and stavudine with the excipients identified to match the dissolution profile of the innovator, thus producing a robust formulation.

Stability studies have been conducted on 3 batches of Lamivudine 150mg and Stavudine 40mg Tablet stored at 25°C/60%RH (18-month), 30°C/65%RH (18-month) and 40°C/75%RH (6-month). Stability results show that Lamivudine 150mg and Stavudine 40mg Tablet confirm with the proposed end of shelf life specification including description, disintegration time, dissolution, assay and degradation products.

**Unique product characteristics**

Lamivudine and Stavudine Tablet is a light pink to pink coloured, circular, flat bevel edged tablets with LS40 engraved on one side and plain on other side.

**Approved indication(s)**

Lamivudine 150mg and Stavudine 40mg Tablet is indicated for the treatment of HIV infection.

**Clinical pharmacology**

Lamivudine is a synthetic nucleoside analogue. Intra cellularly, lamivudine is phosphorylated to its active 5'-triphosphate metabolite, lamivudine triphosphate (L-TP). The principle mode of action of L-TP is the inhibition of HIV-1 reverse transcriptase (RT) via DNA chain termination after incorporation of the nucleoside analogue into viral DNA. L-TP is weak inhibitor of mammalian DNA polymerases  $\alpha$  and  $\beta$ , and mitochondrial DNA polymerase  $\gamma$ .

Stavudine is a nucleoside analogue of thymidine, inhibits the replication of HIV in human cells in vitro. Stavudine is phosphorylated by cellular kinase to the active metabolite stavudine triphosphate. stavudine triphosphate inhibits the activity of HIV reverse transcriptase both by competing with the natural substance deoxythymidine triphosphate and by its incorporation in viral DNA causing a termination of DNA chain elongation because stavudine lacks the essential 3'-OH group.

**Pharmacokinetics**

Lamivudine was rapidly absorbed after oral administration in HIV-infected patients. Absolute bioavailability in 12 adult's patients was  $86\% \pm 16\%$  (mean  $\pm$  SD) for the 150-mg tablets and  $87\% \pm 13\%$  for the oral solution. Lamivudine was excreted as the trans-sulfoxide metabolite in the urine. Serum concentrations of this metabolite have not been determined. The majority of lamivudine is eliminated unchanged in urine. The pharmacokinetic properties of lamivudine have been determined in small group of HIV -infected adults with impaired renal function and impaired hepatic function.

Stavudine has been evaluated in HIV infected adult and paediatric patients. Peak plasma concentration ( $C_{max}$ ) and area under the plasma concentration time curve (AUC) increased in proportion to dose after both single and multiple doses ranging from 0.03 to 4 mg/kg.

Stavudine is rapidly observed with peak plasma concentration occurring within 1 hour after dosing. Stavudine distributes equally between red blood cells and plasma. The metabolic fate of stavudine has not been elucidated in human. Renal elimination accounted for about 40% of the overall clearance regardless of the route of administration.

**Drug Interactions; related side effects and contra indications****Lamivudine.**

Lamivudine is predominantly eliminated in the urine by active organic cationic secretion. The possibility of interactions with other drugs administered concurrently should be considered, particularly when their main route of elimination is active renal secretion via the organic cationic transport system (e.g. trimethoprim). Trimethoprim 160 mg/sulphamethoxazole 800 mg once daily has been shown to increase lamivudine exposure (AUC). No change in dose of either drug is recommended. There is no information regarding the effect on lamivudine pharmacokinetics of higher doses of TMP/SMX such as those used to treat *Pneumocystis carinii* pneumonia. No data are available regarding interactions with other drugs that have renal clearance mechanisms similar to that of lamivudine.

Lamivudine and zalcitabine may inhibit the intracellular phosphorylation of one another. Therefore, use of lamivudine in combination with zalcitabine is not recommended.

**Stavudine.**

Zidovudine may competitively inhibit the intracellular phosphorylation of stavudine. Therefore, use of zidovudine in combination with stavudine is not recommended.

## Clinical Efficacy

### Controlled studies

**Title: A comparison of stavudine plus lamivudine versus zidovudine plus lamivudine in combination with indinavir in antiretroviral naive individuals with HIV infection: selection of thymidine analog regimen therapy (START I).**

Squires KE, Gulick R, Tebas P, Santana J, Mulanovich V, Clark R, Yangco B, Marlowe SI, Wright D, Cohen C, Cooley T, Mauney J, Uffelman K, Schoellkopf N, Grosso R, Stevens M.

University of Alabama at Birmingham, 35294-2050, USA.

AIDS. 2000 Jul 28; 14 (11):1591-600.

**BACKGROUND:** No clinical trial results directly comparing two nucleoside analog pairs in a drug regimen for HIV that includes a protease inhibitor are available. **OBJECTIVE:** To compare the safety and efficacy of stavudine (d4T) + lamivudine (3TC) with zidovudine (ZDV) + 3TC, each in combination with indinavir (IDV).

**DESIGN:** Randomized, open-label, multi-center.

**SETTING:** Fifteen HIV clinical research centers.

**PATIENTS:** Two-hundred and four antiretroviral-naive HIV-1-infected-patients with CD4 cell counts  $\geq 200 \times 10^6/l$  and HIV-1 RNA  $\geq 10,000$  copies/ml (bDNA assay), modified to 5000 copies/ml.

**INTERVENTION:** d4T 40 mg twice a day, 3TC 150 mg twice a day plus IDV 800 mg every 8 h compared with ZDV 200 mg every 8 h (modified to 300 mg every 12 h) plus 3TC and IDV.

**MEASUREMENTS:** Primary endpoint: plasma HIV-1 RNA  $< 500$  copies/ml. Additional endpoints: HIV-1 RNA  $\leq 50$  copies/ml; change from baseline in HIV-1 RNA and CD4 cell counts; safety and adverse events.

**RESULTS:** For HIV-1 RNA, 62% of patients on d4T + 3TC + IDV and 54% of patients on ZDV + 3TC + IDV had  $< 500$  copies/ml HIV RNA at weeks 40 through 48 [90% confidence interval, -0.204 to 0.036;  $P = 0.213$ ], with 49% and 47% respectively achieving  $\leq 50$  copies/ml at 48 weeks (90% CI, -0.134 to 0.096;  $P = 0.834$ ).

Median change in CD4 cell counts at 48 weeks was  $+227 \times 10^6/l$  and  $+198 \times 10^6/l$  for the d4T- and ZDV-containing arms, respectively. The median time-weighted average change from baseline in CD4 cell counts was significantly greater at 48 weeks in the d4T-containing arm ( $142 \times 10^6/l$  versus  $110 \times 10^6/l$ ;  $P = 0.033$ ). Serious adverse events were not significantly different between treatment arms, but there were significant differences for frequency of adverse events of all severity with increased nausea and vomiting in the ZDV-containing arm, and increased diarrhea and rash in the d4T-containing arm.

**CONCLUSIONS:** These results support the choice of d4T + 3TC as a nucleoside analog pair in combination with a protease inhibitor in an initial HIV treatment regimen

**Title: Efficacy and tolerability of stavudine plus lamivudine in treatment-naive and treatment-experienced patients with HIV-1 infection.**

Katlama C, Valantin MA, Matheron S, Coutellier A, Calvez V, Descamps D, Longuet C, Bonmarchand M, Tubiana R, De Sa M, Lancar R, Agut H, Brun-Vezinet F, Costagliola D. Hopital Pitie-Salpetriere, and INSERM SC4, Institut Saint Antoine de Recherche en Sante, Paris, France.

Ann Intern Med. 1998 Oct 1; 129(7): 525-31.

**BACKGROUND:** A combination of two nucleoside analogues is currently the core of any antiretroviral regimen for HIV-1 infection. Stavudine plus lamivudine has shown an additive effect in vitro, as well as an absence of overlapping toxicity and cross-resistance. **OBJECTIVE:** To evaluate the antiviral efficacy of stavudine plus lamivudine in treatment-naive patients and in patients previously treated with other nucleoside reverse transcriptase inhibitors.

**DESIGN:** Prospective, open-label pilot study.

**SETTING:** Three urban clinical centers in Paris.

**PATIENTS:** 83 patients with CD4+ cell counts between 50 and 400 cells/mm<sup>3</sup> (42 treatment-naive and 41 treatment-experienced patients).

**INTERVENTIONS:** Stavudine, 40 mg twice daily (30 mg twice daily in patients with a body weight  $\leq 60$  kg), and lamivudine, 150 mg twice daily.

**MEASUREMENTS:** Primary end points for efficacy included changes in plasma viral load and CD4+ cell count

at 24 weeks compared with baseline.

RESULTS: Therapy with stavudine plus lamivudine resulted in a median decrease of 1.66 log<sub>10</sub> (10(1.66)) (range, -3.04 to -0.79 log<sub>10</sub>) in plasma HIV-1 RNA; the median increase in CD4+ cell count was 108 cells/mm<sup>3</sup> (range, -58 to 406 cells/mm<sup>3</sup>) at week 24 in treatment-naïve patients. In treatment-experienced patients, the median reduction in plasma HIV-1 RNA was 0.55 log<sub>10</sub> (range, -2.86 to 0.52 log<sub>10</sub>), and the median increase in CD4+ cell count was 46 cells/mm<sup>3</sup> (range, -188 to 311 cells/mm<sup>3</sup>). The percentages of patients with less than 3000 HIV-1 RNA copies/mL and less than 400 copies/mL at 24 weeks were, respectively, 57% (95% CI, 41% to 72%) and 26% (CI, 12% to 40%) among treatment-naïve patients and 22% (CI, 10% to 38%) and 5% (CI, 1% to 17%) among treatment-experienced patients. Of 82 patients, 14 (17%) experienced grade 3 or 4 toxicity and 2 discontinued therapy because of intolerance toward treatment.

CONCLUSION: Stavudine plus lamivudine seems to have a potent antiviral effect in treatment-naïve and treatment-experienced patients. No major drug-limiting toxicity was found. This two-nucleoside combination should be considered in multi-drug therapy for HIV.

### **Clinical studies in special populations**

#### **Renal impairment**

The dose of both lamivudine and stavudine should be reduced for patients with CrCL <50 mL/min. Since Lamivudine and Stavudine Tablet is a fixed-dose combination, it should not be prescribed for these patient populations.

#### **Hepatic dysfunction**

No dose adjustment for lamivudine is required for patients with impaired hepatic function. Safety and efficacy of lamivudine have not been established in the presence of decompensated liver disease. Stavudine pharmacokinetics were not altered in 5 non HIV infected patients with hepatic impairment secondary to cirrhosis (Child-Pugh classification B or C) following the administration of a single 40-mg dose.

### **Clinical Safety**

Safety data on the lamivudine and stavudine has been supported by 2 studies tabulated previously {AIDS. 2000 Jul 28; 14 (11): 1591-600, Ann Intern Med. 1998 Oct 1;129(7):525-31. The safety population includes all subjects who received lamivudine and stavudine from comparative studies.

### **Serious adverse events / deaths**

#### **Lamivudine and stavudine**

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination, including lamivudine and stavudine. Some data suggests that this infrequent but life threatening event may be more often associated with antiretroviral combinations containing stavudine. Female gender, obesity and prolonged nucleoside exposure may be the major risk factors.

Particular caution should be exercised when administering stavudine and lamivudine to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Generalized fatigue, digestive symptoms (nausea, vomiting, abdominal pain and sudden unexplained weight loss); respiratory symptoms (tachypnoea and dyspnoea); or neurologic symptoms (including motor weakness) might be indicative of lactic acidosis development.

Treatment with lamivudine and stavudine should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

#### ***Patients With HIV And Hepatitis B Virus Co-infection***

Safety and efficacy of lamivudine have not been established for treatment of chronic hepatitis B in patients dually infected with HIV and HBV. In non-HIV-infected patients treated with lamivudine for chronic hepatitis B, emergence of lamivudine-resistant HBV has been detected and has been associated with diminished treatment response. Emergence of hepatitis B virus variants associated with resistance to lamivudine has also been reported in

HIV-infected patients who have received lamivudine-containing antiretroviral regimens in the presence of concurrent infections with hepatitis B virus. Post treatment exacerbation's of hepatitis have also been reported.

#### *Post-Treatment Exacerbation's Of Hepatitis*

In clinical trials in non-HIV-infected patients treated with lamivudine for chronic hepatitis B, clinical and laboratory evidence of exacerbation's of hepatitis have occurred after discontinuation of lamivudine. These exacerbation's have been detected primarily by serum ALT (STGP) elevations in addition to re-emergence of HBV and DNA. Although most events appear to have been self-limited, fatalities have been reported in some cases. Similar events have been reported from post-marketing experience after changes from lamivudine-containing HIV treatment regimens to non-lamivudine containing regimens in patient's infected with both HIV and HBV.

The causal relationship to discontinuation of lamivudine treatment is unknown. Patients should be closely monitored with both clinical and laboratories follow up for at least several months after stopping treatment. There is insufficient evidence to determine whether re-initiation of lamivudine alters the course of post treatment exacerbation's of hepatitis.

#### *Neurologic Symptoms*

Motor weakness has been reported rarely in patients receiving combination antiretroviral therapy including stavudine. Most of these cases occurred in the setting of lactic acidosis. The evolution of motor weakness may mimic the clinical presentation of Guillain-Barre syndrome (including respiratory failure). Symptoms may continue or worsen following discontinuation of therapy.

Peripheral neuropathy, manifested by numbness, tingling or pain in the hands or feet, has been reported in patient's receiving stavudine therapy. Peripheral neuropathy has occurred more frequently in patient's with advanced HIV disease, a history of neuropathy or concurrent neurotoxic therapy.

#### *Pancreatitis*

Fatal and nonfatal pancreatitis has occurred during therapy when stavudine was part of a combination regimen that included didanosine.

#### *Fat Redistribution (Lipodystrophy Syndrome)*

Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo lump), peripheral wasting, facial wasting, breast enlargement and "cushingoid appearance" have been observed in patient's receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown. A causal relationship has not been established.

## **5. Overall Conclusion and benefit risk assessment.**

### **Quality**

The quality of this product is considered to be acceptable when used in accordance with the conditions defined in the SPC. Physicochemical and biological aspects relevant to the uniform clinical performance of the product have been investigated and are controlled in a satisfactory way.

### **Bioequivalence**

Lamivudine 150mg and Stavudine 40mg Tablet has shown to be bioequivalent to one capsule of Zerit 40mg and one tablet of Epivir 150mg.

### **Efficacy and Safety**

Regarding clinical efficacy and safety, Lamivudine 150mg and Stavudine 40mg Tablet is considered effective and safe to use when the guidance and restrictions presented in the Summary of Product Characteristics are taken into consideration.

### **Benefit Risk Assessment**

Based on the WHO assessment of data on quality, bioequivalence, safety and efficacy the team of assessors considered by consensus that the benefit risk profile of Lamivudine 150mg and Stavudine 40mg Tablet was acceptable for the following indication: Lamivudine 150mg and Stavudine 40mg Tablet is indicated for the treatment of HIV infection and has demonstrated adequate tolerability to Lamivudine 150mg and Stavudine 40mg Tablet and has advised to include Lamivudine 150mg and Stavudine 40mg Tablet in the list of pre-qualified medicinal products and manufacturers.