# WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

*This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information fromstringent regulatory authorities.*[*]

*The medicine may be authorised for additional or different uses by national medicines regulatory authorities.*

[*]https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

# 1. NAME OF THE MEDICINAL PRODUCT

[HA424 trade name]†

# 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 150 mg lamivudine.

For a full list of excipients see section 6.1

# 3. PHARMACEUTICAL FORM

Film-coated tablet

The tablets are white coloured, capsule-shaped, biconvex film-coated tablets, having score on one side and “ML 1" debossed on other side.

The tablets can be broken for ease of swallowing only.

# 4. CLINICAL PARTICULARS

## 4.1 Therapeutic indications

[HA424 trade name] is indicated as part of antiretroviral combination therapy for the treatment of HIV-1 infection in adults, adolescents and children weighing at least 25 kg.

Treatment regimens should follow most recent WHO treatment guidelines, supplemented by other authoritative guidelines.

[HA424 trade name] may be used as part of a regimen for post-exposure prophylaxis to HIV. For use of antiretroviral agents for post-exposure prophylaxis the most recent official guidelines, e.g., those by WHO, should be consulted.

## 4.2 Posology and method of administration

Oral use.

Antiretroviral therapy should be prescribed by a health care provider experienced in the management of HIV-1 infection.

*Adults, adolescents and children (weighing at least 25 kg)*

The recommended dose of lamivudineis 300 mg daily. This may be administered either as 150 mg (1 tablet) twice daily or 300 mg (2 tablets)once daily (see section 4.4).

*Children weighing less than 25 kg*

[HA424 trade name] is not suitable for children weighing less than 25 kg. For these patients another formulation should be used, e.g. a tablet that can be given at a smaller dose or an oral solution of lamivudine.

*Switching between twice-daily and once-daily regimens*

Patients switching from twice-daily dosing to once-daily dosing should take the first once-daily dose about 12 hours after the last twice-daily dose and then continue the recommended once-daily dose every 24 hours.

Patients switching from once-daily dosing to twice-daily dosing should take the first twice-daily dose about 24 hours after the last once daily dose and then continue the recommended twice-daily dose every 12 hours.

†Trade names are not prequalified by WHO. This is the national medicines regulatory agency’s responsibility.

***Special populations***

*Older people*
No specific data are available; however, special care is advised due to age-associated changes such as the decrease in renal function and alteration of haematological parameters.

*Liver Impairment*
No dose adjustment is necessary.

*Renal Impairment*
Lamivudine concentrations are increased in patients with moderate or severe renal impairment due to decreased clearance. It is recommended that lamivudine dose be modified in patients with reduced creatinine clearance as shown below.

It may be necessary to use alternative formulations such as lamivudine oral solution for patients whose creatinine clearance falls below 30 mL/minute (see below).

*Dosing for patients weighing up to 25 kg with renal impairment*

| **Creatinine clearance** | **First dose** | **Subsequent doses** |
|---|---|---|
| At least 50 mL/minute | 300 mg<br>*or*150 mg | 300 mg once daily<br>*or* 150 mg twice daily |
| 30–50 mL/minute | 150 mg | 150 mg once daily |
| 15–30 mL/minute* | 150 mg | 100 mg once daily |
| 5–15 mL/minute* | 150 mg | 50 mg once daily |
| Less than<br>5 mL/minute* | 50 mg | 25 mg once daily |
| * An alternative formulation such as an oral solution is required for patients with creatinine clearance of less than 30 mL/minute | | |

***Method of administration***
[HA424 trade name] may be taken with food or between meals. Preferably, the tablet should be swallowed whole.

For patients with difficulty swallowing tablets, other lamivudine formulations, e.g. oral solution, may be available. If these are not available, the tablets may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any excipients listed in section 6.1.

## 4.4 Special warnings and precautions for use

[HA424 trade name] is not recommended for use as monotherapy.

*Renal impairment*
In patients with moderate to severe renal impairment, the terminal plasma half-life of lamivudine is increased due to decreased clearance, therefore the dose should be adjusted (see section 4.2).

*Triple nucleoside therapy*
There have been reports of a high rate of virological failure and of emergence of resistance at an early stage when lamivudine was combined with tenofovir disoproxil and abacavir as well as with tenofovir disoproxil and didanosine as a once-daily regimen.

*Mitochondrial dysfunction following exposure in utero*

Nucleoside and nucleotide analogues may cause a variable degree of mitochondrial damage. This is most pronounced with stavudine, didanosine and zidovudine. There have been reports of mitochondrial dysfunction in HIV-negative infants exposed to nucleoside analogues either in utero or after birth; these have predominantly involved regimens containing zidovudine. The main adverse reactions reported are haematological disorders (anaemia, neutropenia) and metabolic disorders (hyperlactataemia, hyperlipasemia). These events have often been transitory. Late-onset neurological disorders have been reported rarely (hypertonia, convulsion, abnormal behaviour). Whether such neurological disorders are transient or permanent is currently unknown.

Mitochondrial damage should be considered for any child exposed in utero to nucleoside and nucleotide analogues, who presents with severe clinical findings of unknown aetiology, particularly neurologic findings. These findings do not affect current guidelines on the use of antiretroviral therapy in pregnant women to prevent vertical transmission of HIV.

*Weight and metabolic parameters*

Weight and levels of blood lipids and glucose may increase during antiretroviral therapy. Such changes may in part be linked to disease control and lifestyle. For lipids, there is some evidence for a treatment effect, while there is no strong evidence relating weight gain to any particular treatment. Established HIV treatment guidelines should be consulted for advice on monitoring of blood lipids and glucose. Lipid disorders should be managed as clinically appropriate.

*Pancreatitis*

Cases of pancreatitis have occurred rarely. However, it is not clear whether these cases were due to the antiretroviral treatment or to the underlying HIV disease. Treatment with [HA424 trade name] should be stopped immediately if clinical signs, symptoms or laboratory abnormalities suggestive of pancreatitis occur.

*Immune reactivation syndrome*

Immune reactivation syndrome has been reported in patients treated with combination antiretroviral therapy. During early stages of treatment, patients whose immune system responds to antiretroviral therapy may develop an inflammatory response to slow-developing or residual opportunistic infections (such as *Mycobacterium avium* infection, cytomegalovirus retinitis, *Pneumocystis jirovecii* pneumonia, or tuberculosis). These reactions may require further evaluation and treatment.

Autoimmune disorders (such as Graves' disease, autoimmune hepatitis, polymyositis, and Guillain-Barré syndrome) have also been reported in the setting of immune reactivation; however, the reported time to onset is more variable and these events can occur many months after starting antiretroviral treatment.

*Opportunistic infections*

Patients receiving [HA424 trade name] or other antiretroviral medicines may still develop opportunistic infections and other complications of HIV infection. Therefore,heath care providers experienced in the treatment of these associated HIV diseases should keep patients under close clinical observation.

*Liver disease*

Lamivudine should be given cautiously to patients with hepatitis B coinfection. Lamivudine inhibits hepatitis B virus (HBV) replication. Discontinuation of lamivudine or virologic failure resulting from HBV developing resistance to lamivudine may cause hepatic deterioration and a hepatitis flare. Periodic monitoring of liver function and markers of HBV replication is recommended for at least 4 months if lamivudine is discontinued in HBV-coinfected patients.

Patients with chronic hepatitis B or C and treated with combination antiretroviral therapy are at higher risk of severe and potentially fatal hepatic adverse events. In case of concomitant antiviral therapy for hepatitis B or C, refer also to the product information for these medicines.

If [HA424 trade name] is discontinued in patients coinfected with hepatitis B virus, periodic monitoring of liver function tests and markers of HBV replication is recommended, as withdrawal of lamivudine may result in an acute exacerbation of hepatitis.

Patients with liver dysfunction, including chronic active hepatitis, have higher frequency of liver function abnormalities during combination antiretroviral therapy, and should be monitored according to standard practice. If liver disease worsens in such patients, interruption or discontinuation of treatment must be considered (see section 4.8).

*Paediatric population*

A study (see section 5.1) found lower rates of virologic suppression and more frequent viral resistance in children receiving lamivudine oral solution compared to those receiving tablets. Lamivudine should preferably be usedas tablet formulationin children.

*Osteonecrosis*

Osteonecrosis has been reported, particularly in patients with advanced HIV-disease or after long-term combination antiretroviral therapy. Its aetiology is considered to be multifactorial and includes corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index. Patients should be advised to seek medical advice if they have joint aches and pain, joint stiffness or movementdifficulty.

*Drug Interactions*

[HA424 trade name] should not be taken with any other medicine that contains lamivudine.

Because of overlapping resistance and lack of additive antiretroviral effects, [HA424 trade name] should not be taken with emtricitabine (see section 4.5).

The combination of lamivudine with cladribine is notrecommended (see section 4.5).

## 4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Metabolic interactions with lamivudineare less likelybecause of its limited metabolism and plasma protein binding and almost complete renal clearance.

Lamivudine metabolism does not involve CYP3A and interactions with medicines metabolised by this system (e.g.protease inhibitors) are unlikely.

Sulfamethoxazole/trimethoprim increases plasma concentrations of lamivudine but a clinically significant effect is not expected; the patient should be monitored for lamivudine toxicity in case of marked renal impairment or if high doses of sulfamethoxazole/trimethoprim are used (e.g. for treating *Pneumocystis jirovecii* pneumonitis).

Medicines which are main eliminated by renal secretion via the organic cationic transport system, e.g. trimethoprim, may interact with lamivudine. Medicines (e.g. ranitidine, cimetidine), which are eliminated only in part by this mechanism, were shown not to interact with lamivudine.

Due to similarities, [HA424 trade name] should not be administered concomitantly with other cytidine analogues, such as emtricitabine.

In vitro lamivudine inhibits the intracellular phosphorylation of cladribine, raising the possibility of a loss of cladribine's efficacy if the two are used concomitantly. Some clinical findings also support a possible interaction between lamivudine and cladribine. Therefore, the concomitant use of lamivudine with cladribine is not recommended.

Co-administration of sorbitol solution (3.2, 10.2, and 13.4 g) with a single 300-mg dose of lamivudine oral solution to adults resulted in dose-dependent decreases of 14, 32, and 36% in lamivudine exposure ($AUC_{\infty}$) and 28, 52, and 55% in the $C_{max}$ of lamivudine. When possible, chronic co-administration of lamivudine with medicines containing sorbitol or other osmotic-acting polyalcohols or monosaccharide alcohols (e.g.lactitol,

maltitolmannitol,xylitol) should be avoided. More frequent monitoring of HIV-1 viral loadshould be considered when chronic co-administration cannot be avoided.

The co-administration of sulfadiazine and cisplatin with lamivudine has a potential for renal toxicity and would require monitoring of renal function.

The co-administration of flucytosine with lamivudine has potential for haematological toxicity which requires monitoring of haematological parameters and dose reduction should be considered.

### 4.6 Fertility, pregnancy and breastfeeding

*Pregnancy*
WHO HIV Treatment guidelines recommend lamivudine-containing therapy for pregnant women and women of childbearing potential.
No increased risk of birth defects has been reported for lamivudine (www.apregistry.com).

*Breastfeeding*
Lamivudine is excreted into the breast milk of lactating mothers.
Current recommendations on HIV and breastfeeding (e.g. those from the WHO) should be consulted before advising patients on this matter.
Preferred options may vary depending on the local circumstances.

*Fertility*
Studies in animals showed that lamivudine had no effect on fertility (see section 5.3).

### 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
Nevertheless, the clinical status of the patient and the adverse reaction profile of [HA424 trade name]should be borne in mind when considering the patient's ability to drive or operate machinery.

### 4.8 Undesirable effects

The following adverse reactions have been reported during therapy for HIV disease with lamivudine.

The adverse reactions considered at least possibly related to the treatment are listed below by body system, organ class and absolute frequency. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000).

| System Organ Class | Common | Uncommon | Rare | Very Rare |
|---|---|---|---|---|
| **Blood and lymphatic system orders** | | Neutropenia and anaemia (both occasionally severe), thrombocytopenia | | Pure red cell aplasia |
| **Metabolism and nutrition disorders** | | | | Lactic acidosis |
| **Nervous system disorders** | Headache, insomnia | | | Peripheral neuropathy (or paraesthesia) |
| **Respiratory, thoracic and mediastinal** | Cough,<br>Nasal symptoms | | | |

| | | | | |
|---|---|---|---|---|
| **disorders** | | | | |
| **Gastrointestinal disorders** | Nausea, vomiting, abdominal pain or cramps, diarrhoea | | Pancreatitis, elevations in serum amylase | |
| **Hepatobiliary disorders** | | Transient elevations in liver enzymes (AST, ALT) | Hepatitis | |
| **Skin and subcutaneous tissue disorders** | Rash, alopecia | | Angiooedema | |
| **Musculoskeletal and connective tissue disorders** | Arthralgia, muscle disorders | | Rhabdomyolysis | |
| **General disorders and administration site conditions** | Fatigue, malaise, fever | | | |

Weight and levels of blood lipids and glucose may increase during antiretroviral therapy (see section 4.4)

In HIV-infected patients with severe immune deficiency at the time of initiation of combination antiretroviral therapy, an inflammatory reaction to asymptomatic or residual opportunistic infections may arise. Autoimmune disorders (such as Graves' disease) have also been reported to occur in the setting of immune reactivation; however, the reported time to onset is more variable and these events can occur many months after initiation of treatment (see section 4.4).

Cases of osteonecrosis have been reported, particularly in patients with generally acknowledged risk factors, advanced HIV disease or long-term combined antiretroviral exposure. The frequency of which is unknown (see section 4.4).

*Paediatric population*

1206 HIV-infected paediatric patients aged 3 months to 17 years were enrolled in a clinical trial, 669 of whom received abacavir and lamivudine either once or twice daily (see section 5.1). No additional safety issues have been identified in paediatric subjects receiving either once or twice daily dosing compared to adults.

***Reporting of suspected adverse reactions***

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine's benefits and risks.

## 4.9 Overdose

No specific symptoms or signs have been identified following acute overdose with lamivudine, apart from those listed as undesirable effects.

If overdose occurs the patient should be monitored for toxicity (see section 4.8), and standard supportive treatment applied as necessary. Since lamivudine is dialysable, continuous haemodialysis may be used to treat an overdose, but this has not been studied.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: nucleoside and nucleotide reverse transcriptase inhibitor, ATC Code: J05AF05.

*Mechanism of action*

Lamivudine is a nucleoside analogue which has activity against human immunodeficiency virus (HIV) and hepatitis B virus (HBV). It is metabolised intracellularly to the active moiety, lamivudine 5'-triphosphate. Its main mode of action is as a chain terminator of viral reverse transcription. The triphosphate has selective inhibitory activity against HIV-1 and HIV-2 replication in vitro, it is also active against zidovudine-resistant clinical isolates of HIV. No antagonistic effects in vitro were seen with lamivudine and other antiretrovirals (tested agents: abacavir, didanosine, nevirapine and zidovudine).

*Resistance*

HIV-1 resistance to lamivudine involves the development of a M184V amino acid change close to the active site of the viral reverse transcriptase (RT). This variant arises both in vitro and in HIV-1 infected patients treated with lamivudine-containing antiretroviral therapy. M184V mutants display greatly reduced susceptibility to lamivudine and show diminished viral replicative capacity *in vitro. Invitro* studies indicate that zidovudine-resistant virus isolates can become zidovudine sensitive when they simultaneously acquire resistance to lamivudine. The clinical relevance of such findings remains, however, not well defined.

*In vitro* data tend to suggest that the continuation of lamivudine in anti-retroviral regimen despite the development of M184V might provide residual anti-retroviral activity (likely through impaired viral fitness). The clinical relevance of these findings is not established. Indeed, the available clinical data are very limited and preclude any reliable conclusion in the field. In any case, initiation of susceptible NRTI's should always be preferred to maintenance of lamivudine therapy. Therefore, maintaining lamivudine therapy despite emergence of M184V mutation should only be considered in cases where no other active NRTI's are available.

Cross-resistance conferred by the M184V RT is limited within the nucleoside inhibitor class of antiretroviral agents. Zidovudine and stavudine maintain their antiretroviral activities against lamivudine-resistant HIV-1. Abacavir maintains its antiretroviral activities against lamivudine-resistant HIV-1 harbouring only the M184V mutation. The M184V RT mutant shows a <4-fold decrease in susceptibility to didanosine; the clinical significance of these findings is unknown. In vitro susceptibility testing has not been standardised and results may vary according to methodological factors.

Lamivudine demonstrates low cytotoxicity to peripheral blood lymphocytes, to established lymphocyte and monocyte-macrophage cell lines, and to a variety of bone marrow progenitor cells *in vitro*.

*Clinical efficacy and safety*

Lamivudine has been investigated in several randomised, prospective clinical trials in combination with other antiretroviral drugs. These studies demonstrate significant decrease in plasma HIV RNA and increase in CD4 cell counts when lamivudine is used in combination with another nucleos(t)ide analogue and third agent of a different therapeutic class, e.g. a non-nucleoside reverse transcriptase inhibitor (NNRTI), protease inhibitor (PI) or integrase strand transfer inhibitor (INSTI). In recent studies by intention-to-treat analysis 88% of subjects achieved plasma HIV RNA ≤ 50 copies/ml after 48 weeks of combination antiretroviral treatment.

*Paediatric subjects*

Clinical trial evidence from paediatric patients receiving lamivudine with other antiretroviral drugs (abacavir, nevirapine/efavirenz or zidovudine) has shown that the resistance profile observed in paediatric patients is similar to that observed in adults, in terms of the genotypic substitutions detected and their relative frequency.

In a randomised clinical trial the safety and efficacy of once-daily dosing with twice-daily dosing of lamivudine and abacavir, in combination with a third antiretroviral drug was compared in 1206 paediatric patients aged 3 months to 17 years. After 36 weeks on a regimen including twice daily abacavir and lamivudine, 669 eligible subjects were randomised to either continue twice daily dosing or switch to once daily abacavir and lamivudine for at least 96 weeks. The abacavir + lamivudine once daily dosing group was demonstrated to be non-inferior to the twice daily group according to the pre-specified non-inferiority margin of -12%, for the primary endpoint of <80 c/ml at Week 48 as well as at Week 96. Analyses by formulation demonstrated the proportion of subjects with HIV-1 RNA of less than 80 copies per mL at randomisation and Week 96 was higher in subjects who had received tablet formulations of lamivudine and abacavir (75% [458/610] and 72% [434/601]) than in those who had received any solution formulation(s)at any time (with lamivudine solution given at weight band-based doses approximating 8 mg per kg per day) (52% [29/56] and 54% [30/56]), respectively. These differences were observed in each different age group evaluated. See section 4.4.

## 5.2 Pharmacokinetic properties

No pharmacokinetic data are available for [HA424 trade name]. A bioequivalence study was conducted with [HA425 trade name]that is essentially the same as [HA424 trade name] in qualitative terms and with respect to the ratio of the active substance and other ingredients.

The absorption characteristics of [HA425 trade name] have been determined after administration of onetablet of [HA425 trade name] in healthy volunteers in the fasting state as follows:

| **Pharmacokinetic variable** | **Mean value ± standard deviation**<br>arithmetic mean ± SD |
|---|---|
| Maximum concentration ($C_{max}$) ng/ml | 3062 ± 849 |
| Area under the curve ($AUC_{0-\infty}$), a measure of the extent of absorptionng.hour/ml | 13791 ± 4246 |
| Time to attain maximum concentration ($t_{max}$) hour | 0.97 ± 0.43 |

*Pharmacokinetics of lamivudine*

| | |
|---|---|
| **Absorption** | |
| Oral bioavailability | 80–85% |
| Food effect | not clinically relevant |
| **Distribution** | |
| Volume of distribution (mean) | 1.3 L/kg |
| Plasma protein binding in vitro | < 36% |
| **Metabolism** | |
| | Only minor route (< 10%) |
| Active metabolite(s) | Information not available |
| **Elimination** | |
| Elimination half life | 18-19 h<br>16-19 h for intracellular lamivudine triphosphate |
| Mean systemic clearance | 0.32 L/h/kg |
| % of dose excreted in urine | > 70% [predominantly cleared unchanged] |

| | |
|---|---|
| **Pharmacokinetic linearity** | Linear pharmacokinetics |
| **Drug interactions *(in vitro*)** | |
| Transporters | OCT (organic cationic transporters) |

*Pharmacokinetics in pregnancy*

The pharmacokinetics of lamivudine and zidovudine during pregnancy were similar to that of non- pregnant women. Nevirapine clearance increases in pregnant women resulting in lower AUC and $C_{max}$ compared to non-pregnant women.

*Pharmacokinetics in children*

The absolute bioavailability of lamivudine (about 58–66%) was reduced in children below 12 years of age.Paediatric pharmacokinetic studies with bothoral solution and tablet formulations found that once-daily dosing provides equivalent $AUC_{0\text{-}24h}$ to twice-daily dosing of the same total daily dose.

### 5.3 Preclinical safety data

Administration of lamivudine in animal toxicity studies at high doses was not associated with any major organ toxicity. At the highest dosage levels, minor effects on indicators of liver and kidney function were seen together with occasional reductions in liver weight. The clinically relevant effects noted were a reduction in red blood cell count and neutropenia.

*Mutagenecity and carcinogenecity*

Lamivudine was not mutagenic in bacterial tests but, like many nucleoside analogues, showed activity in an in vitro cytogenetic assay and the mouse lymphoma assay.Based on the totality of the available data it is concluded that lamivudine should not represent a genotoxic hazard to patients undergoing treatment.
The results of long-term carcinogenicity studies in rats and mice did not show any carcinogenic potential relevant for humans.

*Reproductive toxicology*

In reproductive toxicity studies in animals, lamivudine was shown to cross the placenta. Lamivudine was not teratogenic in animal studies and data on early embryonic deaths were not consistent between species. Data from monkey studies demonstrated that foetuses exposed in utero to the combination of zidovudine and lamivudine sustained a higher level of nucleoside analogue-DNA incorporation into multiple foetal organs and showed evidence of more telomere shortening than in those exposed to zidovudine alone. The clinical significance of these findings is unknown.
A fertility study in rats has shown that lamivudine had no effect on male or female fertility.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

*Core tablet:* Magnesium stearate
Microcrystalline cellulose
Sodium starch glycolate

*Film coat*: Hypromellose
Macrogol (polyethylene glycol 400)
Polysorbate 80
Titanium dioxide

This medicine is essentially ‘sodium-free’. It contains less than 1 mmol sodium (23 mg) per tablet.

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

36 months (Blister pack)
48 months (HDPE bottle)

### 6.4 Special precautions for storage

Store below 30°C in a dry place and protected from light. Keep out of reach of children.

### 6.5 Nature and contents of container

HDPE bottle package comprising a white HDPE bottle with white polyethylene screw cap and containing pack insert and 1 g pillow pack with adsorbent.
Each bottle contains 60 tablets.

Blister package comprising pre-printed aluminium foil coated with heat seal lacquer and clear PVC/PVdC film.
Each blister card contains 10 tablets.
The pack size is 6 blister packages of 10 tablets packed in a carton (6x10).

### 6.6 Special precautions for disposal and other handling

Not applicable

## 7. SUPPLIER

Macleods Pharmaceuticals Limited,
Atlanta Arcade, 3rd floor, Church Road, near Leela Hotel,
Andheri-Kurla Road,
Andheri (East),
Mumbai 400 059,
India
Telephone: + 91 22 56 26 28 00
Fax: + 91 22 29 25 65 99
Email: exports@macleodspharma.com
vijay@macleodspharma.com
sjadhav@macleodspharma.com

## 8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

HA424

## 9. DATE OF PREQUALIFICATION

14 December 2010

## 10. DATE OF REVISION OF THE TEXT

June 2023

Section 6 was updated in May 2024

***References***

*General reference sources for this SmPC include:*

Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – second edition. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/handle/10665/208825

Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations: 2022(7) https://www.who.int/publications/i/item/9789240052390

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European SmPCs of Epivir available at:
https://www.ema.europa.eu/en/documents/product-information/epivir-epar-product-information_en.pdf

*Further references relevant to sections of the SmPC include:*

Section 4.4
On combination therapy
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*Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/pqweb/medicines*