

ABACAVIR (ABC)

GENERAL INFORMATION

- Therapeutic class: Nucleoside reverse transcriptase inhibitor (NRTI).
- WHO guidelines: Indicated for first- and second-line for adults, adolescents and children.^{6,22}
- Originator company and product brand name: GlaxoSmithKline (GSK), Ziagen. In April 2009, Pfizer and GSK jointly announced the creation of ViiV, a new joint venture focusing solely on the R&D and commercialisation of HIV medicines.
- First approval by U.S. Food and Drug Administration (FDA): December 1998.²³
- WHO Model List of Essential Medicines (EML): Included in the 17th edition.²⁴
- World sales of originator product: 2010: Sales not reported. 2009: US\$ 160 million; 2008: \$175 million; 2007: \$215 million; 2006: \$230 million; 2005: \$268 million; 2004: \$290 million.^{25, 26, 27, 28, 29, 30}
- Patents: The basic patents on ABC were applied for by GSK in 1989³³ and 1990,³¹ and these expired in 2009 and 2010, respectively. GSK subsequently applied for additional patents related to new intermediates in 1995,³² to the hemisulfate salt of ABC in 1998³³ and to compositions of ABC particularly relevant for paediatric use in 1999, which³⁴ are due to expire in 2015, 2018 and 2019, respectively.

PRICE INFORMATION

Developing country prices in US\$ per patient per year, as quoted by companies.

The price in brackets corresponds to the price of one tablet/ml of oral solution. Products quality-assured by US FDA or WHO prequalification (as of May 2011) are in **bold**.

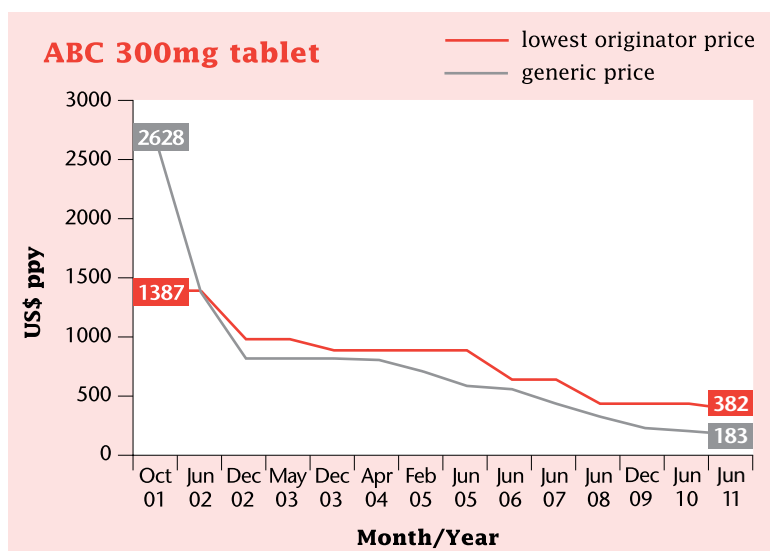
	Daily dose	ViiV	Aspen	Aurobindo (CF)	Cipla (CF)	Hetero	Matrix (CF)	Ranbaxy	Strides
Who can access this price?		See annex 2							
ABC 20mg/ml oral solution	10 ml	347 (0.095/ml)	153 (0.042/ml)	212 (0.058/ml)	139 (0.038/ml)				
ABC 60mg tablet	4			146 (0.100)	158 (0.108)		134 (0.092)		
ABC 300mg tablet	2	382 (0.523)		195 (0.267)	231 (0.317)	231 (0.317)	183 (0.250)	261 (0.358)	292 (0.400)

(CF) The Clinton Foundation has negotiated with this manufacturer for reduced prices on some formulations for countries in their consortium. See annex 13 for details.

Evolution of the lowest price quoted for eligible developing countries since 2001:

As of May 2011, six generic sources of ABC 300mg tablet were quality-assured by US FDA or WHO prequalification. The one with the lowest price is shown here.

Since 2001, the originator price has decreased by 72%, while generic prices have dropped by 93%.



Continued overleaf ❖

SPOTLIGHT ON ACCESS ISSUES

In 2010, WHO released new recommendations for antiretroviral therapy for HIV in adults and adolescents. For second-line treatment, protease inhibitors such as ritonavir-boosted atazanavir (ATV/r) or lopinavir (LPV/r), and simplified NRTI options are recommended. Abacavir (ABC) (along with didanosine (ddI)) is therefore no longer recommended as one of the NRTI backbones in second-line therapy.⁷

Price remains an issue. Even though the generic price of ABC has fallen by 93% since 2001, the current lowest price is more than twice the lowest price of tenofovir (TDF) or zidovudine (AZT).

In addition, in 2011, ViiV clarified their pricing structure (see annex 2), confirming that their standardised price discounts were not in fact available to all fully-financed Global Fund or PEPFAR programmes, contrary to previous announcements. Global Fund financed programmes in middle-income countries have not been and will not be eligible for those prices, and will have to negotiate prices on a case-by-case basis. With some developed countries paying over \$3,500 ppy, the price is prohibitive for many developing countries that need to access the product.³⁵

In February 2011, Shionogi-ViiV Healthcare announced the start of a phase III trial for a new fixed-dose combination including ABC, lamivudine (3TC)³⁶ and a new integrase inhibitor S/GSK1349572 (an investigational drug known as dolutegravir, now in phase III clinical development).³⁷

Patents

The price of ABC decreased significantly with the arrival of generic competition. GSK could not apply for the basic patents on ABC in countries with generic production capacity such as India, which did not grant patents on pharmaceuticals at the time.

However, patents have been granted in China.³⁸

In addition, GSK applied for patents on the hemisulfate salt of ABC in India but withdrew this application in October 2007 after it was opposed by civil society groups in a pre-grant opposition procedure.³⁹

GSK also applied for a patent on compositions of ABC particularly relevant for paediatric use, which was granted in December 2007.⁴⁰ This patent raises concerns over the continued generic availability of the ABC paediatric formulation, which is an important option for young children with HIV/TB co-infection.

Paediatrics

ABC is approved for use in children. In its 2010 guidelines for antiretroviral therapy for HIV in infants and children, WHO recommends ABC as one of the possible NRTIs to be given with 3TC and either an NNRTI or a PI in the first-line. WHO guidelines recommend a preferential order of NRTIs to be used in first-line regimens, with AZT preferred over ABC, and ABC preferred over d4T.²²

ABC can also be part of second-line regimens, depending on what has been used as a first-line.²²

ABC will continue to be an important drug for HIV/TB co-infected young children, not least because children have limited treatment options – there are interactions between TB drugs and nevirapine (NVP), and the dosage data on efavirenz (EFV) for children under three is lacking.

However, a recent survey regarding paediatric second-line carried out by the TREAT Asia Paediatric HIV Observational Database (TApHOD) found that ABC was more difficult to access in Asia and that its relatively high cost could act as a deterrent to wider use.⁴¹ This applies particularly in countries where ABC is patented, where the generic ABC 60mg tablet is not available. In the public sector in Malaysia, ViiV's ABC solution costs more than \$1200 ppy.⁴²

Paediatric ABC comes in a liquid formulation. In addition, as of April 2011, three generic sources of ABC 60mg paediatric tablet are quality-assured by either US FDA or WHO prequalification.

Generic manufacturers have also been developing both double and triple fixed-dose combinations containing ABC. As of May 2011, two sources of paediatric double FDC and one triple FDCs containing ABC were quality-assured by either US FDA or WHO prequalification. All are produced by generic companies.

Once-daily dosing of ABC is only recommended for patients over 12 years of age; more studies are needed to confirm the safety of daily dosing of ABC in children.⁴³