ABACAVIR (ABC)

GENERAL INFORMATION

- **Therapeutic class:** Nucleoside reverse transcriptase inhibitor (NRTI).
- **2016 WHO Guidelines:** ABC is recommended for infants and children under 10 years of age as a preferred first-line NRTI, and for second-line treatment if a thymidine analogue was used in first-line treatment. In adolescents, ABC is recommended as an alternative first-line ARV. For adults, other treatment options are preferred for first-line; ABC is part of second- or third-line regimens.
- Originator company and product brand name: GlaxoSmithKline (GSK); Ziagen. In April 2009, Pfizer and GSK announced the creation of ViiV Healthcare, a joint venture focusing solely on research and development and commercialisation of HIV medicines.
- First approved by US Food and Drug Administration (FDA): December 1998.
- WHO Model List of Essential Medicines (EML): Included in the 19th edition for adults and the 5th edition for children.
- World sales of originator product: 2009: US$160 million; 2008: $175 million; 2007: $215 million; 2006: $230 million; 2005: $268 million; 2004: $290 million. After 2010, sales were not reported in the company's annual report.

PRICE INFORMATION

Developing country prices in US$ per person per year, as quoted by companies.
The price in brackets corresponds to the unit price of one capsule/tablet/ml of oral solution.
Products that are quality-assured by US FDA or WHO prequalification (as of May 2016) are in **bold.**

	Daily Dose	ViiV	Aspen	Aurobindo	Cipla	Hetero
ABC 20mg/ml oral solution (paediatrics)	12ml	**289 (0.066)**	249 (0.057)	**228 (0.052)**		**123 (0.028)**
ABC 60mg tablet (paediatrics)	4				**97 (0.067)**	

SPOTLIGHT ON ACCESS ISSUES

ABC is crucial for people who cannot tolerate zidovudine or tenofovir. For paediatric treatment, ABC is as part of first-line regimens for infants and children up to 10 years of age.

Paediatrics: The 2016 WHO guidelines recommend ART initiation for all children who are less than a year old to 10 years old. The ABC/3TC scored FDC tablet is included in the 2016 IATT optimal paediatric ARV formulary.[1]

PATENTS
(Patent information may be updated in 2016 to fully reflect the evolving landscape of patents, other forms of intellectual property, licensing and use of flexibilities for the particular drug.)

GSK's basic patent on ABC expired in 2010 in most countries, including middle-income countries such as China[2,3] and Ukraine,[3] and high-income countries such as the United States. GSK applied for secondary patents to extend its patent monopoly, including one on the hemisulfate salt of ABC, filed in 1998.[4]

India: generic production and supply protected

In India, generic production and capacity to supply ABC are protected, thanks to a number of safeguards available in its patent law. GSK could not apply for the basic patent on ABC in India, as it did not grant product patents on pharmaceuticals prior to the full implementation of the TRIPS Agreement. GSK withdrew its secondary patent application (on the hemisulphate salt) in India in 2007, after the Initiative for Medicines, Access and Knowledge (I-MAK) helped the Indian Network of Positive People (INP+) file an opposition against the application.[5]

Remaining challenges in other countries due to patent barriers

Today, ABC for adults and paediatric versions of ABC/3TC are produced by Indian generics manufacturers and available for export to developing countries, although intellectual property (IP) barriers may prevent some of these countries from importing more affordable generic versions of the adult formulation. For instance, the secondary patent on the ABC hemisulphate salt is being enforced by GSK in China, Malaysia, Ukraine and other countries, thereby posing a barrier until 2018.[3]

In September 2012, the Indonesian government issued compulsory licences (CLs) for several key ARVs, including ABC. The CL will last until May 2018, when the ABC patent expires.[6]

In August 2012, GSK filed a claim to stop the supply and procurement of generic ABC, using an infringement of the hemisulfate salt patent as a threat against four Ukrainian companies and distributors that submitted bids to supply the adult formulation of ABC to the Ukrainian Ministry of Health. GSK also filed for an injunction to prohibit these companies from selling and importing generic ABC from Cipla and Mylan, which was granted in August 2012. GSK's patent infringement claim is being considered by the Kiev commercial court.[7] This litigation has had a chilling effect on generic suppliers of the drug in Ukraine, who are no longer bidding to sell the drug to the Ministry of Health. Ironically, GSK has not been able to use the evergreening hemisulphate

salt patent to block generics from the US market, where a number of Indian and Canadian generics are registered.[8]

ViiV also holds patents on different ABC-containing combinations in high-income and many middle-income countries; these can block access to generic versions. For instance, in the United States, ViiV's combination patent on the dual combination of lamivudine and abacavir (3TC/ABC), and a triple combination of lamivudine, abacavir and zidovudine (3TC/ABC/ZDV) was upheld by a District Court after Teva challenged it.[9,10] But the court also ruled that Teva's generic product did not infringe on ViiV's patented product.[9,10] The combination patent of abacavir/doultegravir/lamivudine (ABC/DTG/3TC) has been filed in a number of developing countries such as Brazil, China, Indonesia and countries of the Africa Regional Intellectual Property Office (ARIPO),[3] and has been granted in countries like Ukraine and Colombia.[3] GSK also holds patents on fixed-dose combinations of ABC with 3TC or emtricitabine (FTC), and with AZT in China, Russia, ARIPO and OAPI countries.[3] This may hinder access to generic versions of this combination, especially in countries that were excluded from the voluntary licence (VL) signed between ViiV and the Medicines Patent Pool (MPP) in 2013.[11]

In November 2012, Ecuador issued a compulsory licence on ABC/3TC. The licence was issued to Ecuadorean manufacturer Acroxmax, in a bid to reduce the price by 75%.[12]

MPP licence: limited effects

In February 2013, the MPP and ViiV announced a VL agreement for paediatric ABC in 118 countries.[13] Many high burden middle-income countries, including Brazil, China, Mexico, Peru, Russia, Uruguay, Ukraine, and Venezuela are excluded from the licence agreement. In many of these countries, the secondary patents listed in the licence will not expire until after 2018.[3]

The MPP and ViiV also entered into a separate, non-binding Memorandum of Understanding,[14] which promises collaboration on paediatric licencing of pipeline ARVs, development of novel combination paediatric formulations, and availability of novel paediatric formulations outside of the licenced territories.

GSK: recent statement on relaxing patents in developing countries

In March 2016, GSK released a statement[15] on its future patenting policy in developing countries, including a waiver on submitting patent applications on new drugs in Least-Developed Countries (LDCs); LDCs already benefit from a waiver extension, until 2033, from implementing TRIPS obligations, including pharmaceutical patents. GSK's waiver includes low-income countries, but a number of generic-producing middle-income countries are excluded from it, including Brazil and China.

While GSK's announcement recognises "that improving access around the world requires a flexible and multi-faceted approach to intellectual property (IP)"[15], its lawsuit in Ukraine and the limitations of its MPP VL for ABC show that the company does not address the access barriers to ABC that many high burden, middle-income countries are facing. GSK still enjoys a monopoly in many jurisdictions for ABC, although it was invented in the 1980s; this highlights the dangers of evergreening claims being granted.

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