



REYATAZ[®] (atazanavir) Capsules Approved for Paediatric Use by The European Commission

(PARIS, July 7, 2010) – Bristol-Myers Squibb announced that on 5th of July, the European Commission has approved boosted REYATAZ[®] (atazanavir sulfate) capsules to treat HIV-1 infection in paediatric patients aged six to eighteen years and greater than 15 kg, as part of combination HIV therapy.¹ This decision grants marketing authorisation in the 27 countries of the European Union.

“Globally, more than two million children under 15 years of age are living with HIV, and between 1,000 and 1,500 become newly infected with HIV every day. Once a child is infected with HIV, he/she faces a high chance of illness and death, unless treatment is provided. In countries of North America and Europe, where treatment options are accessible, the vast majority of children infected around the time of birth are surviving into adulthood. Despite the availability of treatment options, there are still many unmet needs in this patient population,” said Dr Gareth Tudor-Williams, Reader in Paediatric Infectious Diseases, Department of Medicine at Imperial College London and Consultant in Paediatric Infectious Diseases, St. Mary’s Hospital. “The European Commission approval of REYATAZ[®] is a milestone in addressing these challenges for children with HIV. We look forward to REYATAZ[®] capsules being available for our paediatrics patients across the European Union.”

In 2004, REYATAZ[®] was the first once-daily protease inhibitor to be launched in the European Union for pre-treated HIV patients.^{1,2,3} The use of boosted REYATAZ[®], in combination with other antiretrovirals, was approved for treatment-naïve patients in the European Union in June 2008.⁴ The United States Food and Drug Administration (FDA) approved REYATAZ[®] capsules in 2008 to treat HIV-1 infection in paediatric patients aged six

years and older, as part of combination HIV therapy.⁵ The safety, tolerability and efficacy of REYATAZ[®] capsules with ritonavir have been established in paediatric patients at least six years of age from the open-label, multicentre clinical trial, PACTG 1020A.¹

About PACTG 1020A Study

The Pediatric AIDS Clinical Trial Group (PACTG) 1020A study is a multicentre, open-label, phase I/II study conducted in HIV-infected children from 3 months to 21 years of age in the United States and South Africa to determine pharmacokinetics, safety, tolerability and efficacy of REYATAZ[®] in paediatric population⁶.

Overall in this study, 182 paediatric patients antiretroviral-naïve or experienced received once daily atazanavir, with or without ritonavir, in combination with two NRTIs¹. Forty-one of them (16 treatment-naïve and 25 experienced paediatric patients 6 years to less than 18 years of age) were treated with REYATAZ capsules with ritonavir. The clinical data derived from these 41 patients support the new paediatric indication.

Clinical Trial Results

About Efficacy

The 48-week PACTG 1020A study results confirmed that dosing ATV capsules, administered with RTV in naïve and experienced patients, was generally safe and efficacious.¹

The response rates for HIV RNA < 50 copies/ml were: 81% (13/16) in ARV-naïve patients and 24% (6/25) in ARV-experienced patients. The response rates for HIV RNA < 400 copies/ml were 88% (14/16) and 32% (8/25) in ARV naïve and experienced patients, respectively.¹

About Safety

In clinical studies, the safety profile of REYATAZ[®] was overall comparable to that seen in adults. Both asymptomatic first-degree (23%) and second-degree (1%) atrioventricular block were reported in paediatric patients. The most frequently reported laboratory abnormality in

paediatric patients receiving REYATAZ[®] was elevation of total bilirubin (≥ 2.6 times ULN, Grade 3-4) which occurred in 45% of patients.¹

About HIV in Children

Recent statistics suggest that, globally, approximately 2.1 million children younger than 15 years of age have HIV, out of 33 million patients worldwide.⁷ About 90% of HIV-positive children live in sub-Saharan Africa.⁸ Generally, HIV and AIDS have affected Western Europe more than Central Europe.⁹ Switzerland has the highest HIV prevalence, followed closely by France, Italy, Portugal and Spain.⁹ The European Region of the World Health Organization (WHO), particularly its Eastern countries, has one of the fastest-growing HIV/AIDS epidemics in the world.¹⁰ This is likely due to the steady rise of HIV-infected women, and subsequently, the rise in the transmission rate of HIV infection to newborn babies.¹⁰ Most children acquire the virus from their HIV-infected mothers during pregnancy, birth or breastfeeding.¹¹ Currently, children represent nearly 16% of the newly HIV-infected population.⁷

AIDS has become one of the major killers of young children. In 2008, two million people died from HIV, 14% of which were children.⁷ Worldwide, one in seven people dying of HIV-related illness is a child under 15 years old.¹²

The number of children receiving antiretroviral therapy increased from about 75,000 in 2005 to almost 200,000 in 2007.¹¹

About REYATAZ[®]

Developed by Bristol-Myers Squibb, REYATAZ[®] is an antiviral drug used in combination with other medicines to treat individuals infected with the human immunodeficiency virus-1 (HIV-1).¹ REYATAZ[®] was the first once-daily protease inhibitor launched in Europe.^{2,3}

Important Information About REYATAZ® (atazanavir sulfate) for Paediatric Patients

Ages 6 years and older

INDICATION:

REYATAZ® capsules, co-administered with low dose ritonavir, are indicated for the treatment of HIV-1 infected adults and paediatric patients 6 years of age and older in combination with other antiretroviral medicinal products.¹

Based on available virological and clinical data from adult patients, no benefit is expected in patients with strains resistant to multiple protease inhibitors (≥ 4 PI mutations). There are very limited data available from children aged 6 to less than 18 years.¹

The choice of REYATAZ® in treatment-experienced adult and paediatric patients should be based on individual viral resistance testing and the patient's treatment history. Available data do suggest that atazanavir in combination with ritonavir may not be effective in treatment experienced children with very few (<3) PI mutations.¹

The dosing of REYATAZ® capsules for paediatric patients is based on body weight as follows:

Body Weight (kg)	REYATAZ® dose QD	ritonavir dose QD
15 to less than 20	150 mg	100 mg
20 to less than 40	200 mg	100 mg
at least 40	300 mg	100 mg ¹

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company committed to discovering, developing and delivering innovative medicines that help patients prevail over serious diseases.

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