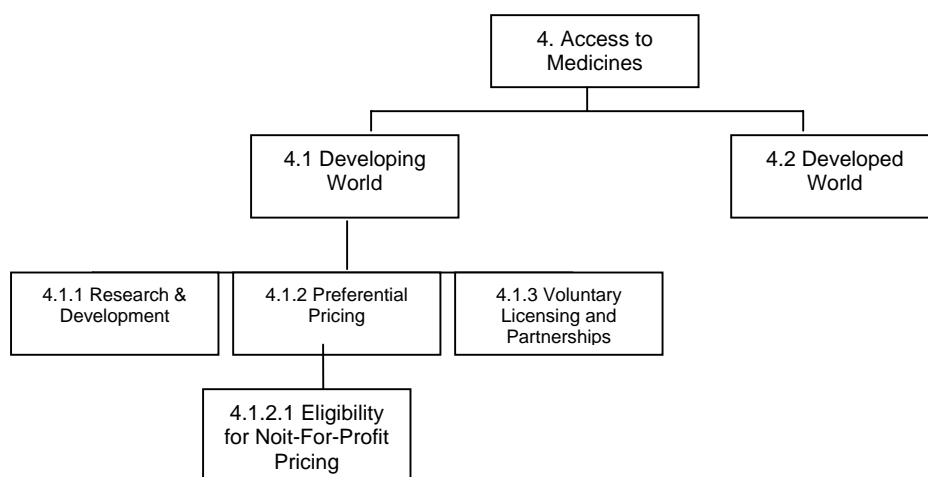


ACCESS TO MEDICINES



Access 4

Access to Medicines

Corporate responsibility principle

We will continue to research and develop medicines to treat diseases of the developing world. We will find sustainable ways to improve access to medicines for disadvantaged people, and will seek partnerships to support this activity.

Access to healthcare is a significant challenge in many parts of the world. Millions of poor people in both developed and developing countries cannot obtain the medicines they need.

This section describes how GSK is helping to improve access, and our progress in 2004. It covers our:

- contribution to the developing world through research, not-for-profit pricing, partnerships and voluntary licences
- preferential pricing arrangements and discount cards for middle-income countries
- Patient Assistance Programs and discount cards to help uninsured patients in the US

We also support under-served communities worldwide through donations, funding and practical support, see Community Investment in the website.

Case study

Improving Access to Medicine in Lithuania

GSK's new *Orange Card* in Lithuania is giving all senior citizens better access to the medicines they need.

Patients in Lithuania must contribute towards the cost of prescription medicines. Many senior citizens don't get the treatment they need because they cannot afford to pay this cost and do not have private medical insurance to cover the expense. Doctors are aware of this and may sometimes prescribe based on the patient's ability to pay rather than the best option available. In general, the access to innovative treatment is very limited in Lithuania. The standard of living of seniors is relatively poor and healthcare financing is one of the lowest in the EU. All of these causes encouraged GSK Lithuania to implement the *Orange Card* scheme launched successfully in the US.

The *Orange Card* helps to tackle this problem by giving all senior citizens a discount of up to 100% of the patient's contribution on all GSK prescription medicines. Patients can apply by completing a simple form and if eligible they will receive their *Orange Card* by post.

The card was launched in July 2004 through a national advertising campaign and promotional material sent to pensioner organisations, doctors and pharmacies. By February 2005 more than 3,500 patients had applied for an *Orange Card* and 107 pharmacies had registered to participate.

Our target is for 18,000 patients and 125 pharmacies to have joined the programme by July 2005.

Developing World

There is a healthcare crisis in many parts of the developing world. Millions of people do not have access to adequate food and clean water. Their governments do not have the resources to fund the clinics and staff needed to deliver healthcare. The AIDS pandemic has made these problems worse, creating a generation of orphans and depriving communities of their greatest asset – fit and healthy people.

Tackling this crisis is a complex challenge. Poverty is the fundamental cause and a huge barrier to progress. Significant political will and extra funding are needed from new national and international sources to aid development and build healthcare infrastructure.

We believe that it is the responsibility of governments and intergovernmental agencies, supplemented by the work of many NGOs, to work in partnership to deliver the healthcare needed in these countries. However, the pharmaceutical industry can play a significant role in supporting their work.

We make an important contribution through:

- Investing in research and development that targets diseases disproportionately affecting developing countries
- Providing antiretrovirals (ARVs), anti-malarials and vaccines at specially reduced prices
- Developing partnerships and granting voluntary licences to local manufacturers.

We also support programmes to improve health and education through our community investment programme. Partnerships focus on four major diseases -- lymphatic filariasis, malaria, HIV/AIDS and diarrhoeal disease. Support is given through donations of cash and medicines, as well as employee involvement. See Community Investment in the website.

Research and Development

To learn more about R&D for the developing world visit our website

The research and development (R&D) of new drugs is essential to improve health in the developing world. There are still no effective treatments for some widespread and life-threatening diseases. Many existing treatments for diseases such as malaria are becoming less effective due to drug resistance.

Many of these diseases disproportionately affect developing countries. This means there is often no viable commercial market for new treatments. New ways are required to encourage R&D and to ensure that new medicines and vaccines reach the people who need them. One solution is the Public Private Partnership (PPP) model. This encourages R&D and can often accelerate the product's uptake in the developing world on a scale that cannot be achieved by a company on its own.

PPPs involve companies and the public sector (eg governments, the WHO and other UN bodies, academia, and philanthropic foundations) working together. They are helping to address this lack of effective markets. Companies provide technology, development, manufacturing and distribution expertise. Public sector partners help fund R&D and delivery costs, ensuring that new medicines and vaccines get to the people who need them. GSK is a partner in several PPPs including the Medicines for Malaria Venture (MMV), Global Alliance for TB and the Malaria Vaccine Initiative (MVI). PPPs such as these are transforming the landscape of R&D into diseases of the developing world.

GSK has created a dedicated group in our pharmaceutical R&D organisation, based in Spain, the UK and the US, to focus on diseases disproportionately affecting developing countries. Projects are prioritised according to their social and public health benefits rather than their commercial returns. A similar group exists in our vaccines organisation based in Belgium.

We believe GSK is currently the only company researching both new vaccines and treatments for HIV/AIDS, TB and malaria – the World Health Organisation's three priority diseases.

HIV/AIDS affects both developed and developing countries. This means there is a commercial market for new treatments, which encourages investment in the required R&D. GSK is the industry leader in research into HIV/AIDS treatment, and currently has three major clinical development programmes in progress, each with a different mode of action.

In total GSK has 14 clinical programmes for medicines and vaccines against 9 diseases¹ particularly relevant to the developing world. Seven of these projects are for diseases that disproportionately affect developing countries.

¹ HIV/AIDS, malaria, leishmaniasis, dengue fever, TB, hepatitis E, N. meningitis, cervical cancer and pneumonia

Development Pipeline at end of 2004 for diseases relevant to the developing world*

Focus	Pre-clinical activity	PHASE I	PHASE II	PHASE III	MARKETED
HIV	✓		CCR5 antagonist NNRTI Protease Inhibitor		<i>Retrovir, Epivir, Combivir, Ziagen, Trizivir, Agenerase, Epzicom/Kivexa, Lexiva/Telzir</i>
Vaccines	✓	HIV TB Dengue fever	N. meningitidis Malaria Hepatitis E	<i>Streptorix</i> (S. pneumoniae paediatric) <i>Cervarix</i> (cervical cancer)	<i>Rotarix</i> – (Rotavirus) <i>Havrix</i> - (Hepatitis A) <i>Enerix-B</i> - (Hepatitis B) <i>Twinrix</i> - (Hep A&B) <i>Infanrix</i> - (Diphtheria, Tetanus, acellular Pertussis) <i>Tritanrix</i> - (Diphtheria, Tetanus, wholecell Pertussis) Polio Sabin - (Polio) <i>Priorix</i> - (Measles, Mumps and Rubella) <i>Typherix</i> - (Typhoid) <i>Hiberix</i> - (Haemophilus influenzae type b) <i>Mencevax ACW</i> (meningitis)
Malaria	✓	pyridone**	CDA (chlorproguanil, dapsone + artesunate)	tafenoquine	<i>Lapdap, Halfan, Malarone</i>
TB	✓				
Other	✓			sitamaquine (visceral leishmaniasis)	<i>Zentel</i> (de-worming agent) <i>Pentostam</i> (visceral leishmaniasis)

* more detailed information on our product pipeline can be found in the Annual Report [link]

**the pyridone project should enter phase 1 in 2005

Progress in 2004

Malaria

- Phase IIb clinical trials of our malaria vaccine for children showed unprecedented results. Data from the trials, conducted with the Malaria Vaccine Initiative (MVI), showed the vaccine protected a significant percentage of children against uncomplicated malaria, malaria infection and even severe forms of the disease for at least six months. Dr Melinda Moree, Director of MVI, commented that “The findings represent a breakthrough in the science of malaria vaccines”.
- GSK is working with the Medicines for Malaria Venture (MMV), the World Health Organisation (WHO) and academic partners to develop an affordable fixed-dose artemisinin combination treatment for malaria in Africa, based on GSK’s *Lapdap*.
- We received the MMV’s Project of the Year award for our Pyridone Project, investigating a new class of compounds for use against malaria. The project was chosen by the MMV’s Expert Scientific Advisory Committee - a group of 12 experts in malaria and drug development - for its rapid success in identifying a drug candidate. We have since signed an agreement with the MMV to take a lead compound into clinical development.

HIV/AIDS

- We have also made progress on R&D into HIV/AIDS. *Epzicom/Kivexa*, a new fixed dose combination of *Epivir* and *Ziagen*, was approved in the US and Europe. This new once-a-day combination tablet will help to simplify treatment regimens for patients. We plan to register it across the developing world in 2005 once it has received a European Certificate of Pharmaceutical Product. *Telzir*, a new protease inhibitor, was approved in Europe in 2004 and is being registered in the developing world, where it will provide yet another treatment option.
- In September we signed a material transfer agreement with the International Partnership for Microbicides (IPM). Under the agreement, GSK's HIV drug candidates will be tested for use in microbicides to prevent transmission of HIV and help women reduce their vulnerability to HIV infection during sexual intercourse.
- Phase II clinical trials of our CCR5 antagonist, a new class of AIDS therapy, produced positive data. The therapy will now be tested in further clinical studies. If trials are successful the therapy may benefit people living with HIV who have developed viral resistance to existing HIV treatments.
- Proof of concept trials and drug interaction studies are underway for two additional HIV/AIDS compounds, a protease inhibitor (PI) and non-nucleoside reverse transcriptase inhibitor (NNRTI), and results are expected to be reported in 2005.
- GSK is supporting clinical trials that are sponsored by external organisations - such as the WHO, the UK's Medical Research Council and US National Institutes of Health (NIH) - through our HIV-collaborative research programme for resource-poor settings. Twenty trials are currently underway mainly focussing on public health-related issues and involving more than 13,000 patients in the developing world.
- Phase I clinical trials on our most advanced HIV vaccine candidate continued in 2004 with no major milestones to report.

TB

- GSK and Corixa, a US pharmaceutical company, began phase I clinical trials of a new vaccine for tuberculosis in 2004. This is the first study of this vaccine candidate to be conducted in humans.
- During 2004 GSK continued to screen compounds for possible use as new classes of anti-TB drugs against enzymatic targets of *Mycobacterium tuberculosis* and *M. tuberculosis* whole cells. Should our search be successful the leads identified from screening will be progressed to candidates for development.

Rotavirus

- Our rotavirus vaccine, *Rotarix*, for the prevention of gastroenteritis, was launched in Mexico in January 2005. Rotavirus infection is the leading cause of severe diarrhoea and vomiting (gastroenteritis) in children under two and kills around 600,000 children each year - one child every minute - mostly in developing countries. *Rotarix* was tested in the largest phase III clinical trial ever performed for a vaccine, involving over 60,000 children. We are now seeking regulatory approval for the vaccine in other developing countries.

Cervical Cancer

- Clinical trials of our cervical cancer vaccine, *Cervarix*, produced positive results. Cervical cancer is the number one cause of cancer deaths in women in the developing world. Current studies suggest *Cervarix* could reduce by 70% a woman's lifetime risk of developing cervical cancer. We hope to launch the vaccine in Europe and our International region during 2007.

Leishmaniasis

- GSK is developing sitamaquine, a new oral treatment for visceral leishmaniasis which affects at least half a million people a year in the developing world and is usually fatal if untreated. A new treatment for leishmaniasis is urgently needed since current medicines are either impractical or becoming ineffective due to drug resistance. Sitamaquine has shown good efficacy in phase II studies and clinical development is ongoing.

Preferential Pricing

To learn more about preferential pricing visit our website

There are many barriers to healthcare in developing countries. Most significantly, poverty, and a lack of political will, have led to a lack of medical infrastructure – hospitals, clinics and medical professionals – that prevents poor people accessing the healthcare they need.

The affordability of medicines is also important and there are two elements to this. First is the ability of governments or patients to pay for medicines. Solving this problem will require developed country governments and inter-governmental agencies to make significant additional financial resources available to developing countries.

The second element is the price at which medicines are sold, an area GSK can help to address. We are making key medicines available to developing countries at more affordable prices and in sufficient quantities for as long as they are required. This is a major commitment that we call 'preferential pricing'.

All our AIDS and malaria treatments are available at not-for-profit prices to public sector customers and not-for-profit organisations in over 100 developing countries, including all the countries covered by the US President's Emergency Plan for AIDS Relief (PEPFAR). [Link to eligibility criteria and How to Guide] Our prices are sustainable – we do not make a profit on them, but we do cover our manufacturing and distribution costs. Therefore we can sustain supply of these products for as long as they are needed.

We aim to reduce not-for-profit prices for our ARVs and anti-malarial medicines whenever improvements in manufacturing, or economies of scale, allow. For example, *Combivir*, one of our key ARVs, is now available at \$0.65 a day, compared with \$1.70 in April 2003. This equates to around \$237 per patient per year and includes delivery costs, which compares favourably with generic tablets. The February 2005 pricing report by *Medecins Sans Frontieres* shows that the average cost of generic equivalents is \$0.75 a day and the lowest priced generic equivalent costs \$0.55 a day.

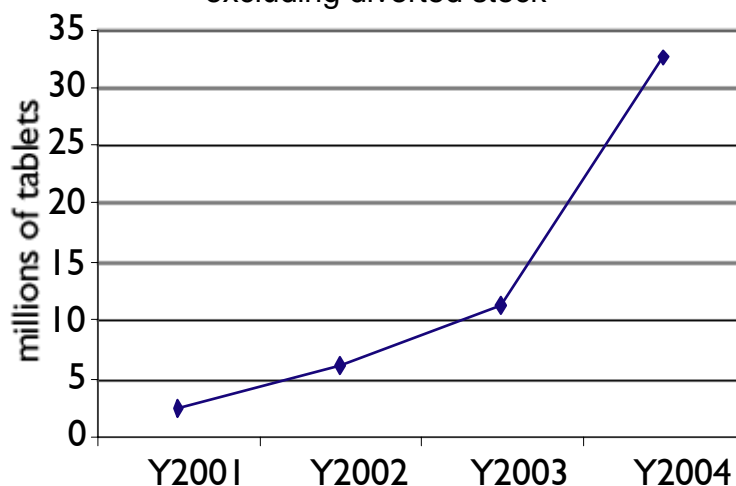
In addition, we negotiate public sector prices with middle-income developing countries on a case-by-case basis. These combine a viable and sustainable commercial return for GSK with increased affordability for the healthcare systems concerned.

GSK vaccines are also available at preferential prices. Here we work with multinational organisations such as UNICEF, the World Health Organisation and the Pan American Health Organisation, governments and non-governmental organisations, to provide appropriate and affordable vaccines for the developing world.

Progress in 2004

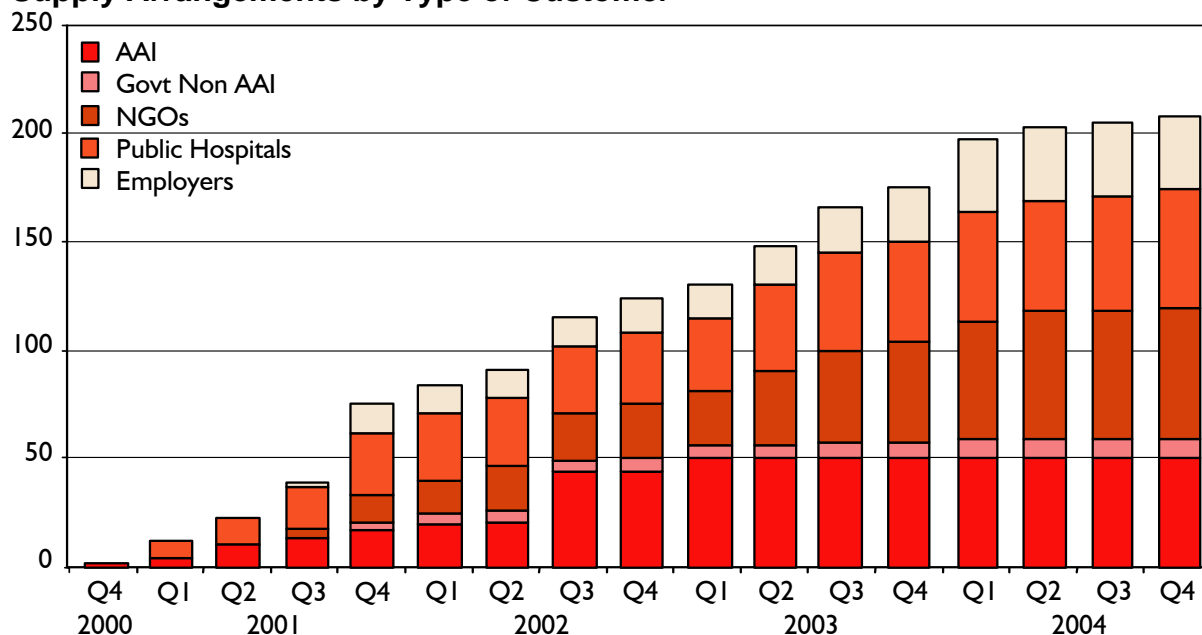
- In 2004 we shipped 32.7 million preferentially-priced *Combivir* tablets to the developing world, with over 80% of these going to Africa. This is nearly three times the 11 million tablets shipped in 2003. We do not routinely collect data for our other preferentially-priced medicines but a similar increase has been experienced for *Epivir*, another of our ARVs. Overall shipments are still low given the scale of the AIDS epidemic in Africa but the growth is encouraging. More doctors, hospitals and clinics are needed to treat more patients and ensure better take up of preferentially priced medicines.

Shipments of preferentially priced Combivir
excluding diverted stock



- It is difficult to estimate the number of patients treated as a result of our preferential pricing agreements, since GSK does not control healthcare provision. A report from the UN-led Accelerating Access Initiative (AAI), suggests that by September 2004 more than 333,000 patients in developing countries were receiving ARV treatments supplied by the seven pharmaceutical companies in the AAI. This includes 157,500 patients in Africa, a 50% increase since September 2003. For more on GSK's work with the AAI see Accelerating Access Initiative in the website.
- At the end of 2004 we had 208 arrangements to supply preferentially-priced ARVs in 57 countries. This includes 30 agreements with private employers.
- We added new supply agreements with a number of middle-income countries during 2004. These include an agreement with the Chinese Ministry of Health for preferentially priced *Epivir* tablets to support China's national HIV treatment programme, and a number of arrangements in Central and Eastern Europe.
- We are also introducing discount cards for senior citizens in several middle-income countries, see Developed Countries in this report.

Supply Arrangements by Type of Customer



- Product diversion, where not-for-profit medicines are illegally shipped back for sale in wealthier countries, undermines our ability to provide not-for-profit prices and denies treatment to the intended patients in poorer countries. We can only afford to supply products at low prices in the world's poorest countries if we can still make an adequate return on them in wealthier markets. We have introduced different packaging and tablet colours for many of our not-for-profit medicines to help prevent product diversion. Special tri-lingual 'access packs' are now approved for *Combivir*, *Epivir* and *Trizivir* in over 50 countries, and we are now receiving regulatory approvals for the red *Epivir* and *Combivir* tablets. GSK has nine ARVs registered under the EU's Anti-Diversion Regulation. We are the only company to have registered products under this Regulation.
- We have set up five pilot projects in collaboration with NGOs in Tanzania, Uganda, Nigeria, Zambia and Malawi to assess the impact of extending preferential pricing to a wider range of products. Initial results show that lack of healthcare capacity and infrastructure are major barriers. When capacity (for example the number of healthcare professionals) or funding is improved there is an increase in take up of preferentially-priced medicines. For example two of the pilot sites have received funding from the US President's Emergency Plan for AIDS Relief for the treatment of opportunistic infections. This has led to an increase in orders for antibiotics. A report on the findings from the pilots will be prepared at the end of 2005.

Eligibility for Not-for-Profit Prices

Our not-for-profit prices are available in over 100 countries. This includes all the Least Developed Countries (LDCs) and all of sub-Saharan Africa (SSA) – a total of 64 countries. In addition, all private employers in sub-Saharan Africa who provide care and treatment to their uninsured staff can purchase our ARVs at not-for-profit prices. The not-for-profit prices are also offered to all projects fully funded by the Global Fund and the 15 countries covered by the US President's Emergency Plan for AIDS Relief (PEPFAR).

We offer these prices where we believe the need is greatest. This is to governments, NGOs and agencies that are providing treatment on a not-for-profit basis in the poorest and worst affected countries. We also seek not-for-profit arrangements with individual countries to facilitate access for core public employees such as teachers, nurses, police and fire-fighters who are not covered by private health insurance schemes.

We negotiate prices with the private health sector on a case-by-case basis. We depend on revenues from sales to the private market to maintain a local presence and much-needed infrastructure in developing countries. Without this local capacity we would be unable to provide essential services such as training healthcare workers to use our products, product support, safety monitoring and registration and launch of new products.

Voluntary Licensing and Partnerships

Learn more about voluntary licensing in the website

Learn more about partnerships in the website

We want to play an active role in addressing the healthcare crisis in developing countries. We believe preferential pricing arrangements are the best way to do this because we are able to ensure delivery of a safe, quality product at an affordable price for as long as it is needed. This is where we focus our efforts. But in some situations partnerships and voluntary licences may also help to increase the supply of medicines.

Voluntary Licences

Voluntary licences (VL) enable local manufacturers to produce and sell generic versions of our products. GSK has granted six VLs for our antiretrovirals (ARVs) in Africa where HIV/AIDS is having a devastating impact. This is a creative response to a unique situation.

A decision to grant a VL depends on a number of factors including the severity of the HIV/AIDS epidemic in that country, local healthcare provision and the economic and manufacturing environment. VLs are not a universal solution to HIV/AIDS but a specific response to a particular set of circumstances.

We discuss VLs with potential partners on a case-by-case basis. Selecting the most appropriate licensees is key. We need to be sure that the manufacturer will be able to provide a long-term supply of good-quality medicines and will implement safeguards to prevent the diversion of medicines to wealthier markets. (See Preferential Pricing in the website).

We do not seek to prevent voluntary licence holders from combining the active ingredients they have licensed from us with other licensed active ingredients to produce Fixed Dose Combinations. They can also use the US Food and Drug Administration's fast track approval process for ARVs to accelerate the availability of generic ARVs for PEPFAR programmes in Africa.

There has been much discussion about the use of compulsory licences, under which intellectual property rights are taken away from rights holders. Compulsory licenses are one of the flexibilities in the World Trade Organisation's TRIPs agreement on intellectual property, which can be used for humanitarian purposes. However, widespread use of compulsory licences will undermine the intellectual property framework and be counter-productive in the long term. R&D into new treatments, especially where commercial markets exist, such as for HIV/AIDS, depends on protection for intellectual property.

Progress in 2004

- GSK granted five VLs in 2004, four in South Africa and one in Kenya.
- We have now granted a total of five VLs to South African generics companies for the sale of some of our antiretrovirals² to public and private sector customers in South Africa. Three of these VLs also include rights to sell in other countries in sub-Saharan Africa.
- In 2004 we granted a similar VL to Cosmos, a Kenyan pharmaceutical company, for manufacture and sale in Kenya and other countries in East Africa.

Partnerships

HIV treatment is complex, often requiring patients to take a combination of different tablets at different times of the day. This increases the risk of patients missing a dose or taking their medicine at the wrong time, which can reduce the effectiveness of treatment.

In July 2004, GSK and Boehringer Ingelheim (BI) agreed to assess the development of co-packaging for *Combivir* and *Viramune* (BI's HIV treatment sometimes used in conjunction with GSK ARVs) for use in developing countries. Given the complexities of HIV treatment, we recognise the need for multiple treatment options and support efforts to simplify treatment regimens. Aspen Pharmacare is developing the combined pack through the voluntary licences granted by both GSK and BI.

² lamivudine, zidovudine, and the combination containing lamivudine and zidovudine.

Developed World

Learn more about Patient Assistance Programs in the website

Access to medicines is not just an issue for the developing world. Even in developed countries some patients cannot afford the medicines they need. This is a particular problem in the US where many people do not have health insurance. GSK has developed Patient Assistance Programs and discount cards in the US to help patients without insurance.

We are also introducing discount cards in several middle-income countries to enable qualifying patients to obtain prescription medicines at a discount price

Programmes in the US

Patient Assistance Programs provide prescription medicines to low-income, uninsured patients free or at minimal cost. GSK operates two Patient Assistance Programs. Commitment to Access covers cancer treatments; Bridges to Access covers other medicines for outpatients. Patients are registered through one phone call from a patient advocate and receive medicine at their local pharmacy or by mail order. In 2004, 475,000 patients received GSK medicines worth \$372.5 million through these programs (based on the wholesale acquisition cost (WAC) of these medicines).

GSK was the first pharmaceutical company in the US to offer a card providing savings on medicines to low-income senior citizens and disabled people. Known as the *Orange Card* this enables these people to buy GSK outpatient prescription medicines at a discount. Introduced in 2001, the *Orange Card* provides savings of up to 40%. In 2004, 37,319 patients, received 73,740 prescriptions. This resulted in WAC savings of \$2.9 million for patients.

In 2002, GSK and six other pharmaceutical companies established the *Together Rx* card which provides discounts on over 155 prescription medicines for low-income senior citizens who are eligible for Medicare. In 2004, over 190,000 patients received 683,364 GSK medicines through this programme, saving \$12.3 million (based on WAC).

In January 2005, GSK and nine other pharmaceutical companies created a new card to improve access to medicines for other uninsured Americans, not just seniors. The *Together Rx Access* card provides savings of 25-40% on more than 275 medicines. Approximately 36 million people, around 80% of uninsured people in the US, are eligible to enrol.

We also offer discounts on our prescription medicines through cards launched by the Centers for Medicare & Medicaid Services, a US government agency, in 2004.

Orange Cards in Middle Income Countries

During 2004 we introduced *Orange Cards* providing discounts on certain GSK prescription medicines for eligible patients in Bulgaria, Lithuania, and Ukraine.

The nature of the discounts varies between countries, depending on the needs of the patient and the way in which the healthcare system operates.

Our *Orange Card* in the Ukraine gives all asthma and chronic obstructive pulmonary disease patients who are under 25 or over 50, an average discount of 19% on GSK's *Seretide* asthma medicine. Asthma patients of any age who suffer disabilities or who are affected by the Chernobyl nuclear disaster are also eligible. Eligibility is assessed by the patient's doctor and patients can receive the medicine at participating pharmacies. A hotline number has been set up to help patients find their nearest pharmacy, and so far 1,100 patients are enrolled.

In Lithuania, patients must pay towards the costs of their medicines. This is known as patient co-payment. Our *Orange Card* gives senior citizens an average discount of 40% on the patient co-payment on all GSK prescription medicines. By February 2005 more than 3,500 patients had applied for an *Orange Card* and 107 pharmacies had registered to participate. (see *Improving Access to Medicine in Lithuania case study*)

A GSK *Orange Card* was also introduced in Bulgaria in May 2004 for low-income patients with chronic diseases such as asthma, chronic obstructive pulmonary disease and diabetes. Card holders receive an average 35% discount on four GSK prescription medicines, and over 16,000 patients have registered so far.

Summary of GSK Discount Programmes

Country	GSK programme	Number of patients	Value of benefit to patients
US	Patient Assistance Programmes - Free or minimal cost medicines for low-income, uninsured patients.	475,000 received prescriptions	\$372.5 million
US	Orange Card - Discounts for low income senior citizens and disabled people.	37,000 received prescriptions	\$2.9 million
US	Together Rx - Discounts for low income senior citizens. Joint industry programme.	190,000 received prescriptions	\$12.3 million
US	Together Rx Access - Discounts for all low-income uninsured patients. Joint industry programme.	N/a	Launched in 2004
Bulgaria	Orange Card - Discounts for low-income patients with chronic diseases.	16,000 enrolled	Launched in 2004
Lithuania	Orange Card - Discounts for senior citizens.	3,500 enrolled	Launched in 2004
Ukraine	Orange Card - Discounts on asthma medicine for patients under 25 or over 50.	1,100 enrolled	Launched in 2004