Patient safety and product security

The safety of the patients who take our medicines is of fundamental importance to us. All drugs have potential side effects and our aim is to minimise the risks and maximise the benefits of each of our medicines. We also take extremely seriously the counterfeiting of medicines as this illegal trade poses a serious and global risk to patient safety.

Our approach

From the discovery of a potential new medicine and continuing throughout its development, launch and marketing we work to ensure that we become aware of any risks to patient safety such as side effects or cases of product counterfeiting.

During the development phase, extensive and rigorous pre-clinical and clinical testing is done to establish a potential new medicine’s safety and efficacy. For some studies, we use independent external safety data-monitoring boards to further strengthen the safety evaluation process. Once we establish an acceptable benefit and risk profile, we submit comprehensive information, including clinical trial data, to the regulatory authorities responsible for approving medicines in each country or region in which we want to launch the product.

Clinical trials cannot replicate the complete range of patient circumstances that exist among larger and more diverse patient populations. Rare side effects can often be identified only after a medicine has been launched and used in far greater numbers of patients and over longer periods of time. Therefore, pharmacovigilance, the practice of monitoring the effects of medical drugs after they have been licensed for use, is a responsibility to our patients that we take very seriously.

Product counterfeiting (an illegal activity) is also a serious patient safety concern as counterfeit medicines often fail to provide effective treatment and sometimes cause direct harm to patients. It is impossible to estimate on a global scale how common counterfeiting is due to its nature. It is not possible to know, for example, how many counterfeit medicines go undetected. Counterfeits can be found for all types of medicines, both branded and generic, and in all regions throughout the globe. Although the scale, complexity and covert nature of counterfeiting activity mean it is impossible to prevent entirely, we aim to protect patients by: disrupting counterfeiting networks and operations; and making it as difficult as possible for people to counterfeit our products.
Patient safety

Our Chief Medical Officer has overall accountability for the benefit and risk profiles of the products we have in development and those on the market. He and the Head of Global Regulatory Affairs, Patient Safety and Quality Assurance are supported by a dedicated patient safety function that monitors the safety of our investigational products and marketed medicines, and maintains our patient safety systems.

Building a culture of accountability

Our Code of Conduct requires all AstraZeneca employees to report any possible adverse effects relating to our medicines within 24 hours through our established procedures.

Our safety standards are global and apply in all countries where we operate. We audit our patient safety systems regularly to make sure our policies and standards are being implemented. Audits of the pharmacovigilance systems within our marketing companies are done on a risk-based approach. In some countries, particularly emerging markets, national systems for safety reporting are not yet well-established and doctors, regulators and others are less likely to report potential safety issues. As our business expands in these markets, we are working with regulators to improve safety reporting.

Patient safety risk management plans

We develop patient safety risk management plans for our medicines to help us identify and reduce risks to patients and, where appropriate, we provide these to the regulatory authorities as part of our submission for approval to market a new medicine.

Plans are reviewed regularly and updated with new safety information as our knowledge of the medicine’s safety profile evolves. Our global patient safety database is the central source of information for those responsible for patient safety across our organisation, and for reporting to regulatory authorities.

Patient safety risk management plans

Each plan has three parts:

Safety specification

Information on all known risks and side effects associated with the medicine. This includes potential side effects where more research is needed to establish or refute a link to the product. We also highlight missing information. For example, the medicine may not have been studied in certain patient groups such as children.

Pharmacovigilance plan

The activities we are going to undertake to confirm or refute potential risks or to fill in missing information. For example, plans to carry out further research studies.

Risk minimisation activities

All plans include routine risk management activities such as product labelling and safety monitoring. For some medicines with potentially more serious side effects we may need to take further steps. For example, we may run an awareness campaign to educate doctors or restrict the groups of patients who may receive the medicine.
Clear patient communication

A vital aspect of our commitment to patient safety is making sure that accurate and up-to-date information is provided to support effective use of our medicines. During the new medicine approval process, we work with regulators to develop prescribing information that provides healthcare professionals with the benefit and risk information they need to make appropriate prescribing decisions. This information includes indications for use, dosing recommendations, warnings and contra-indications, as well as what side effects might be experienced. We also make information available directly to patients, as appropriate, about our medicines and how they should be taken.

We continue to provide information throughout a medicine’s life. We have comprehensive and rigorous systems in place for detecting and rapidly evaluating adverse effects, including mechanisms for highlighting those that require immediate attention. We work to ensure that any new safety data that becomes available through our continuous monitoring processes is provided to regulators, doctors, other healthcare professionals and, where appropriate, patients.

If, as a result of our monitoring, we find a new side effect, the actions we take may include carrying out further clinical trials, modifying the prescribing information, and communicating with healthcare professionals and others. In some situations it may be appropriate to stop a clinical trial or withdraw a medicine from the market.

We also provide updates to regulators on the safety of our medicines on more serious safety issues as they arise or through periodic safety update reports. This is governed by local regulation and the frequency depends on the country and how long the medicine has been marketed in that country. For example, in the US, safety reports are required every three months for the first three years. In Europe, reports are required every six months for the first two years. We are fully compliant with the new pharmacovigilance legislation in Europe and have implemented the format for safety updates through submission of Periodic Benefit Risk Evaluation Reports.

If further research confirms a link to our medicine, we will update the product label and prescribing information to include warnings on the side effect or act to restrict the use of the medicine to certain patient groups. We use journal articles and our sales representatives to make sure doctors are aware of the change.

If we identify a very serious potential side effect, we may tell doctors about it before we have confirmed a definite link to our medicine. We use emails and letters sent directly to all doctors who may prescribe the product. Other channels could include advertisements in newspapers, radio and television. We work closely with national regulatory agencies and their networks, and in the most serious cases, we may withdraw the product from the market.
Product security

Our Global Product Security strategy aims to protect our patients from the dangers of counterfeit and illegally traded medicines by focusing on three key areas:

- **Building strong, collaborative partnerships**
  to strengthen enforcement, raise awareness and provide advocacy to increase the effectiveness and efficiency of regulation in this area.

- **Working in enforcement**
  to combat illegal activity through reporting and professional investigation of suspicions.

- **Securing our products**
  through the introduction of pack features and enhanced integrity of the end-to-end supply chain.

Our Anti-Counterfeiting and Illegal Trade Standard for Supply Chain Partners requires our partners to take the necessary steps to ensure the authenticity of the product through the supply chain. It also identifies the actions to be taken by AstraZeneca when a supply chain partner has been involved in counterfeiting or illegal trade, either knowingly or through lack of adequate controls.

Our Code of Conduct also requires all AstraZeneca employees to report suspicions of possible illegal trade of medicines that come to their attention.

**How our anti-counterfeiting strategy works**

The counterfeiting of medicines is not a problem AstraZeneca can tackle alone. We work closely with other pharmaceutical companies through, for example, industry trade associations (IFPMA, EFPIA and PhRMA) and coalitions EAASM (European Alliance for Access to Safe Medicines) and ASOP-EU (Alliance for Safe Online Pharmacy – Europe), to raise awareness of the threat of counterfeit medicines.

One such initiative to help raise awareness among patients, healthcare professionals and regulators is the IFPMA ‘Fight the Fakes’ campaign and their ‘False Friends’ video.

Our Global Security investigators are responsible for the enforcement activities for AstraZeneca and work closely with law enforcement agencies, Interpol and Customs to dismantle counterfeiting operations/networks.

In addition, Global Security works closely with other pharmaceutical companies through the Pharmaceutical Security Institute, a not-for-profit organisation, to identify cases of counterfeiting and coordinate investigations.

As there is no global law enforcement agency or regulator, pharmaceutical companies like AstraZeneca can often act as an interface between authorities in different countries. Investigations conducted by Global Security helped secure the arrest of over 100 people involved in illegal activities in the Asia Pacific and Latin America regions alone in 2014. After a counterfeiting incident in Latin America, our Global Security investigation led to law enforcement dismantling an entire organised crime gang.

**100 arrests**

Our investigations helped secure the arrest of over 100 people involved in illegal activities in Asia Pacific and Latin America.
Security along our value chain
We include security features on our packs to enable us to distinguish legitimate products from counterfeits. We also work to improve security in our supply chains (bespoke product security audits, collaborating with others to share best practice and supply chain integrity principles for supply chain design) to inhibit the entry of counterfeit medicines. This includes:

- Strengthening our due diligence processes for third parties and adding product security clauses in our contracts with supply chain partners
- Training our third parties to report any suspicions and to maintain secure distribution channels
- Using seals and/or unique identification numbers (a serial number) on some packs to make it more difficult and expensive for counterfeiters to copy our packaging, and help identify packs that have been tampered with. Applying serial numbers to packs is now becoming a legislative requirement in some markets as governments recognise this as part of their anti-counterfeiting strategy.

Finding and investigating counterfeit medicines
We find counterfeits through the work of our Global Security investigators, by monitoring internet pharmacies, via reports from sales representatives, customs, other law enforcement agencies, healthcare professionals, patients and others. Our Global Security investigators gather the evidence needed for a prosecution and pass this to relevant local law enforcement agencies, for example.

The work of the Global Security investigators is recorded and fully auditable, and complies with globally acceptable standards of ethics and human rights. Our Global Security investigators have also been asked to act as witnesses during court cases, helping to secure convictions.

We analyse suspect counterfeit samples and if the samples are found to be counterfeit, our global team works with our local markets to report counterfeit medicine cases to the relevant health authority. We will agree with our local market/health authority any local action; for example, we may alert doctors, pharmacists or wholesalers via letters or other channels. We rely on their cooperation and the local health authority to stop counterfeit medicines from reaching patients.

We will vigorously pursue anyone who makes, distributes or sells counterfeit versions of our products and seek prosecution of offenders to the fullest extent of the law.

Driving greater protection
As counterfeiting is an illegal activity and therefore hard to measure, we do not publish performance targets around our anti-counterfeiting work. However, we continue to make positive progress on all three areas of our strategy.

As an industry, there has been a lot of progress in terms of raising awareness of the dangers of counterfeit medicines, including the dangers of buying medicines online, but there is more work still to be done. While the counterfeiting of any product is illegal, we need to ensure that patients recognise the potentially life-threatening risks specifically associated with counterfeit medicines.

We are also encouraging regulators to address the issue by enacting legislation that will better protect patient safety and by ensuring that the sentencing of those convicted of producing and distributing counterfeit medicines reflects the seriousness of the crime.