

GASTROINTESTINAL (GI) MEDICINES

MARKETED PRODUCTS

Nexium (esomeprazole) is the first proton pump inhibitor (PPI) for the treatment of acid-related diseases to offer clinical improvements over other PPIs and other treatments.

Losec/Prilosec (omeprazole) was the first PPI, and is used for the short-term and long-term treatment of acid-related diseases.

Entocort (budesonide) is a locally acting corticosteroid for the treatment of inflammatory bowel disease (IBD) with better tolerability than other corticosteroids and greater efficacy than aminosalicyclic acid medicines.

2007 IN BRIEF

- > **Sales of Nexium down 2% to \$5.2 billion.**
- > **Losec/Prilosec sales of over \$1 billion with sales growth in Japan and China. Overall sales down 20%.**
- > **European Patent Office rulings that the European process patent for Nexium and the European patent for the Multiple Unit Pellet (MUPS) formulations of Losec and Nexium, which expire in 2015, are valid in amended form.**
- > **Patent litigation continuing in the US against generic manufacturers following abbreviated new drug applications relating to Nexium.**

PERFORMANCE

	2007			2006			2005	2007 compared to 2006		2006 compared to 2005	
	Sales \$m	Growth underlying \$m	exchange effects \$m	Sales \$m	Growth underlying \$m	exchange effects \$m		Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
<i>Nexium</i>	5,216	(104)	138	5,182	555	(6)	4,633	(2)	1	12	12
<i>Losec/Prilosec</i>	1,143	(277)	49	1,371	(266)	(15)	1,652	(20)	(17)	(16)	(17)
Other	84	2	4	78	8	-	70	3	8	11	11
Total	6,443	(379)	191	6,631	297	(21)	6,355	(6)	(3)	4	4

PIPELINE

Compound	Mechanism	Areas under investigation	Phase			Estimated filing date		
			I	II	III	Europe	US	
NCEs								
AZD3355	inhibitor of transient lower oesophageal sphincter relaxations (TLESR)	GERD	■	■			2011	2011
AZD2066	metabotropic glutamate receptors subtype 5	GERD		■				
AZD1386	vanilloid receptor 1 antagonist	GERD		■				
Line extensions								
<i>Nexium</i>	proton pump inhibitor	peptic ulcer bleeding	■	■	■		2Q 2008	2Q 2008
<i>Nexium</i> sachet formulation	proton pump inhibitor	GERD	■	■	■		Approved ¹	Launched
<i>Nexium</i> low dose aspirin combination	proton pump inhibitor	low dose aspirin associated peptic ulcer	■	■	■			1H 2009
<i>Nexium</i>	proton pump inhibitor	extra-oesophageal reflux disease	■	■			2H 2009 ²	2H 2009 ²

¹ Approved by EU reference member state, mutual recognition procedure ongoing.

² Project Extraesophageal reflux disease (reflux asthma) will be completed but will not result in a regulatory filing.

For discontinued projects see page 30.

GASTROINTESTINAL (GI) MEDICINES CONTINUED

WE AIM TO DEVELOP OUR LEADING POSITION IN GI TREATMENTS BY FOCUSING ON LIFE CYCLE INITIATIVES FOR NEXIUM TO GAIN FURTHER MARKET PENETRATION BY BROADENING ITS USE, COUPLED WITH INNOVATIVE RESEARCH AND DEVELOPMENT OF NEW THERAPIES FOR GASTRO-OESOPHAGEAL REFLUX DISEASE (GERD).

PRODUCTS

Nexium, for the treatment of acid-related diseases such as gastro-oesophageal reflux disease (GERD), was first launched in Sweden in August 2000 and is now available in approximately 100 markets, including the US, Canada and all EU countries. It has been generally well received by patients and physicians alike and close to 746 million patient treatments were administered by the end of 2007. *Nexium* has been evaluated in clinical studies involving around 85,000 patients in over 62 countries and offers very effective acid inhibition.

GERD is a common disease that affects patients' daily lives. In the treatment of reflux oesophagitis, *Nexium* provides healing in more patients than *Losec/Prilosec*, lansoprazole or pantoprazole. It is an effective, long-term therapy for patients with GERD, with or without oesophagitis (in the US, the long-term indication is only for patients with GERD with oesophagitis). For the treatment of active peptic ulcer disease, seven-day *Nexium* triple therapy (in combination with two antibiotics for the eradication of *H.pylori*) heals most patients without the need for follow-up anti-secretory therapy.

Nexium is approved for the treatment of children aged 12 to 17 years with GERD in both the US and the EU. During 2007, *Nexium* was also approved for the age group one to 11 years in Canada and Sweden, and an approvable letter for this group was received in the US. *Nexium* is approved in the US, the EU, Canada and Australia for the treatment of patients with the rare gastric disorder, Zollinger-Ellison syndrome.

Nexium is approved in Europe for the healing and prevention of ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy. In the US, *Nexium* is approved for the reduction in the risk of gastric ulcers associated with continuous NSAID therapy in patients at risk of developing gastric ulcers. Trials are continuing to further evaluate a combination of *Nexium* and low-dose acetylsalicylic acid (ASA, for example Aspirin™) in patients at risk from low-dose ASA-associated peptic ulcers. These patients need to stay on low-dose ASA for CV protection but also need protection from the risk of developing peptic ulcer (due to the ulcerative properties of ASA).

The parenteral form of *Nexium*, which is used when oral administration is not applicable for the treatment of GERD and upper GI side effects induced by NSAIDs, is approved in 86 countries including the US and all EU countries. A continuing study of *Nexium* for the treatment of patients with peptic ulcer bleed will be finalised during 2008.

The US Food and Drug Administration (FDA) made a public announcement in August 2007 about differences in cardiac event rates reported from two small, non-blinded, long-term, clinical studies in patients with GERD, comparing anti-reflux surgery with either omeprazole or *Nexium* treatment. The announcement was in response to a communication sent to all health authorities by us in May 2007. After further assessment, the FDA issued its final assessment of the two studies in December 2007, which stated that the "FDA continues to believe that long-term use of omeprazole or esomeprazole is not likely to be associated with an increased risk of heart problems and recommends that healthcare providers continue to prescribe and patients continue to use these products in the manner described in the labelling for the two products".

In December 2006, the European Patent Office (EPO) ruled that one of the European substance patents for *Nexium* would be rejected following an appeal from the German generic manufacturer, ratiopharm GmbH. The original expiry date for this patent was 2014. Although disappointed with the EPO decision, we continue to have full confidence in the intellectual property portfolio protecting *Nexium*. This portfolio includes process, formulation, method of use and additional substance patents with expiration dates ranging from 2009 to 2018. In October 2007, the EPO Opposition Division ruled that the European process patent for *Nexium* is valid in amended form, in response to opposition proceedings commenced by ratiopharm. In January 2008, ratiopharm filed a notice of appeal against this decision. In November 2007, the EPO Opposition Division ruled that a European patent for the multiple unit pellet (MUPS) formulations of *Losec* and *Nexium* is valid in amended form, in response to opposition proceedings from generic manufacturers. Both the process patent and the MUPS patent expire in 2015. In addition to these patents, *Nexium* has data exclusivity valid until 2010 in most major European markets.

In the US, we are continuing to pursue patent litigation against various generic manufacturers who have filed abbreviated new drug applications (ANDAs) and are seeking to market esomeprazole magnesium products before the expiration of certain of our patents relating to *Nexium*.

During 2007, we received additional notices that ANDAs had been filed by generic drug manufacturers in respect of 20 and 40mg delayed-release esomeprazole magnesium capsules. Details of these ANDA filings and of continuing litigation are set out in Note 27 to the Financial Statements on page 158.

The rejection of our European substance patent relating to *Nexium* should not have any substantive impact on our ability to uphold and enforce our *Nexium* patents in the US. We have several US patents covering *Nexium*, all of which can be differentiated from the rejected European patent. As a result of the expiration of 30-month stays during which the FDA may not approve ANDAs, an 'at risk' launch by a generic drug manufacturer of 20 and/or 40mg delayed-release esomeprazole magnesium capsules may occur in the US in 2008.

We continue to have full confidence in our intellectual property protecting *Nexium* and will vigorously defend and enforce it.

Patients have benefited from over 889 million treatments with *Losec/Prilosec* (up to the end of October 2007) since its launch in 1988. Continued sales growth of *Losec/Omepral* was seen in Japan in 2007. Patent protection for omeprazole, the active ingredient in *Losec/Prilosec*, has expired (the first patent expiration was in Germany in 1999). We continue to maintain formulation patent property in respect of *Losec/Prilosec*. Further information about the status of omeprazole patents and patent litigation, including details of generic omeprazole launches, is set out in Note 27 to the Financial Statements on page 158.

Our appeal to the European Court of First Instance regarding the European Commission's Decision in 2005 to impose fines on us totalling €60 million (\$75 million) for alleged infringements of European competition law relating to certain omeprazole intellectual property and regulatory rights is still pending. Further information about this case is set out in Note 27 to the Financial Statements on page 158.

Entocort is increasingly accepted as first-line therapy for mild to moderate, active Crohn's disease and is approved in 44 countries.

PIPELINE

Our pipeline includes life cycle management initiatives for approved products mentioned above, as well as development compounds. Our focus is on developing novel approaches to treating GERD by inhibition of reflux with or without concomitant treatment of gastro-oesophageal hypersensitivity. During 2007, AZD3355, which inhibits transient lower oesophageal sphincter relaxations, was tested in patients with GERD and showed positive effects in a phase IIa study. The development of AZD3355 in phase II is progressing.

PERFORMANCE 2007

Reported performance

Gastrointestinal sales fell by 3% to \$6,443 million in 2007 from \$6,631 million in the previous year.

Underlying performance

After excluding the effects of exchange, gastrointestinal sales fell by 6%. Worldwide, *Nexium* sales fell by 2% to \$5,216 million. In the US, *Nexium* sales for the full year were \$3,383 million, down 4%. Estimated volume growth was 2% for the year. *Nexium* market share in the branded segment of the PPI market increased by 1.5 percentage points in 2007; however, generic omeprazole's share of the prescription PPI market increased to 27.4% by December 2007, an increase of nearly 7 percentage points since December 2006. Realised prices declined by around 8% for the year. *Nexium* sales in other markets were up 2% for the full year to \$1,833 million, as growth in Emerging Markets more than offset the declines in Western Europe. We expect *Nexium* sales to be lower in 2008.

For the full year, *Losec* sales declined by 20% to \$1,143 million. *Prilosec* sales in the US were down 3% to \$226 million. *Losec* sales in other markets were down 24%, although sales increased in Japan and China; sales in these two markets now account for almost 30% of the brand's performance.

PERFORMANCE 2006

Reported performance

Gastrointestinal sales grew by 4% to \$6,631 million, up from \$6,355 million in 2005. The performance of *Nexium* (particularly in the US) more than compensated for the continued decline in *Losec/Prilosec* sales.

Underlying performance

After excluding the effects of exchange, GI sales grew by 4%.

In the US, *Nexium* sales increased by 13% to \$3,527 million. Dispensed tablet volume for *Nexium* increased by 17%; all other PPI class brands in aggregate declined by 4%. *Nexium* volume growth more than offset lower realised prices from contracted sales.

Sales of *Nexium* in other markets reached \$1,655 million for the full year (up 10%) as good volume growth in France and Italy helped mitigate the significant price erosion in Germany. As a result, Europe sales improved by 6% to \$1,166 million, whilst Asia Pacific revenues increased by 14% to \$195 million, driven by Japan and China.

Losec/Prilosec sales were down 16% to \$1,371 million. *Prilosec* sales were down 12% in the US and *Losec* sales in other markets were down 17%. Sales in Japan were up 7% at \$227 million, whilst sales in China were flat.