The Decline of use of Paroxetine in England

Introduction

Official drug statistics for England show that the use of paroxetine in England grew annually for the first 11 years since 1991 in spite of the increasing weight of scientific and clinical evidence that this drug does induce suicide in some and dependence in others. Annual consumption of all forms of paroxetine peaked in Q4 2001 it but Q4 2003 it had fallen by 25%. Some reasons for the growth in patient awareness and rejection of Seroxat are examined in this paper.

By chance this overall decline of use of paroxetine coincided with the lapse of the UK GSK patent in Q1 2002. In six months GSK had lost 94% of the supply of the 20mg tablets to the (unnamed) generic competitor in a market that was itself in a very steep decline. The transition between GSK and Generics for the 20 mg. tablet is shown in detail in appendix 1 and this raises some important questions. This study includes all paroxetine dose concentrations from both GSK and Generics. All results are for England, division by 0.82, the population factor gives UK figures.

The IMR model has been designed and developed to calculate the total flow of patients to and from any SSRI as a function of the amount of medication that is used. Hitherto it has always operated with huge consumption growth. In this study IMR has been used to model the considerable reduction of consumption of paroxetine in the last two years. The consequent reduction in patient numbers indicates that perhaps over 200 potential victims have been saved from induced suicide in the last two years.

It has taken some time to detect this decline in England due to the difficulty in obtaining the data. It could also be happening in the rest of the world where the data is even less available but mitigated only by the delay in international patient awareness of the officially denied dangers of SSRIs. However Ed Silverman (Newark Star Ledger) already reports a 10% drop in scripts for children since the February meeting with FDA in Washington…………

1.0 Paroxetine in England 1991 to 2003.

The study was carried out using quarterly consumption totals of each variant of the drug used in UK, 20mg, 30mg and liquid 10mg/5ml. Quarterly data increases the precision and enables possible patient awareness triggers like Panorama or MHRA admissions to be plotted or associated more exactly. Paroxetine (or any SSRI) consumption has to grow at a certain rate each year just to maintain the ever increasing population of dependants/addicts called Long Term Patients (LTP). New patients will only occur if there is any excess as happened from 1991 to 2001.

In 2001 new patients in England peaked at 339K, 682K patients were treated overall in that year, 207 suicides were induced, one of these was that of my wife, Rhona after just 11 days on Seroxat. However the small decline in consumption (c.f. Ed Silverman) from 2001 to 2002 reported in earlier IMR documents, before the 2003 data was available was in fact the start of an avalanche. The sum of the collective efforts by a few for so long began to take effect. Consumption fell in Q1 2002, held steady in Q2, fell again in Q3, then, in early Q4, "Secrets of Seroxat" by Panorama delivered a devastating exposure of Seroxat to an estimated audience of 5M. Paroxetine consumption went into a much steeper dive and has been diving without hesitation for the last 18 months (up to Q4 2003).

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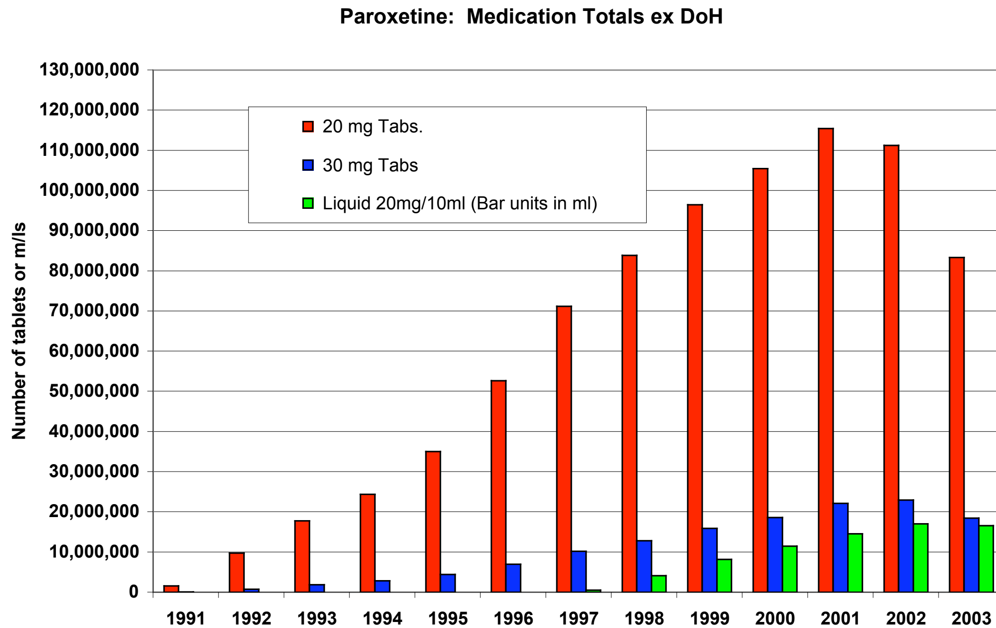
Perhaps the days are gone forever when paroxetine is handed out in ignorance by doctors for inappropriate conditions, when patients are neither aware nor warned of the real danger of induced suicide. It is earnestly hoped that what England does today the world will do tomorrow. Chart 1 below shows the decline in each dose variant.



2.0 Medication Units.

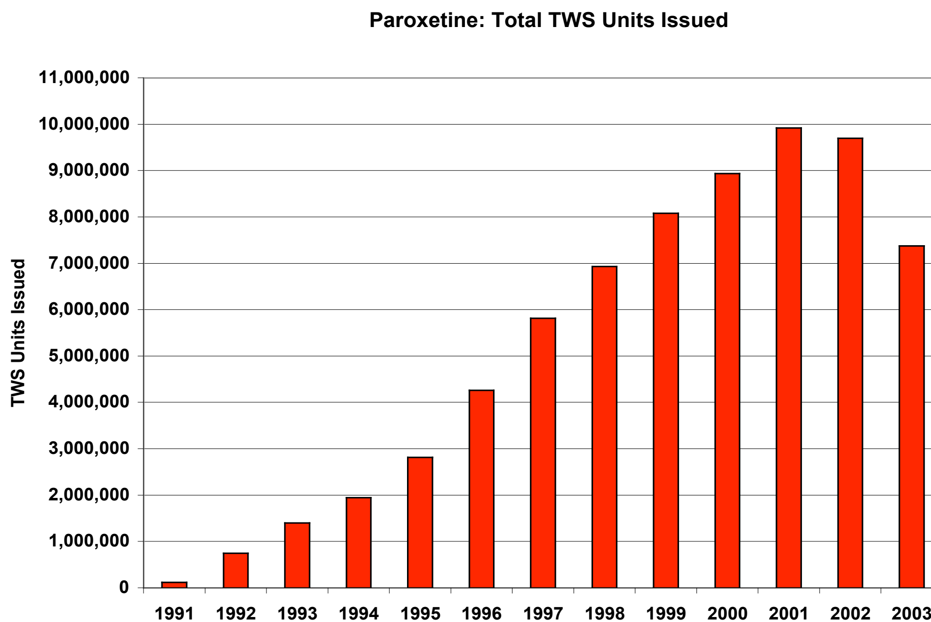


Chart 2 (above) shows the accumulation for paroxetine in England and illustrates the life saving decline in this ill validated drug

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IMR uses the common medication unit called TWS, (Two Weeks Supply), this enables the medication to be accumulated under one universal label regardless of form or concentration. Chart 2 was plotted using annual data, rather than quarterly data. It shows that the annual consumption of paroxetine in all its forms grew by more than 1.15 million units per year for 7 years up to 2001, then it fell by 2.7 M units i.e. 25% from 2001 to 2003. In fact this decline is much worse if the higher precision quarterly data is used; from the peak at Q4 2001 to Q4 2003 the fall was 36%. Annual totals can disguise higher rates of change defined by the quarters within the years (frequently exploited in financial marketing.)

3.0 Individual Medication.

3.1 30 mg Tabs and Liquid 10mg/5ml

Chart 3 below shows the growth and decline of paroxetine 30 mg tablets and liquid 10mg/5ml. These forms have always been supplied by GSK, there is no generic alternative.

Liquid has grown steadily the first 4 years of availability, although the share only grew from 0.4% to 1.5% of the total annual consumption of paroxetine. Liquid use has declined in absolute terms by 13% from Q4 2002 to Q4 2003. This evidence suggests that liquid is probably not being used in dilution to any great extent, to assist the withdrawal of LTP from fixed dose tablets, otherwise it would have grown in absolute terms whilst other forms declined.

The decline in 30 mg tablet use started in Q4 2002. Use has fallen by 30% in the last 18 months.

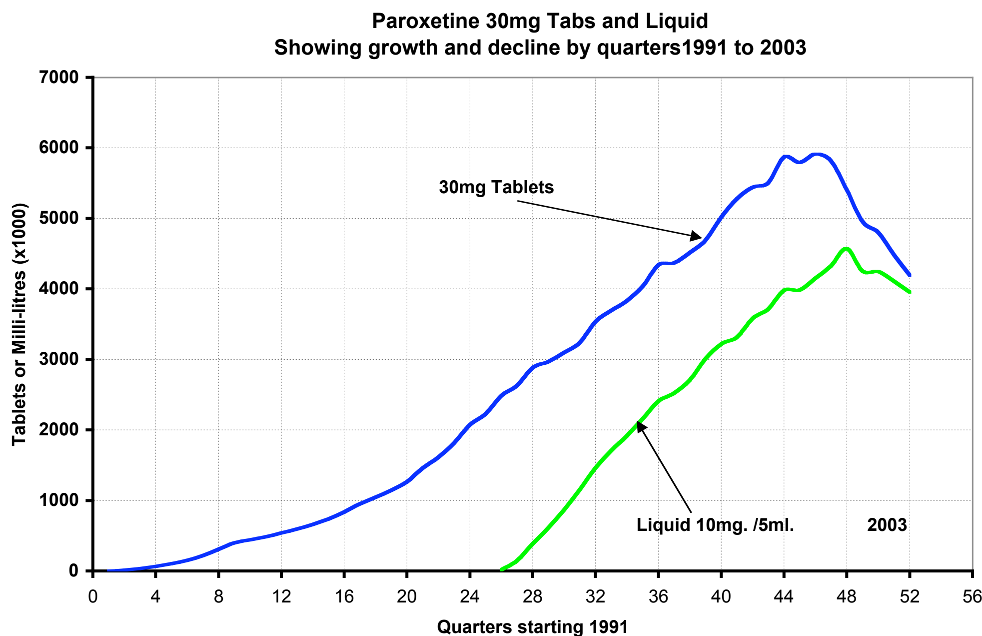

Chart 3

3.2 Paroxetine 20mg Tablets

In chart 4, the GSK and generic supply (from Q2 2002 onwards) have been added together. The use of 20 mg tablets peaked at end of 2001, since then the decline has been fast. By the end of 2003 use had fallen by 38%, (Q4 2001 to Q4 2003). This is shown in the chart below.

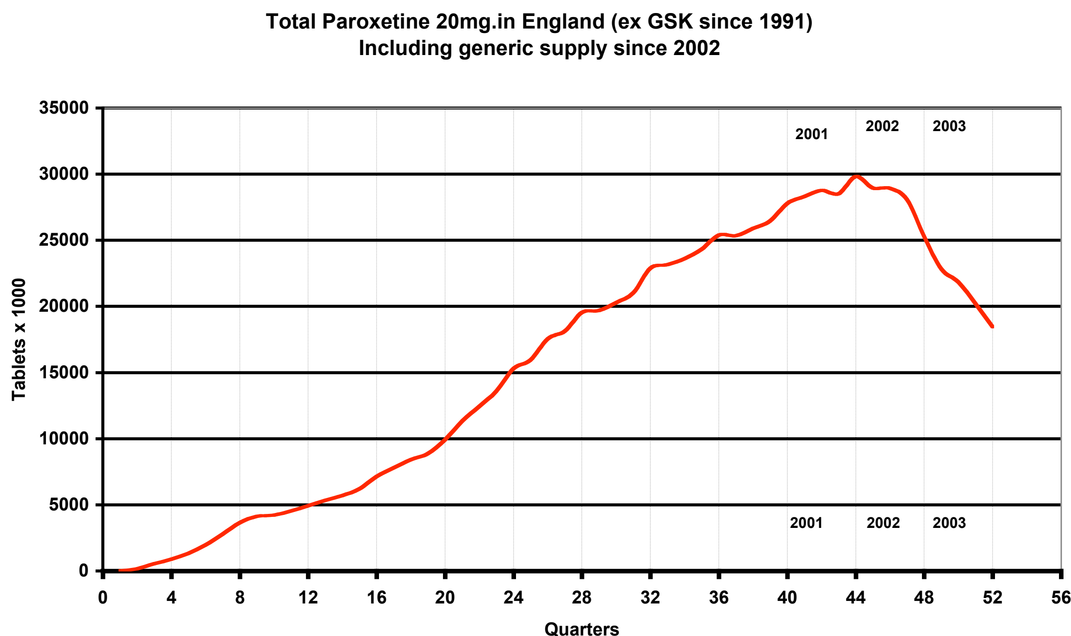

Chart 4: Paroxetine 20mg in England

4.0 Modelling the Decline of Paroxetine with IMR.

The sudden 25% reduction in consumption following nine years of continuous annual growth indicated that both an abnormal exodus of existing long term users and a considerable reduction of new patients must have occurred. Such cohort specific patient response can be modelled in IMR by adjusting various parameters specific to the years in question. Using this flexibility, the radically different patient behaviour between the early years, 1995 to 2001 (rapid rise) and 2002, 2003 (rapid decline) can co-exist and be accommodated in IMR.

Several possible scenarios of the decline in patient numbers relative to the diminishing medication were examined. It was reasonable to assume that both existing long term users and new potential users would each develop awareness of danger and respond accordingly. This provided a range of solutions from which the most plausible was selected. This gave a reduction of new patients joining the drug from 250 K in 2002 to 83K in 2003, an endorsement of growing patient and doctor awareness, in a climate of almost monthly adverse SSRI publicity from MHRA/CSM announcements and inquest findings critical of Seroxat.

Table 2 below quantifies the decline in use of Seroxat in 2002, 2003.

Table 2: Some details of the exodus from Paroxetine in England

	2000	2001	2002	2003
New Patients (K)	**282**	**339**	**250**	**83**
Total Treated (K)	**600**	**682**	**633**	**423**
Long Term Pats (K)	**295**	**325**	**284**	**211**
Induced Suicides	**172**	**207**	**153**	**31**

The table shows that in 2002, 2003 about 300K potential patients choose not to start Seroxat, in addition about 114 K long term patients managed to withdraw. This has saved 220 potential patients from drug induced suicide compared to 2001. *(The suicide rate used is the lowest at 32 excess suicides/100K patients based on background of 20 and OR=2.62)* For UK figures divide England figures in table 2 by 0.82.
Some reduction in demand could be explained by dose tapering by long term patients trying to withdraw from the drug (cutting tablets or diluting liquid). This effectively stretches the existing medication so that it can support patients for longer. This might reduce the exodus figures depending on the duration of tapering. However all the evidence is against this, the use of liquid declined by 13% just when it might be expected to rise spectacularly to support tapering as patients switched from tablets to liquid. Prozac and sertraline show no extra growth.

5.0 Related Events
It is important to see this decline in the perspective of any events that may have triggered it. The usage of paroxetine for the last 4 years in England is plotted in Chart 5 together with some events that must have contributed to the new awareness and caused the decline.

The successful Tobin v GSK (USA June 2001) trial had no noticeable effect in the UK, in fact, usage increased to maximum by Q4 2001. The MCA failed once again to react to specific documented warnings from Dr David Healy (Social Audit website) on his return. The Agency ignored the significance of the Tobin trial verdict even though it had explicitly found against the fundamental safety of Seroxat. In particular the MCA failed to demand full access to the undisclosed Healthy Volunteer results (1988) kept secret by GSK, the key evidence in the Tobin verdict.

With no fall out from the Tobin verdict, 2001 was the peak Seroxat growth year in England, trusting new patients continued to be prescribed Seroxat in vast numbers, like Rhona who was one of 339K new patients and 207 new victims.

Chart 6 clearly shows that the sequence of investigative TV programmes, Mind Games, Bitter Pill, Secrets of Seroxat and Emails from the Edge were fundamental in both creating awareness in very large audiences of the undisclosed dangers of SSRIs and exposing the failures of drug safety regulation by the complacent MCA. The importance of the programmes is that they were not just preaching to the converted, but reaching a vast new audience who saw for the first time the undisclosed danger for themselves or their families of the indiscriminate use of improperly validated SSRIs.

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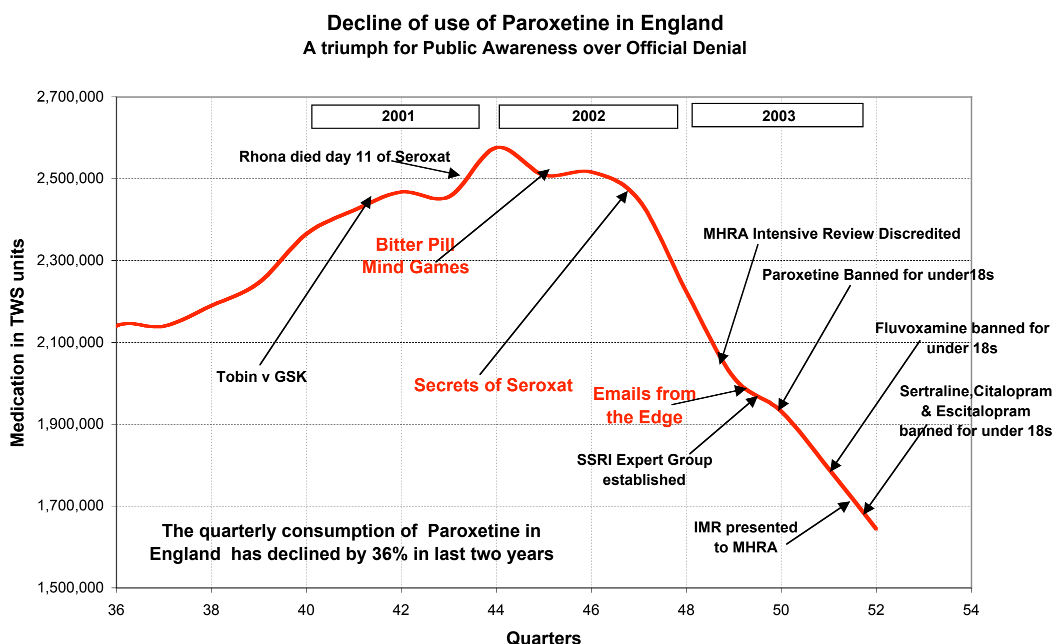
The growth of patient awareness and choice in UK has subsequently been fed by a progression of reluctant statements from MHRA in which they have been forced to admit that all SSRIs can cause suicide in those just under 18 years old but, incredibly, SSRIs are perfectly safe for patients just over 18 years of age. This offence against science, logic or just ordinary common sense reveals the culture and mentality of the Agency responsible for drug safety in the UK.

In February 2004, MHRA had to admit what they had known since 1991, that doses greater than 20mg paroxetine are "unsafe" for most conditions and therefore represent an overdose. MHRA initial attempts to cover this up led to the heroic resignation of Richard Brook from the so-called Expert Review on SSRIs and this forced the official admission. Analysis of the 30 mg drug stream using IMR, shows that 493K patients have been prescribed 30 mg tablets since 1991 in the UK, 15% of the total patients treated in England. MHRA refuse to comment. *(See Usage of 30mg Paroxetine in UK Graham Aldred TBA)*

Chart 5: Events during the decline of use of paroxetine in England.



6.0 Conclusions.

Chart 5 demonstrates the immense value to Society of free and independent Public Service Broadcasting and Internet communication. This combination has triggered the growth of awareness of SSRI danger. It has united the many thousands of victims of SSRIs across the world with some professionals who have laboured so long in a cause for saving lives, seeking justice and exposing dysfunctional drug regulation. Chart 5 shows that the tide has turned in the UK. Great encouragement should be taken from this life saving victory. However efforts must continue both to expose the known risks of paroxetine (Seroxat, Paxil) and all the other ill validated SSRIs and to call for the establishment an effective independent Drug Safety Regulator in every country, the absence of which is the root cause of this ongoing officially supported tragedy.

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Appendix 1 GSK and Generics.

Competition for the 20mg tablet market from a generic supplier.

The GSK patent for paroxetine lapsed on or before the end of Q1 2002. In Q2 a generic competitor immediately took 29% of the 20mg supply, in Q3 it was 94%. The supply was shared as follows in Table 1 as the overall demand for all forms of paroxetine itself declined,

Quarter	GSK Share of 20mg supply
2002 Q1	100%
2002 Q2	71.51%
2002 Q3	5.94%
2002 Q4	5.63%
2003 Q1	5.38%
2003 Q2	5.10%
2003 Q3	4.82%
2003 Q4	4.54%

Table 1: GSK share of 20mg paroxetine supply

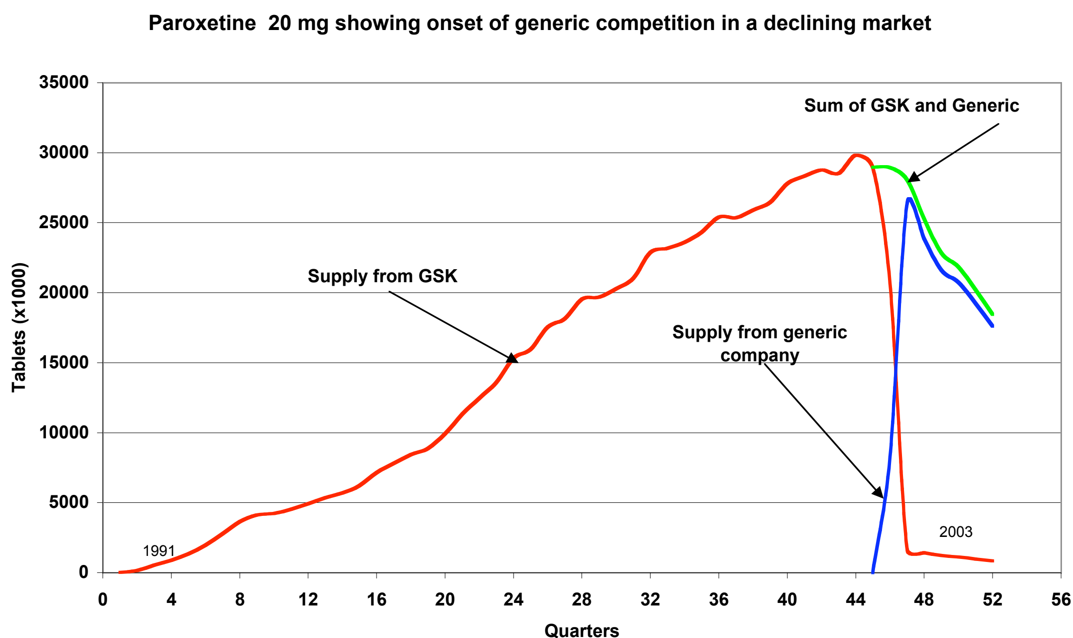

Chart 6.

Chart 6 illustrates this transition in suppliers just as the demand declined radically, Approximately 82 % of the paroxetine consumed in England is in 20 mg tablet form. The curious lack of response by GSK to defend its market share raises some questions.

GSK Response to Generic Competition.

Past evidence shows that GSK has been motivated by profit above other considerations. GSK knew when they would lose the monopoly of supply of paroxetine in the UK at end 2001 and they could anticipate that they would be undercut on price. Any normal commercial company would react to this by lowering product price to diminish the margin with the competition. GSK could have afforded to do this after 11 years price monopoly, particularly as they had not funded very much costly scientific research on paroxetine, which they acquired second hand. But GSK did nothing. They had a monopoly in a market that grew by 1 Million units per year for 10 years and they did nothing. Why ?

a) Poor business planning?
b) They did not want the money ?
c) Did not anticipate that they would lose so much of the 20mg market (95%)
d) GSK wanted to distance itself from adverse publicity re paroxetine?
e) Perhaps GSK are still making the paroxetine?

Reason (e) is plausible, perhaps GSK actually still make all the paroxetine that is used in the generic 20 mg tablets. The substance may be sold in bulk to the "Generic Company" to be packaged and distributed at a small added value. The profit is in the substance, paroxetine, not the packaging and distribution. GSK definitely have the manufacturing capacity available. This explanation fits the lack of response from GSK in giving up such a lucrative market without even a tiny reactive gesture in pricing.

For patients there is one important consequence of a single manufacturer of paroxetine. Any quality control and process problems that may lead to the apparently random and unexplained harm to adults, children and healthy volunteers, would then continue in both the proprietary and generic drugs because it actually comes from the same manufacturing plants. A genuinely independent generic drug manufactured under other quality control disciplines may not show the same symptoms in patients. Pharma's production processes are not quality audited or inspected by MHRA or FDA. In any diagnosis it is always necessary to prove that the unthinkable is untrue.

Reason (d) is compatible with (e). By not fighting the competition commercially, GSK have ensured that the generic company appears to be the major supplier of paroxetine within less than 6 months, obtaining 95% of the 20 mg supply, and therefore 76% of the whole paroxetine supply in UK. It is possible that having a generic fall guy to share the predicted adverse publicity and the foreseeable litigation is a deliberate company strategy.

Graham Aldred 17 May 2004