CASE AUTH/2312/4/10

ALLERGAN v PFIZER

Promotion of Xalatan

Allergan complained about the promotion of Xalatan (latanoprost) and Xalacom (latanoprost plus timolol) by Pfizer. The items at issue were a POAG (primary open angle glaucoma) Budget Impact Model for Xalatan and Xalacom and a journal advertisement, 'Is your prescribing optimised?'. Allergan supplied Lumigan (bimatoprost) and Ganfort (bimatoprost plus timolol).

Allergan stated that Pfizer's long-standing campaign centred around the loss of patent in July 2011 on Xalatan and Xalacom. The campaign encouraged prescribing of Xalatan or Xalacom now in preference to other medicines, in order to realise future cost savings when they came off patent. Price predictions had been made for the corresponding generic medicines and those of competitors including Lumigan and Ganfort. Annual treatment costs had been calculated based on these projected estimates, which had then been used to arrive at comparative cost-saving claims quoted over a period of up to five years.

Although NHS budget holders would be interested in discussing areas for potential reduction in medicine expenditure it was impossible for Pfizer to accurately forecast generic medicine prices and it certainly could not predict the future pricing behaviour of its competitors. Allergan failed to see how a campaign based on pure speculation could be acceptable. Any cost saving claims so formulated were highly likely to be inaccurate. When extrapolated over a long time period, they became increasingly unsupportable and misleading whilst artificially inflating the potential savings.

Allergan did not consider the statements at the beginning of the model to acknowledge the inability to accurately predict future prices of medicines and to put the responsibility on the customer for any data entered, did not make the principle of the model acceptable.

Allergan also had major concerns about the following statement (or similar) which had featured prominently on all campaign materials, including the budget impact model and advertisement at issue:

> **'The current assumption is that Xalatan and Xalacom will come off patent in the UK in July 2011. However, a paediatric development programme is ongoing in Europe which, if all the requirements of the EU Paediatric Medicines Regulation are met, may result in an extension of 6 months.'**

Allergan believed this statement was teaser advertising and promotion of a medicine outside the terms of its marketing authorization.

The detailed response from Pfizer is given below.

The Panel noted that the advertisement at issue was headed 'Is your prescribing optimised?' below which it stated 'Xalatan and Xalacom will be the first prostaglandins to come off patent'. Readers were told that initiating patients on Xalatan or Xalacom now meant that they had the prospect of realising significant long-term savings when generic versions became available without having to interrupt patient treatment. Readers were invited to find out more. Xalacom and Xalatan were currently more expensive than some of the competitor products and thus initiating patients now on Pfizer's products might mean more expensive treatment costs until July 2011 or January 2012 whenever the products came off patent. It was of course likely that savings would be made once generic versions were available. A footnote explained that the current assumption was that Xalatan and Xalacom would come of patent in July 2011. However, a paediatric development programme was ongoing in Europe, which, if all the requirements of the EU Paediatric Medicines Regulations were met, might result in an extension of 6 months. The Panel thus noted that Xalatan and Xalacom might not come off patent until January 2012 ie almost two years after the advertisement was prepared. In that regard the Panel questioned the use of the claim 'Significant savings are in sight'.

The Panel noted that both the advertisement and the budget impact model which clearly promoted Xalatan and Xalacom, referred to the paediatric development programme. The Xalatan summary of product characteristics (SPC), however, stated that safety and effectiveness in children had not been established. Xalatan was therefore not recommended for use in children. The Panel considered that it was important to give an idea of time scale regarding when the products would come off patent however there was no need to explain the reason why. The Panel considered that the advertisement and the budget impact model insomuch as they also referred to the ongoing paediatric development programme, were inconsistent with the particulars listed in the Xalatan and Xalacom SPCs. A breach of the Code was ruled. The Panel further considered that such promotion of a medicine meant that high standards had not been maintained. A further breach of the Code was ruled.

The Panel did not consider that the statement regarding the paediatric development programme

constituted 'teaser' advertising which was material issued to elicit interest in something which would follow at a later date without providing any information about it. Information about Xalatan and Xalacom had been provided. No breach was ruled in this regard.

The Panel noted that the five year budget impact model compared the acquisition costs of Xalatan and Xalacom with that of its competitors and explored possible five-year cost savings that might be achieved when Xalatan and Xalacom came off patent. The users of the model were informed that: 'The predicted dates for loss of exclusivity (LOE) for [the products featured] are estimates based on current understanding. Please be aware that it is not possible to accurately predict the price of Xalatan, Xalacom, Lumigan, Travatan, Saflutan, Duo Trav and Ganfort post-LOE. The predicted prices will be estimates based on your current understanding, therefore all post LOE prices used in the model are assumptions as selected by you. All analyses within the model that incorporate LOE are therefore also assumptions and may not provide an accurate reflection of the value of Xalatan and Xalacom in the future'.

The Panel noted that by their nature, financial models could only give estimates and that the audience would understand such constraints. The question was whether such estimates were reasonable. The Panel considered that while it might be acceptable for a company to present short-term budget models about its own medicines, over which it could be assumed to have reasonable control, to present a long-term model which generated comparative claims vs competitor products introduced many uncertainties. The model at issue covered five years; the date of the loss of patent for Xalatan and Xalacom was dependent upon the outcome of an ongoing paediatric development programme. The model could be modified to take account that Travatan was expected to come off patent within five years; the prices of generic versions of Xalatan and Xalacom were decided upon by the health professional. Pfizer could not accurately predict competitors' pricing strategies as the dynamics of the market changed. Nor could Pfizer accurately predict government strategy as noted in the model itself, 'Product prices are correct based on the current situation. However prices are subject to change and may go up or down as a result of UK PPRS requirements'. The fact that in the short-term, depending on the date of loss of exclusivity, it would be more expensive to initiate patients on Xalacom and Xalatan than some of the competitors had not been made clear.

Overall, the Panel considered that the budget impact model was based on too many assumptions and uncertainties such that the comparative data generated was too speculative and in that regard it was misleading. The Panel ruled breaches of the Code. The Panel considered that its comments about the budget impact model were relevant in relation to the cost savings claims such as 'significant saving are in sight' in the advertisement and similarly ruled breaches of the Code.

Allergan Ltd complained about the promotion of Xalatan (latanoprost) and Xalacom (latanoprost plus timolol) by Pfizer Limited. The items at issue were a POAG (primary open angle glaucoma) Budget Impact Model for Xalatan and Xalacom and an advertisement in Prescriber, 19 March, 'Is your prescribing optimised?'. Inter-company dialogue had failed to resolve the issues. Allergan supplied Lumigan (bimatoprost) and Ganfort (bimatoprost plus timolol).

COMPLAINT

Allergan stated that Pfizer had run a long-standing campaign centred around the loss of patent in July 2011 of its two major medicines for the treatment of glaucoma, Xalatan and Xalacom. The campaign encouraged health professionals to prescribe Xalatan or Xalacom now in preference to other medicines, in order to realise future cost savings when they came off patent. Price predictions had been made for the corresponding generic medicines and those of competitors including Lumigan and Ganfort. Annual treatment costs had been calculated based on these projected estimates, which had then been used to arrive at comparative cost-saving claims quoted over a period of up to five years.

Allergan acknowledged that NHS budget holders would be interested in discussing areas for potential reduction in medicine expenditure. However Allergan considered that Pfizer's materials used to instigate these discussions did not comply with the Code. It was impossible for Pfizer to accurately forecast generic medicine prices and it certainly could not predict the future pricing behaviour of its competitors. Allergan failed to see how a campaign based on pure speculation and not fact could possibly be acceptable under the Code. Any cost saving claims so formulated were highly likely to be inaccurate. When extrapolated over a long time period, they became increasingly unsupportable and misleading whilst artificially inflating the potential savings to a primary care trust (PCT). Allergan thus alleged that the budget impact model and any materials associated with it were in breach of Clauses 7.2 and 7.3 of the Code.

Allergan also had major concerns about the following statement (or similar) which had featured prominently on all campaign materials, including the budget impact model and advertisement at issue:

> 'The current assumption is that Xalatan and Xalacom will come off patent in the UK in July 2011. However, a paediatric development programme is ongoing in Europe which, if all the requirements of the EU Paediatric Medicines Regulation are met, may result in an extension of 6 months.'

Allergan believed this statement was teaser

advertising intended to elicit interest in this area and also promotion of a medicine outside the terms of its marketing authorization. Allergan alleged that the budget impact model and advertisement were in breach of Clauses 3.2, 9.1 and 9.2.

Allergan understood that representatives used the budget impact model at issue to demonstrate potential five-year cost savings to health professionals. Allergan understood from its discussion with Pfizer that the model itself was not left with customers. However, the 'print' and 'save' functions within the model implied that the information and potential outputs from the model could be left with the customer to share with colleagues.

The model compared acquisition costs for the four first-line prostaglandin monotherapies: Xalatan (latanoprost), Lumigan (bimatoprost), Travatan (travoprost) and Saflutan (tafluprost); and the three second-line prostaglandin combination therapies: Xalacom (latanoprost plus timolol), DuoTrav (travoprost plus timolol) and Ganfort (bimatoprost plus timolol).

The model itself, relatively simple in design, was based entirely on predicted medicine costs which were then used to calculate savings for any given PCT population. It did not take into account other aspects of glaucoma treatment which might impact cost savings, for example additional therapy which might be required in addition to the chosen medicine and additional clinic visits.

Allergan did not consider that the statements at the beginning of the model to acknowledge the inability to accurately predict future prices of medicines and to put the responsibility on the customer for any data entered, made the principle of the model acceptable.

Allergan alleged that Pfizer's statements that '… NHS staff are aware of changes in drug costs and are able to reach their own conclusions on pricing changes ...' and that '… the model allows a simple way of exploring potential cost changes with the impact of loss of exclusivity, and will be based on the clinician's own opinion…' was disingenuous. The major driving factor of the model outcomes was the predicted estimate of the price of generic Xalatan/Xalacom and its competitors. This required an adequate understanding of pricing behaviour in the market following loss of patent to make the estimate accurate and valid. Allergan considered that in the majority of cases, this would inevitably be representative-led due to the likely minimal knowledge of health professionals in this area.

If the customer was unsure as to what figures to input, Allergan understood that the representatives had been briefed as to appropriate suggestions that might be made. Allergan was concerned about the nature of this guidance, which was based on IMS research conducted for Pfizer in January 2008.

Pfizer had stated that '…the IMS data used as a basis for discussion on pricing post loss of exclusivity are real life data for a range of products that have lost exclusivity in the recent past …'. Allergan considered that there were several weaknesses to this data and hence any conclusions based upon this material. Aside from the overriding fact that the data entered remained a theoretical estimate, these concerns included:

- The products chosen by IMS for analysis. In Allergan's opinion, determining comparators for analogue modelling was subjective depending on the screening questions to access the respective markets. Allergan considered that the six products chosen for the Pfizer model were not truly representative of, or relevant to, the glaucoma market. For example it was very difficult to draw conclusions from the hypertensive market to the glaucoma market given such different dynamics. Considering that predictions of the likely pricing behaviour of Xalatan/Xalacom generics were based on what Allergan believed were unrepresentative analogues for modelling, it was concerned that the cost-saving calculations subsequently formulated would be misleading.
- The simplistic nature of the research. This focused only on the impact of a lead brand loss of product patent and did not consider the impact on the second or third brand from the loss of a lead brand patent, such as that of the impact of latanoprost loss of patent on travoprost or bimatoprost.
- The failure to consider the loss of patent of subsequent brands, such as that of travoprost in 2014, which was within the scope of the model's projected five-year calculations.
- The nature of the briefing given to representatives as to what data to enter into the model. Allergan had doubts as to whether the price selected for input would be fair and reflect the gradually declining prices as suggested by the research. In this regard Allergan noted that it had received reports from some of its customers that Pfizer representatives had referred to the lowest prices quoted within the IMS data.

The following statement had been included in all campaign materials that Allergan was aware of to date, including the current budget impact model:

'... The current assumption is that Xalatan and Xalacom will come off patent in the UK in July 2011. However, a paediatric development programme is ongoing in Europe which, if all the requirements of the EU Paediatric Medicines Regulation are met, may result in an extension of 6 months…'.

Allergan strongly disagreed with Pfizer's opinion that to not include the above statement in materials would be misleading. Similarly Allergan did not agree with Pfizer's previous assertions that it was only '…a brief factual statement' that was not promotional and '…has been included for complete transparency…'. Allergan submitted this was an opportunity to elicit interest and promote a

potential new indication outside of the terms of the current marketing authorization.

Allergan noted that the advertisement at issue (ref XT1583c) urged health professionals to initiate patients on Xalatan or Xalacom now to have the prospect of realising 'significant long-term savings when generic versions became available …'. No specific mention was made of the budget impact model in this advertisement. However, one would assume that this would be offered for discussion should the reader decide to 'find out more', as directed in the advertisement. For all the reasons stated previously, Allergan believed the significant savings to which Pfizer alluded were based purely on speculation not fact and were thus unacceptable under the Code.

In summary, Allergan alleged that the materials and associated activities outlined above were in breach of the Code. It failed to see how a campaign based on pure speculation and not fact could possibly be acceptable under the Code. Any cost saving claims so formulated were highly likely to be inaccurate. When extrapolated over a long time period, they became increasingly unsupportable and misleading whilst artificially inflating the potential savings to a PCT. Therefore, in Allergan's view the model and any materials associated with it were in breach of Clauses 7.2 and 7.3.

RESPONSE

Pfizer stated that it was committed to building and establishing trust between itself and the UK healthcare system. The UK environment was now such that many customers, whether they were payers or prescribers, valued a conversation with the pharmaceutical industry about the current and future cost of medicines. Pfizer strongly believed that these conversations allowed it to engage and collaborate in a more transparent way, thereby creating openness and integrity.

Pfizer noted that the budget impact model and advertisement covered the loss of exclusivity of its medicines Xalatan (latanoprost) and Xalacom (latanoprost plus timolol), which would be the first of the prostaglandin-based treatments for glaucoma to lose exclusivity in 2011. Allergan had alleged that the model made unreasonable and speculative claims, and did not take into account loss of exclusivity of competitor brands.

The NHS was very alert to cost of treatments and the UK had one of the highest usage of generic medicines. The increased focus on NHS budgets, exacerbated by the current financial climate, had accentuated the focus of prescribers and payers on the cost of treatment and had made prescribers increasingly accountable for their medicine budgets.

Prescribers, budget holders and medicines managers were responsible for forecasting costs and must anticipate potential cost savings from the availability of generic medicines following loss of exclusivity of a major brand. The budget impact model had therefore met with great interest from prescribers and budget holders as the information which it provided could demonstrate how cost savings might be realised.

The model allowed customers to model potential cost savings over a five year period by comparing the prescribing costs of Xalatan or Xalacom with that of competitor products taking into account the dates of loss of exclusivity. The figures calculated in the model were in the first instance based on the current NHS prices of medicines updated monthly from MIMS. The model allowed customers to input their own data which might differ from NHS prices. Customers could use their experience to estimate prices they were likely to pay following loss of exclusivity. This could be supported by evidence from reviewing price reductions for six major products before and after they lost exclusivity using IMS data. The price of Xalatan or Xalacom and their competitors could be independently altered depending on the customer's wishes. Contrary to Allergan's claims, the model could be modified to take into account dates of the competitors' loss of exclusivity. The model offered a dynamic assessment of projected costs in the future.

Although any form of forecasting was inexact, this method allowed customers to model a number of different scenarios and observe the effect on their budget. In addition, and in the interests of transparency, the model could be printed or saved and a record left with the customer. The budget impact model made no quantitative claims around future cost savings or efficacy of medicines. Pfizer believed therefore that the budget impact model was not in breach of Clauses 7.2 or 7.3.

The associated advertisement highlighted to prescribers and budget holders that Pfizer's medicines would be the first of the topical prostaglandins to lose exclusivity. Pfizer did not consider that the claim in the advertisement, 'significant cost savings are in sight' was misleading as major brands in the UK losing exclusivity tended to experience rapid generic competition as evidenced by the IMS data. Optimal prescribing considered the needs of the patient, the prescriber and the budget holder, namely efficacy, tolerability, adherence and price. Therefore Pfizer did not believe the advertisement was in breach of Clauses 7.2 or 7.3.

Pfizer submitted that it had now completed a paediatric investigation plan the results of which were currently being evaluated by the European Medicines Agency. If Pfizer successfully completed the regulatory process, it intended to apply for the six month extension to the supplementary protection certificate for latanoprost in eligible EU countries (including the UK) in accordance with the EU Paediatric Regulation. Although the paediatric investigation plan was not complete when the budget impact model and advertisement were launched, Pfizer considered that it would be misleading not to disclose the significant possibility

of this exclusivity extension to customers, given the context and purpose of the budget impact model. In the interest of transparency, Pfizer therefore included a statement explaining the current situation on all material relating to the issue of loss of exclusivity. As this statement was clear and not misleading Pfizer did not consider that it was advertising as described in the supplementary information to Clauses 9.1 and 9.2. The arguments around cost savings still held with a six month exclusivity extension, as the loss of exclusivity date would still be significantly earlier than that of any of the competitors. There was the facility to model either date in the budget impact model. Pfizer's representatives had been clearly briefed that its products were not yet licensed for paediatric use and so Pfizer refuted that it had tried to promote its products before marketing authorization. Pfizer did not believe the inclusion of a statement regarding potential changes in loss of exclusivity date breached Clauses 3.2, 9.1 and 9.2.

In summary, the budget impact model was an innovative method to help NHS prescribers and budget holders make informed decisions on comparative five year prescribing costs based on evidence of previous experience in price falls after loss of exclusivity. All prices in the model were checked monthly and revised accordingly.

In response to a request for further information Pfizer provided a copy of the briefing material for the original Budget Impact Model and customer letters. The updated briefing material highlighting the most recent changes had already been provided. The customer letters were not used with the current version of the budget model as a disclaimer screen had now been incorporated into the model itself.

In response to a further request for further information, Pfizer referred to the lack of initial savings demonstrated with Xalatan or Xalacom and stated that initiating patients on the less expensive medicines might be cheaper in the short term, but the budget impact model sought to demonstrate that savings over the longer term (five years) could be achieved with the advent of loss of exclusivity and inevitable fall in price of Xalatan and Xalacom. The print-out provided to the Authority showed the framework of the model. The data boxes were not populated at the start but became populated as the representative's interaction with the health profession progressed. It was difficult to illustrate this dynamic process on paper.

Pfizer stated that the model explored possible five-year cost savings with reference to the date of loss of exclusivity of Xalatan and Xalacom, due to occur at either July 2011 or January 2012. The choice of loss of exclusivity date lay with the health professional. Once the date was selected the module calculated price after loss of exclusivity by applying a percentage reduction to the price of Xalatan or Xalacom in the appropriate box in the price modulation table. The scenarios discussed between representative and the health professional were not fixed but were open to variation and formed the basis for their discussion.

In summary, whilst initially current prices of Xalatan and Xalacom might be higher than competitors, the model might demonstrate cost savings over a five year period due to loss of exclusivity.

PANEL RULING

The Panel noted Pfizer's submission that many of its customers valued a conversation with the pharmaceutical industry about the current and future cost of medicine. The Panel accepted that that might well be so but nonetheless any activity in this regard had to comply with the Code. The Panel noted that the advertisement at issue promoted Xalatan and Xalacom as did the budget impact model. The requirements of the Code with regard to the promotion of medicines thus applied.

The advertisement at issue was headed 'Is your prescribing optimised?' below which it stated 'Xalatan and Xalacom will be the first prostaglandins to come off patent'. Readers were told that initiating patients on Xalatan or Xalacom now meant that they had the prospect of realising significant long-term savings when generic versions became available without having to interrupt patient treatment. Readers were invited to find out more by telephoning a free-phone number or by contacting an email address. Xalacom and Xalatan were currently more expensive than some of the competitor products and thus initiating patients now on Pfizer's products might mean more expensive treatment costs until July 2011 or January 2012 whenever the products came off patent. It was of course likely that savings would be made once generic versions were available. A footnote explained that the current assumption was that Xalatan and Xalacom would come of patent in July 2011. However, a paediatric development programme was ongoing in Europe, which, if all the requirements of the EU Paediatric Medicines Regulations were met, might result in an extension of 6 months. The Panel thus noted that Xalatan and Xalacom might not come off patent until January 2012 ie almost two years after the advertisement was prepared. In that regard the Panel questioned the use of the claim 'Significant savings are in sight'.

The Panel noted that both the advertisement and the budget impact model which clearly promoted Xalatan and Xalacom, referred to the paediatric development programme. The Xalatan summary of product characteristics (SPC), however, stated that safety and effectiveness in children had not been established. Xalatan was therefore not recommended for use in children. The Panel considered that it was important to give an idea of time scale regarding when the products would come off patent however there was no need to explain the reason why. The Panel considered that the advertisement and the budget impact model insomuch as they also referred to the ongoing paediatric development programme, were

inconsistent with the particulars listed in the Xalatan and Xalacom SPCs. A breach of Clause 3.2 was ruled. The Panel further considered that such promotion of a medicine meant that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel did not consider that the statement regarding the paediatric development programme constituted 'teaser' advertising which was material issued to elicit interest in something which would follow at a later date without providing any information about it. Information about Xalatan and Xalacom had been provided. No breach of Clauses 9.1 and 9.2 was ruled in this regard.

The Panel noted that the five year budget impact model compared the acquisition costs of Xalatan and Xalacom with that of its competitors and explored possible five-year cost savings that might be achieved when Xalatan and Xalacom came off patent. In that regard the Panel considered that the impact model promoted Xalatan and Xalacom and made comparative claims vs their competitors. The users of the model were informed that: 'The predicted dates for loss of exclusivity (LOE) for [the products featured] are estimates based on current understanding. Please be aware that it is not possible to accurately predict the price of Xalatan, Xalacom, Lumigan, Travatan, Saflutan, Duo Trav and Ganfort post-LOE. The predicted prices will be estimates based on your current understanding, therefore all post LOE prices used in the model are assumptions as selected by you. All analyses within the model that incorporate LOE are therefore also assumptions and may not provide an accurate reflection of the value of Xalatan and Xalacom in the future'.

The Panel noted that having discussed the budget impact model with a representative, a health professional was required to sign a letter accepting the above. The letter also referred to the provision of print outs.

The Panel noted from the representatives' briefing material that the monthly price for a competitor product could not be altered within the five year projected period. The percentage reduction in price for a product was to be based on discussions with the NHS customer.

The Panel noted that by their nature, financial models such as that at issue could only give estimates and that the audience would understand such constraints. The question was whether such estimates were reasonable. The Panel considered that while it might be acceptable for a company to present short-term budget models about its own medicines, over which it could be assumed to have reasonable control, to present a long-term model which generated comparative claims vs competitor products introduced many uncertainties. The model at issue covered five years; the date of the loss of patent for Xalatan and Xalacom was dependent upon the outcome of an ongoing paediatric development programme. The model could be modified to take account that Travatan was expected to come off patent within five years; the price of generic versions of Xalatan and Xalacom were decided upon by the health professional. Pfizer could not accurately predict competitors' pricing strategies as the dynamics of the market changed. Nor could Pfizer accurately predict government strategy as noted in the model itself, 'Product prices are correct based on the current situation. However prices are subject to change and may go up or down as a result of UK PPRS requirements'. The fact that in the short-term, depending on the date of loss of exclusivity, it would be more expensive to initiate patients on Xalacom and Xalatan than some of the competitors had not been made clear.

Overall, the Panel considered that the budget impact model was based on too many assumptions and uncertainties such that the comparative data generated was too speculative and in that regard it was misleading. The Panel ruled breaches of Clauses 7.2 and 7.3 as alleged. The Panel considered that its comments about the budget impact model were relevant in relation to the cost savings claims such as 'significant saving are in sight' in the advertisement and similarly ruled breaches of Clauses 7.2 and 7.3 as alleged.

Complaint received **28 April 2010**

Case completed **26 July 2010**