GENERAL PRACTICE PHARMACIST PRACTITIONER v BRISTOL-MYERS SQUIBB and SANOFI-AVENTIS

Aprovel and CoAprovel mailing

The pharmacist practitioner at a general practice complained about a GP mailing for Aprovel (irbesartan) and CoAprovel (irbesartan and hydrochlorothiazide) sent by Bristol-Myers Squibb and Sanofi-Aventis.

The complainant was concerned about the bold heading 'Treat BP to target today…reduce CV [cardiovascular] risk tomorrow'. There were several referenced claims about the superiority of Aprovel over other angiotensin receptor blockers in terms of BP reduction; however there was no substantiation that either Aprovel or CoAprovel reduced cardiovascular risk and as far as the complainant was aware there was no robust evidence to back that claim.

The complainant also referred to the un-referenced claim 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors'. This claim might be referring to a post-hoc analysis of the irbesartan diabetic nephropathy trial (Berl *et al* 2005); however this study appeared to conclude that, in diabetics treated with irbesartan, there were reductions in the risk of strokes and of renal failure but there was a statistically significant increase in the risk of heart attack and a non significant increase in heart failure! This could hardly be reported as helping to reduce cardiovascular risk. Additionally, the authors were cautious to highlight that their conclusions were based upon observational data and therefore recommended that a properly conducted randomised study was needed to clarify the treatment guidelines they proposed.

In the Panel's view the layout and content of the piece was such that all of the claims therein would be assumed to be linked to Aprovel and CoAprovel. There was no clear differentiation of general claims about blood pressure and cardiovascular risk from specific claims for Aprovel and CoAprovel.

The Panel noted that Aprovel and CoAprovel were both indicated for the treatment of essential hypertension. Aprovel was also indicated for the treatment of renal disease in hypertensive patients with type 2 diabetes. A benefit of lowering blood pressure would be a reduction of cardiovascular risk but neither medicine was indicated to reduce cardiovascular risk.

The claim 'Treat BP to target today … reduce CV risk tomorrow' appeared halfway down a page of text and immediately below, and to the left, of the product logos for Aprovel and CoAprovel. Every other claim on the page referred specifically to Aprovel and/or CoAprovel. The Panel considered that, in the context in which it appeared, the claim in question implied that Aprovel and CoAprovel, by treating BP to target, reduced cardiovascular risk. There was no data for Aprovel and CoAprovel in this regard. The Panel considered that the claim was misleading and could not be substantiated. Breaches of the Code were ruled.

The claim 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors' was on a separate page to the claim considered above. The Panel noted that Aprovel was indicated for renal disease in hypertensive type 2 diabetic patients as part of an antihypertensive drug regimen. Aprovel was thus licensed for use in patients with additional risk factors but there was no direct clinical evidence to show that treatment with Aprovel reduced cardiovascular risk in that patient group. The claim was thus misleading and could not be substantiated. Breaches of the Code were ruled.

The pharmacist practitioner at a general practice complained about a GP mailing (ref APR 06/2319) for Aprovel (irbesartan) and CoAprovel (irbesartan and hydrochlorothiazide). Aprovel and CoAprovel were co-promoted by Bristol-Myers Squibb Pharmaceuticals Ltd and Sanofi-Aventis and the matter was taken up with both companies.

COMPLAINT

The complainant was concerned about a bold heading in the centre foldout area that stated, 'Treat BP to target today…reduce CV [cardiovascular] risk tomorrow'. Throughout the document there were several referenced claims about the superiority of Aprovel over other angiotensin receptor blockers in terms of BP reduction; however there was no substantiation that either Aprovel or CoAprovel reduced cardiovascular risk and as far as the complainant was aware there was no robust evidence to back that claim.

The complainant also referred to another un-referenced claim in the first gate foldout section that stated 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors'. This claim might be referring to a post-hoc analysis of the irbesartan diabetic nephropathy trial (Berl *et al* 2005); however this study appeared to conclude that, in diabetics treated with irbesartan, there were reductions in the risk of strokes and of renal failure but there was a statistically significant increase

in the risk of heart attack and a non significant increase in heart failure! This could hardly be reported as helping to reduce cardiovascular risk. Additionally, the authors were cautious to highlight that their conclusions were based upon observational data and therefore recommended that a properly conducted randomised study was needed to clarify the treatment guidelines they proposed.

When writing to the companies, the Authority asked them to respond in relation to Clauses 7.2 and 7.4 of the Code.

RESPONSE

In a joint response the companies noted that no mention of Aprovel or CoAprovel was made within the claim 'Treat BP to target today … reduce CV risk tomorrow' which reflected the widely understood medical and scientific fact that patients with elevated blood pressure were at greater risk of cardiovascular events. This was the basis of antihypertensive treatments and the conclusion of a substantial body of evidence that the reduction of blood pressure would reduce cardiovascular risk.

The claim therefore also reflected widely accepted, current national and international recommendations for the prevention of cardiovascular disease. The Joint British Societies' guidelines, second revision (2005) were one such example and were referred to in the mailing. These stated: 'The object of CVD prevention in these high risk people is the same - namely, to reduce the risk of a non-fatal or fatal atherosclerotic cardiovascular event and to improve both quality and length of life. This can be achieved through lifestyle and risk factor interventions and appropriate drug therapies to lower blood pressure, modify lipids, and reduce glycaemia. We have set targets (see below) for lifestyle, blood pressure, lipids, and glucose for these high risk people'.

The claim 'Treat BP to target today…. reduce CV risk tomorrow' therefore supported the current medical approach of reducing BP, particularly to recommended targets, to reduce a hypertensive patient's cardiovascular risk. The claim clearly referred to the effect on cardiovascular risk of BP lowering per se, rather than that of any specific medicine. This was distinct from specific claims elsewhere on this item which referred only to the effect of Aprovel and CoAprovel on blood pressure and not to any clinical outcome or cardiovascular risk reduction by direct linkage. Hence, no claim was made for a direct benefit of Aprovel or CoAprovel on cardiovascular risk. Equally, there was substantial and current evidence as described above, for the claim which directly linked BP treatment with reduction in cardiovascular risk.

The companies therefore did not believe that the claim was in breach of Clause 7.2 or 7.4.

The companies submitted that the claim 'Aprovel's power to lower blood pressure can help reduce cardiovascular risk in patients with additional risk factors' was not taken from Berl *et al*. In fact the claim was, again, in support of the guidelines that advocated reducing BP to target in order to reduce cardiovascular risk, described above and positioned adjacent to the claim.

Although the claim was not referenced, it referred to one of the main licensed indications for Aprovel (clearly visible to the left of the claim upon opening the mailing) - that was the treatment of hypertensive patients with type 2 diabetes and renal disease. As the claim did not refer to published studies, it was not mandatory to cite references provided that the requirements of Clauses 7.2 and 7.4 were met.

The mailing clearly identified several studies that supported the ability of both Aprovel and CoAprovel to reduce BP. By lowering BP to target, patients could be helped to reduce their cardiovascular risk, as claimed.

Again, the companies considered that these factors confirmed that there had been no breach of Clauses 7.2 and 7.4 of the Code in respect of this claim.

In summary, the companies submitted that the evidence was clearly reflected and substantiated to demonstrate that the information, claims and comparisons used were accurate, balanced, fair and not misleading.

PANEL RULING

The Panel noted that the claims in question were contained in a short promotional mailing for Aprovel and CoAprovel. In the Panel's view the layout and content of the piece was such that all of the claims therein would be assumed to be linked to the two products. There was no clear differentiation of general claims about blood pressure and cardiovascular risk from specific claims for Aprovel and CoAprovel.

The Panel noted that Aprovel and CoAprovel were both indicated for the treatment of essential hypertension. Aprovel was also indicated for the treatment of renal disease in hypertensive patients with type 2 diabetes. A benefit of lowering blood pressure would be a reduction of cardiovascular risk but neither medicine was indicated to reduce cardiovascular risk.

The claim 'Treat BP to target today … reduce CV risk tomorrow' appeared halfway down a page of text and immediately below, and to the left, of the product logos for Aprovel and CoAprovel. Every other claim on the page referred specifically to Aprovel and/or CoAprovel. The Panel considered that, in the context in which it appeared, the claim in question implied that Aprovel and CoAprovel, by treating BP to target, reduced cardiovascular risk. There was no data for Aprovel and CoAprovel in this regard. The Panel considered that the claim was misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 were ruled.

The claim 'Aprovel's power to lower blood pressure

can help reduce cardiovascular risk in patients with additional risk factors' was on a separate page to the claim considered above. The Panel noted that Aprovel was indicated for renal disease in hypertensive type 2 diabetic patients as part of an antihypertensive drug regimen. Aprovel was thus licensed for use in patients with additional risk factors but there was no direct clinical evidence to show that treatment with Aprovel reduced cardiovascular risk in that patient group. The claim was thus misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 of the Code were ruled.

Complaint received **4 December 2006**

Case completed **12 February 2007**