

GLAXOSMITHKLINE v SANOFI PASTEUR MSD

Gardasil journal advertisement

GlaxoSmithKline complained about a journal advertisement for Gardasil (Human Papillomavirus Vaccine (types 6, 11, 16, 18) (Recombinant absorbed)) issued by Sanofi Pasteur MSD. Gardasil was indicated for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts causally related to HPV types 6, 11, 16 and 18.

GlaxoSmithKline alleged that the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was misleading, exaggerated and all embracing, implying that Gardasil had demonstrated efficacy to prevent cervical cancer (with all high-risk HPV types), when in fact it offered protection against two high-risk HPV types, 16 and 18 (around 70% of cervical cancers). This was not made clear and thus the advertisement was misleading and exaggerated the potential benefits of Gardasil in cervical cancer prevention.

The Panel noted that the summary of product characteristics (SPC) included data on the immune response to Gardasil which showed that overall, across all age groups, 99.9%, 99.8%, 99.8% and 99.6% of individuals who received Gardasil became anti-HPV6, anti-HPV11, anti-HPV16 and anti-HPV18 seropositive, respectively, one month after the third dose. The Panel noted that HPV types 16 and 18 were responsible for around 70% of cases of cervical cancer. The Panel considered that given the product's licensed indication the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was not misleading or exaggerated as alleged. No breach of the Code was ruled.

The claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was immediately followed by the claim 'Benefit from 4 types – before and beyond cervical cancer'. GlaxoSmithKline alleged that the proximity and positioning of these two claims implied that Gardasil offered protection against four HPV types that played a causal role in cervical cancer when in fact it offered protection against two (HPV 16 and 18). GlaxoSmithKline further alleged that the claim 'Benefit from 4 types – before and beyond cervical cancer' was ambiguous and its positioning immediately following 'Now there's Gardasil a vaccine that can prevent cervical cancer' was misleading.

The Panel noted that the claim 'Benefit from 4 types - before and beyond cervical cancer' appeared in a relatively small typeface beneath the bold, prominent claim, 'Now there's Gardasil a vaccine that can prevent cervical cancer' on the first page of the double page spread. The second page was headed 'The first vaccine that can prevent cervical cancer' beneath which 2 bullet points discussed the licensed indication of Gardasil and the HPV types 6, 11, 16 and 18. On balance, the Panel

considered that in the context in which it appeared it was not entirely clear what the claim 'Benefit from 4 types - before and beyond cervical cancer' meant and in this regard it was ambiguous and misleading. A breach of the Code was ruled. However, the claim 'Benefit from 4 types - before and beyond cervical cancer' was subsequently subject to an appeal to the Code of Practice Appeal Board in a separate case, Case AUTH/1927/12/06, wherein the Appeal Board ruled no breach of the Code. The ruling in Case AUTH/1927/12/06 would apply and supersede the Panel's ruling in the present case, Case AUTH/1938/1/07. There had thus been no breach.

GlaxoSmithKline alleged that the claim 'Beyond the cervix, Gardasil can also prevent vulval pre-cancers and genital warts and reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18' incorrectly implied that each of the four HPV types played a causal role in each of the disease states listed.

The Panel did not consider that the claim implied that HPV types 6, 11, 16 and 18 all had a causal role in each of the conditions listed. In the Panel's view, most readers would assume that the conditions listed were caused by one or more of the HPV types listed. No breach of the Code was ruled.

GlaxoSmithKline UK Ltd complained about the promotion of Gardasil (Human Papillomavirus Vaccine (types 6, 11, 16, 18) (Recombinant absorbed)) by Sanofi Pasteur MSD Ltd. At issue was a double page advertisement (ref 10/06 09214c) which appeared in 'Doctor'.

GlaxoSmithKline explained that Gardasil was a quadrivalent vaccine against human papillomavirus (HPV) types 6, 11, 16 and 18. It was indicated for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts causally related to HPV types 6, 11, 16 and 18.

There were approximately 15 'high-risk' (cancer-causing) HPV types. HPV 16 and 18 were responsible for around of 70% cervical cancers and the other high-risk types accounted for the remaining 30% of cases. HPV 16 and 18 also played a causal role in approximately 70% of high grade cervical dysplasias (CIN 2/3), 70% of high grade vulvar dysplasias (VIN 2/3) and the majority of high grade vaginal dysplasia (VaIN 2/3).

In contrast, HPV types 6 and 11 were 'low-risk' HPV types responsible for approximately 90% of genital warts; they were not responsible for cervical, vulvar or vaginal cancers or their respective high-grade dysplasias (also referred to as high-grade pre-cancers).

1 Claim 'Now there's Gardasil a vaccine that can prevent cervical cancer'

This claim appeared on the left-hand side of the double page spread.

COMPLAINT

GlaxoSmithKline alleged that this claim was misleading, exaggerated and all embracing, implying that Gardasil had demonstrated efficacy to prevent cervical cancer (with all high-risk HPV types), when in fact it offered protection against two high-risk HPV types, 16 and 18. As highlighted, HPV 16 and 18 accounted for around 70% of cervical cancers. Therefore, based on the available clinical data, Gardasil only had the potential to prevent 70% of cervical cancers. This was not made clear anywhere in the advertisement which was thus misleading and exaggerated the potential benefits of Gardasil in cervical cancer prevention. GlaxoSmithKline alleged breaches of Clauses 7.2 and 7.10.

RESPONSE

Sanofi Pasteur MSD pointed out that although it did not guarantee compliance with the Code, the advertisement was pre-vetted by the Medicines and Healthcare products Regulatory Agency (MHRA).

Sanofi Pasteur MSD noted that GlaxoSmithKline had correctly noted that Gardasil was indicated, amongst other things, to prevent cervical carcinoma (ie cervical cancer) causally related to HPV types targeted by the vaccine. Since HPV types 16 and 18 were responsible for around 70% of cases of cervical cancer it was a statement of fact and a true reflection of the indication that Gardasil could prevent cervical cancer. 'Can' in the claim, 'Now there's Gardasil a vaccine that can prevent cervical cancer', was chosen very carefully to ensure that the claim reflected Gardasil's ability to prevent cervical cancer rather than the certainty that it would prevent cervical cancer.

Sanofi Pasteur MSD submitted that the claim simply stated the facts, Gardasil was available and indicated for the prevention of cervical cancer and therefore was not in breach of Clause 7.2 of the Code. Furthermore, through use of the word 'can', Sanofi Pasteur MSD had made specific efforts to ensure that the claim was not exaggerated. As a result there was no breach of Clause 7.10.

PANEL RULING

The Panel noted that Gardasil was licensed for the prevention of high-grade cervical dysplasia (CIN 2/3), cervical carcinoma, high grade vulvar dysplastic lesions (VIN 2/3), and external genital warts (condyloma acuminata) causally related to HPV types 6, 11, 16 and 18. Section 5.1 of the summary of product characteristics (SPC), Pharmacodynamic properties, discussed data on the immune response to Gardasil which showed that overall, across all age groups, 99.9%, 99.8%, 99.8% and

99.6% of individuals who received Gardasil became anti-HPV6, anti-HPV11, anti-HPV16 and anti-HPV18 seropositive, respectively, one month after dose three. The Panel noted that HPV types 16 and 18 were responsible for around 70% of cases of cervical cancer. The Panel considered that given the product's licensed indication the claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was not misleading or exaggerated as alleged. No breach of Clauses 7.2 and 7.10 was ruled.

2 Claim 'Benefit from 4 types – before and beyond cervical cancer'

This claim appeared on the left-hand page of the double page spread immediately below the claim in question at point 1 above.

COMPLAINT

GlaxoSmithKline noted that claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' was immediately followed by the claim 'Benefit from 4 types – before and beyond cervical cancer'. The proximity and positioning of these two claims implied that Gardasil offered protection against four HPV types that played a causal role in cervical cancer when in fact it offered protection against two (HPV 16 and 18). GlaxoSmithKline strongly disagreed with Sanofi Pasteur MSD's suggestion that the phrase 'before and beyond cervical cancer', made it very clear that it was referring to cervical intra-epithelial neoplasia, and vulval intra-epithelial neoplasia and genital warts, respectively. Sanofi Pasteur MSD also stated that the body of the advertisement contained expanded details relating to this statement. However, clarification in the body of the advertisement was not sufficient – the title claims should stand alone with regard to clarity. GlaxoSmithKline alleged that the claim 'Benefit from 4 types – before and beyond cervical cancer' was ambiguous and its positioning immediately following 'Now there's Gardasil a vaccine that can prevent cervical cancer' was misleading in breach of Clause 7.2.

RESPONSE

Sanofi Pasteur MSD noted that GlaxoSmithKline was concerned that this claim, and its position in the advertisement, was ambiguous and implied that Gardasil offered protection against four HPV types that were responsible for cervical cancer.

Sanofi Pasteur MSD submitted that this claim was not misleading. Section 4.1 of the SPC stated that Gardasil was indicated not just for the prevention of cervical cancer but also for the prevention of cervical dysplasia (pre-cancerous lesions that developed **before** cervical cancer itself), as well as diseases that occurred **beyond** the cervix (ie vulval intra-epithelial neoplasia, genital warts), all causally related to the four HPV types targeted by the vaccine. The statement reflected the benefits of Gardasil over and above protection against cervical cancer. The claim stood alone with regards to clarity and further details were provided in the right-hand side of the advertisement.

Similarly, Sanofi Pasteur MSD submitted that the claim was not ambiguous. As described above, the claim was not about cervical cancer but rather the other benefits of Gardasil that derived from the inclusion of four HPV types in the vaccine. Indeed, these two facts were linked by the inclusion of the hyphen.

For these reasons, Sanofi Pasteur MSD submitted that this claim was neither misleading, nor ambiguous, and was not in breach of Clause 7.2.

PANEL RULING

The claim 'Benefit from 4 types - before and beyond cervical cancer' appeared in a relatively small typeface beneath the bold, prominent claim considered above, 'Now there's Gardasil a vaccine that can prevent cervical cancer' on the first page of the double page spread. The facing second page of the advertisement was headed 'The first vaccine that can prevent cervical cancer' beneath which 2 bullet points discussed the licensed indication of Gardasil and the HPV types 6, 11, 16 and 18. The Panel considered that the claim 'Benefit from 4 types - before and beyond cervical cancer' was ambiguous. Some might consider that the four types referred to HPV types 6, 11, 16 and 18. Given the prominence of the preceding claim 'Now there's Gardasil a vaccine that can prevent cervical cancer' and its reference to cervical cancer some readers might assume that the claim at issue implied that HPV types 6, 11, 16 and 18 each had a role in cervical cancer. It was only by reading the less prominent text in the bullet points on the facing page that the causative effects of the four HPV types became clear. Others might consider that term 'four' referred to the 4 licensed indications. On balance, the Panel considered that in the context in which it appeared it was not entirely clear what the claim 'Benefit from 4 types - before and beyond cervical cancer' meant and in this regard it was ambiguous and misleading. A breach of Clause 7.2 was ruled.

However, an earlier case, Case AUTH/1927/12/06 included a similar complaint about the claim 'Benefit from 4 types - before and beyond cervical cancer'. After the Panel had made its ruling in the present case an appeal in Case AUTH/1927/12/06 was considered by the Code of Practice Appeal Board which ruled no breach of Clause 7.2 of the Code as follows:

Appeal Board Ruling in Case AUTH/1927/12/06

The Appeal Board had some concerns that in the claim 'Benefit from 4 types - before and beyond cervical cancer', 'before ... cervical cancer' related to time ie high-grade cervical dysplasia whereas 'beyond cervical cancer' related to anatomy ie vulva lesions or external genital warts. However the Appeal Board considered it unlikely that readers would assume that 'beyond' referred to a time after which a woman had developed cervical cancer given that the very prominent claim which preceded the claim at issue clearly referred to the prevention of cervical cancer.

The Appeal Board did not consider that the claim implied that HPV types 6, 11, 16 and 18 all caused cervical cancer as alleged.

Although noting its concern above, the Appeal Board considered that, in the context in which it appeared, the claim was not ambiguous or misleading and could be substantiated. No breach of Clauses 7.2 and 7.4 was ruled. The appeal was thus successful.

Although Case AUTH/1938/1/07 did not go to appeal (when the Panel made its ruling the appeal was pending), the Appeal Board's ruling of no breach of the Code would apply to the present case, Case AUTH/1938/1/07 superseding the Panel's ruling. There had thus been no breach.

3 Claim 'Beyond the cervix, Gardasil can also prevent vulval pre-cancers and genital warts and reduce the incidence of vaginal pre-cancers caused by human papillomavirus types 6, 11, 16 or 18'

This claim appeared on the right hand page of the double page spread.

COMPLAINT

GlaxoSmithKline alleged that this claim incorrectly implied that each of the four HPV types played a causal role in each of the disease states listed. Section 5.1 of the Gardasil SPC clearly defined the causal role of the high-risk (16 and 18) and low-risk (6 and 11) HPV types in the various disease states: 'HPV 16 and 18 are responsible for approximately... 70% of high-grade vulvar dysplasia (VIN 2/3)' and 'HPV 6 and 11 are responsible for approximately 90% of genital warts cases'. GlaxoSmithKline alleged that the claim was in breach of Clause 7.2.

RESPONSE

Sanofi Pasteur MSD submitted that the claim accurately reflected Section 5.1 of the SPC (sub-section titled 'Efficacy in subjects naïve to the relevant vaccine HPV type(s))' where only results for CIN 2/3 or adenocarcinoma in situ (AIS) were related to types 16 or 18 alone, whereas all other results were related to types 6, 11, 16 or 18.

The claim was therefore an accurate, balanced, fair, objective and unambiguous reflection of the data presented in the SPC and not in breach of Clause 7.2.

PANEL RULING

The Panel did not consider that the claim implied that HPV types 6, 11, 16 and 18 all had a causal role in each of the conditions listed. In that regard the Panel did not consider that the claim was misleading as alleged. In the Panel's view, most readers would assume that the conditions listed were caused by one or more of the HPV types listed. No breach of Clause 7.2 was ruled.

Complaint received	2 January 2007
Case completed	6 March 2007