CASE AUTH/2253/7/09

CONSULTANT PSYCHIATRIST v JANSSEN-CILAG

Promotion of Risperdal Consta

A consultant psychiatrist and visiting professor of psychiatry, complained about the promotion of Risperdal Consta (prolonged release risperidone) by Janssen-Cilag, Risperdal Consta was indicated for the maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics.

The complainant stated that a Janssen-Cilag representative recently showed a presentation regarding the putative neuroprotective effects of risperidone. When the complainant protested that there was no clarity as to what was meant by 'neuroprotective effects', and that he would be concerned if there was no justificatory evidence for the claim that risperidone might have neuroprotective effects, he was sent a copy of Lieberman *et al* (2008). The paper did not justify any marketing campaign intended to imply neuroprotective effects for risperidone and in fact, appeared to be a review paper, regarding the potential effects of antipsychotics in general.

The complainant was therefore concerned, not necessarily at the actions of the representative, but at those who had designed a campaign to portray risperidone as having neuroprotective effects. The complainant was prepared to concede that risperidone might have neuroprotective effects, but there was currently not sufficient data to make this claim.

The detailed response from Janssen-Cilag is given below.

The Panel noted that Janssen-Cilag had provided part of the presentation; a sub-section which discussed relapse prevention and comprised 16 slides. The product logo appeared in the bottom right hand corner of each slide. The first 4 slides were headed 'Every relapse counts … give your patients the choice of Risperdal Consta earlier' and included the statement 'The first few years of illness have been proposed as a critical period during which an aggressive and relapsing course may lead to accruing morbidity and persistent deficits'. Six subsequent slides discussed early and late grey matter deficits in schizophrenia beneath the heading 'Recurrent relapses can lead to progressive brain tissue loss'. Below diagrams depicting early and late grey matter deficits was the claim 'Risperdal Consta can help prevent relapse and help patients achieve remission'. All the slides included the statement 'Latest thinking'. A pop-up box on slides 9 and 10 referred to a recent review (Lieberman *et al*) which suggested that some aytpicals had greater neuroprotective effects ie preventing or reversing the frontocortical grey matter decline seen in schizophrenia patients compared to conventional agents.

The Panel noted that the representatives were trained verbally on the presentation after which a guidance document was sent to them. This document instructed representatives to create a sense of urgency and to obtain agreement that relapse prevention was a key outcome. When showing the slides which discussed early and late grey matter deficits in schizophrenia (slide 5) representatives were instructed to discuss the impact of recurrent relapses and progressive brain tissue loss. Alongside the pop-up box which referred to neuroprotective effects (slide 9) representatives were told to discuss the 'suggested neuroprotective effects of aytpicals (Lieberman)'. No further guidance was given about the ensuing discussion on neuroprotective effects.

The Panel noted that Lieberman *et al*, a review article, concluded that schizophrenia 'possibly' involved a limited neurodegenerative component. Whilst more work was needed, the bulk of the data supported the authors' tentative conclusion that some antipsychotics, mainly the second generation antipsychotics, might be neuroprotective in schizophrenia.

The Panel considered that although there was no explicit claim about Risperdal Consta and neuroprotection, the slides very clearly linked the two. Representatives were instructed to refer to the suggested neuroprotective effects of atypical antipsychotics. In the Panel's view the overwhelming impression was that Risperdal Consta had neuroprotective effects. The material was misleading and incapable of substantiation in this regard. Consequently, the representative had failed to comply with all the relevant requirements of the Code. Breaches of the Code were ruled.

The Panel noted the clear link in the presentation between Risperdal Consta and neuroprotection and considered that in that regard it was inevitable that the briefing material advocated a course of action likely to lead to a breach of the Code and ruled accordingly.

A consultant psychiatrist and visiting professor of psychiatry, complained to the Medicines and Healthcare products Regulatory Agency (MHRA) about the promotion of Risperdal Consta (prolonged release risperidone) by Janssen-Cilag Ltd, copying his letter to the ABPI. The ABPI passed the letter to the Authority which treated it

as a complaint under the Code.

Risperdal Consta was indicated for the maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics.

COMPLAINT

The complainant stated that a Janssen-Cilag representative recently showed him a PowerPoint presentation regarding the putative neuroprotective effects of risperidone. When the complainant protested that there was no clarity as to what was meant by 'neuroprotective effects', and that he would be concerned if there was no justificatory evidence for the claim that risperidone might have neuroprotective effects, he was sent a copy of Lieberman *et al* (2008). The paper did not justify any marketing campaign intended to imply neuroprotective effects for risperidone and in fact, appeared to be a review paper, regarding the potential effects of antipsychotics in general.

The complainant was therefore concerned, not necessarily at the actions of this representative, but at those who had designed a campaign to portray risperidone as having neuroprotective effects. He was prepared to concede that risperidone might have neuroprotective effects, but his underlying argument was that there was currently not sufficient data to make this claim.

When writing to Janssen-Cilag, the Authority asked it to respond in relation to Clauses 7.2, 7.4, 15.2 and 15.9 of the Code.

RESPONSE

Janssen-Cilag stated that it was committed to working in partnership with health professionals, and it acknowledged its responsibility to them. As a company, it took clinicians' concerns about its marketing activities very seriously.

The material in question was not intended to claim neuroprotective effects and Janssen-Cilag did not believe it did. Nor did Janssen-Cilag believe that the representative concerned made such a claim during the call. The material formed part of an electronic detail aid which was presented by representatives on laptop computers, and was made up of seven major sections: Introduction; Efficacy; Adherence; Value; How to Use; Choice; Tolerability. Janssen-Cilag believed that a sub-section in the Introduction which focused on the importance of relapse prevention was pertinent to this complaint. It aimed to raise awareness of the importance of relapse prevention in schizophrenia. It contained no claims about the neuroprotective effects of Risperdal Consta.

The page Janssen-Cilag believed was at issue provided information, supported by cited references, that recurrent relapses could lead to progressive brain tissue loss. It also showed images of grey matter deficits at baseline and 5 years later in patients with early onset schizophrenia. This link between relapse and brain tissue loss, which was supported by a credible body of evidence, was one of several reasons why preventing relapse was integral to the treatment of schizophrenia.

Janssen-Cilag submitted that its representatives had been trained on the appropriate use of the electronic detail aid verbally at a meeting in May 2009, after which they were sent a hard copy guidance document. The guidance stated that the relevant page was designed to highlight the impact of recurrent relapses, and of the potential for progressive brain tissue loss in schizophrenia. No guidance was given to make any link to Risperdal Consta or risperidone.

The final statement on the page in question 'Risperdal Consta can help prevent relapse and help patients achieve remission' referred to the clinical profile of Risperdal Consta. The statement was in a separate box at the foot of the page, and was supported by relevant literature about relapse prevention and remission data for Risperdal Consta.

A 'pop-up' link from this page, labelled 'Latest Thinking', stated 'A recent review of evidence suggests that some atypicals may have greater neuroprotective effects (i.e. preventing or reversing the frontocortical grey matter decline seen in schizophrenia patients) compared to conventional agents.' This statement accurately reflected the nature of the review article cited, which suggested that typical and atypical antipsychotics might have differential effects in terms of neuroprotection. This article was a recent, comprehensive review by leading experts on the latest thinking in the area of neurodegeneration in schizophrenia and it was this that was sent to the complainant following the representative's call.

Janssen-Cilag stated that the briefing document provided clear guidance to representatives that the information contained within this article provided a suggestion of neuroprotective effects of atypical antipsychotic medications. There was no guidance to them to make any link to Risperdal Consta or risperidone specifically, nor to draw any further conclusions from this paper.

To summarise, the briefing document confirmed that neuroprotection had not been presented as a claim for Risperdal Consta. The current thinking on the link between relapse and progressive brain tissue loss in schizophrenia had been included as relevant information to support the rationale for the importance of relapse prevention in the management of schizophrenia. The referenced information for the section in the 'pop-up' discussed atypical antipsychotics, of which risperidone was one of several available in the UK.

In all directive communication about Janssen-

Cilag's marketing strategy and guidance to the representatives there was no suggestion that they should link the concept of neuroprotection to Risperdal Consta specifically or that any such association was part of Janssen-Cilag's strategy. Wording and supportive guidelines were clear in relation to this.

Given the evidence cited above, Janssen-Cilag believed that the information in the section of the electronic detail in question was accurate, balanced and fair and did not breach Clause 7.2; the information was capable of substantiation and therefore not in breach of Clause 7.4. The representatives were adequately and appropriately briefed on the use of the materials so Janssen-Cilag believed that this was not in breach of Clause 15.9. The actions of the representative were consistent with the guidance given and, as the complainant was not concerned with the actions of the representative in question, Janssen-Cilag did not believe there had been a breach of Clause 15.2. Janssen-Cilag therefore did not agree there had been any breach of Clauses 7.2, 7.4, 15.2 or 15.9 in relation to the issues raised by the complainant.

However, as mentioned above, Janssen-Cilag took the views of health professionals very seriously. It strove to be a trusted partner to the health professionals with whom it interacted. It was extremely concerned that a clinician had found cause to complain about its marketing activities. In light of this, although it did not believe its materials to be misleading, as a clinician had raised concerns, it would further review them to ensure they transparently reflected Janssen-Cilag's intended communication.

PANEL RULING

The Panel noted that it had not been provided with a copy of the entire presentation at issue. Janssen-Cilag had identified and disclosed the section it considered pertinent to the complaint; a sub-section which discussed relapse prevention and comprised 16 slides. The product logo appeared in the bottom right hand corner of each slide. The first 4 slides were headed 'Every relapse counts … give your patients the choice of Risperdal Consta earlier' and included the statement 'The first few years of illness have been proposed as a critical period during which an aggressive and relapsing course may lead to accruing morbidity and persistent deficits'. Six subsequent slides discussed early and late grey matter deficits in schizophrenia beneath the heading 'Recurrent relapses can lead to progressive brain tissue loss'. Below diagrams depicting early and late grey matter deficits was the claim 'Risperdal Consta can help prevent relapse and help patients achieve remission'. All the slides included the statement 'Latest thinking'. A pop-up box on slides 9 and 10 referred to a recent review (Lieberman *et al*) which suggested that some aytpicals had greater neuroprotective effects ie preventing or reversing the frontocortical grey matter decline seen in schizophrenia patients compared to conventional agents.

The Panel noted that the representatives were trained verbally on the presentation at issue, after which the guidance document was sent to them. The guidance document instructed representatives to create a sense of urgency and to obtain agreement that relapse prevention was a key outcome. When showing the slides which discussed early and late grey matter deficits in schizophrenia (slide 5) representatives were instructed to discuss the impact of recurrent relapses and progressive brain tissue loss. Alongside the pop-up box which referred to neuroprotective effects (slide 9) representatives were told to discuss the 'suggested neuroprotective effects of aytpicals (Lieberman)'. No further guidance was given about the ensuing discussion on neuroprotective effects.

The Panel noted that Lieberman *et al*, a review article, concluded that schizophrenia 'possibly' involved a limited neurodegenerative component. Whilst more work was needed, the bulk of the data supported the authors' tentative conclusion that some antipsychotics, mainly the second generation antipsychotics, might be neuroprotective in schizophrenia.

The Panel considered that although there was no explicit claim about Risperdal Consta and neuroprotection, the slides very clearly linked the two. The first four slides referred to relapse and persistent deficits. The next six slides referred to relapses, progressive brain tissue loss and early and late grey matter deficits. All of these slides included a claim that Risperdal Consta '… can help prevent relapse and help patients achieve remission' and the product logo. Representatives were instructed to refer to the suggested neuroprotective effects of atypical antipsychotics. In the Panel's view the overwhelming impression was that Risperdal Consta had neuroprotective effects. The material was misleading and incapable of substantiation in this regard. A breach of Clauses 7.2 and 7.4 was ruled. Consequently, when presenting the material, the representative had failed to comply with all the relevant requirements of the Code. A breach of Clause 15.2 was ruled.

The Panel noted the clear link in the presentation between Risperdal Consta and neuroprotection and considered that in that regard it was inevitable that the briefing material advocated a course of action likely to lead to a breach of the Code. A breach of Clause 15.9 was ruled.

During its consideration of this matter the Panel noted the tentative conclusion of Lieberman *et al* ie that the atypical antipsychotics might have a neuroprotective effect in schizophrenia. The supplementary information to Clause 7.2, emerging clinical or scientific opinion, stated that when a clinical or scientific issue existed which had not been resolved in favour of one generally

accepted viewpoint, particular care must be taken to ensure that the issue was treated in a balanced manner in promotional material. In the Panel's view claims that a medicine or a class of medicines might do to something rarely negated the impression that they did do something. Lieberman *et al* was a literature review and the authors noted the inconsistency and variability of the results of the studies reviewed; not all of the atypical antipsychotics had been fully evaluated. The Panel asked that Janssen-Cilag be advised of its concerns in this regard.

Complaint received **29 July 2009**

Case completed **8 September 2009**