CASE AUTH/2794/9/15

BAYER v ACTAVIS

Promotion of Levosert

Bayer complained about a Levosert leavepiece issued by Actavis UK. Bayer marketed Mirena. Both Levosert and Mirena were intrauterine delivery systems (IUSs) each containing 52mg levonorgestrel; both were indicated as long acting, reversible contraceptives and of particular use in women with heavy menstrual bleeding who required contraception. Levosert was effective for 3 years and then should be removed; Mirena was effective for 5 years and then should be removed. Mirena was additionally indicated for protection from endometrial hyperplasia during oestrogen replacement therapy and was effective in that regard for 4 years after which it should be removed.

The detailed response from Actavis is given below.

Bayer alleged that the claim 'Can a single IUS be suitable for so many women?' was ambiguous, misleading, did not encourage the rational use of Levosert and could not be substantiated; it implied that Levosert was suitable for the majority of women/more women than other IUSs. Bayer noted that Levosert had a more limited licence than Mirena, with fewer indications and a shorter licensed duration of use, limiting its suitability for some women.

The Panel noted that although the title of the leavepiece 'Can a single IUS be suitable for so many women?' was presented as a question, the claim implied that Levosert was suitable for more women than other IUSs. In that regard, the Panel noted that Levosert was indicated for use in fewer women than Mirena as it was not indicated for protection from endometrial hyperplasia during oestrogen replacement therapy. As a contraceptive, Levosert was contraindicated in more women than Mirena as it could not be used in those with active or previous severe arterial disease such as stroke or myocardial infarction; such conditions were only contraindications for Mirena when it was used in conjunction with an oestrogen for hormone replacement therapy.

The Panel noted Actavis's reference to a 2005 review of Mirena which stated that the device was generally not recommended as the first method of choice in young, nulliparous women. Further, that the guidance had changed. In its updated clinical guideline on long-acting reversible contraception (LARC), the National Institute for Health and Care Excellence (NICE) now stated that all LARC methods were suitable for nulliparous women. Mirena was not contraindicated in nulliparous women. Overall the Panel considered that the claim implied that Levosert had a broader use than other IUSs which was not so. In the Panel's view the claim was misleading, could not be substantiated and did not encourage the rational use of Levosert. Breaches of the Code were ruled.

Bayer further alleged that the claim 'Levosert is available at a low acquisition cost. 25% saving compared to Mirena' was inaccurate and misleading. Levosert could not be compared with other IUSs and that the comparison with Mirena in particular could mislead by placing undue emphasis on the acquisition cost saving, without clearly stating that it had different licensed indications and duration of use. It was not a like-for-like comparison. For five years Mirena cost less per year than Levosert.

The Panel noted that the claim, on a page entitled 'Effective contraception for so many women', appeared in a prominent red circle on a white background. Above the circle was the statement 'All these benefits at a competitive price'. The Panel noted that the duration of effect of Levosert was shorter than that of Mirena and so in that regard their 'usage rates' differed. Levosert was effective for three years after which it had to be removed (a new IUS could be inserted if required); Mirena was effective for 5 years after which it had to be removed (again, a new IUS could be inserted if required). Levosert cost £66 (£22/year) and Mirena £88 (£17.60/year). The Panel noted that Actavis had submitted data to show that on average, women only retained Mirena for approximately 2 years and 10 months. From a population of 2,572, 53% of women retained Mirena for up to 3 years (ie for no longer than they could have retained Levosert). For these women it would have been less expensive if they had been prescribed Levosert. However, 47% of women used Mirena for longer than three years and for up to eight years. For women who used Mirena for no more than 8 years, it would have been less expensive to prescribe Mirena for the first five years and then switch to Levosert. The cost calculations were not straightforward.

The Panel considered that the claim at issue implied that the cost of contraception with Levosert would always be 25% less than with Mirena, which was not so. In the Panel's view the claim did not provide enough information for the prescriber to make a well informed decision. The Panel considered that the claim was misleading as alleged and a breach of the Code was ruled.

Bayer alleged that high standards had not been maintained.

The Panel noted its rulings of breaches of the Code above and considered that high standards had not been maintained. A breach of the Code was ruled.

Bayer complained about a four page Levosert leavepiece (ref UK/LE/0001/01-15b) issued by Actavis UK Ltd. Bayer marketed Mirena. Both Levosert and Mirena were intrauterine delivery systems (IUSs) each containing 52mg levonorgestrel; both were

indicated as long acting, reversible contraceptives (LARCs) and of particular use in women with heavy menstrual bleeding who required contraception. Levosert was effective for 3 years and then should be removed; Mirena was effective for 5 years and then should be removed. Mirena was additionally indicated for protection from endometrial hyperplasia during oestrogen replacement therapy and was effective in that regard for 4 years after which it should be removed.

1 Claim 'Can a single IUS be suitable for so many women?'

This claim appeared as the title on the outside cover of the leavepiece.

COMPLAINT

Bayer alleged that the claim was ambiguous and misleading. Although it was posed as a stylised question, it was an implied claim which indicated that 'a single IUS' ie Levosert was suitable for the majority of women/more women than other IUS options. Bayer noted that Levosert had a more limited licence than Mirena, with fewer indications and a shorter licensed duration of use, limiting its suitability for some women. Bayer alleged that the ambiguous statement did not encourage the rational use of Levosert, it was all-embracing and could not be substantiated. Bayer alleged breaches of Clauses 7.2, 7.4 and 7.10.

RESPONSE

Actavis submitted that Bayer's comparison with Mirena was irrelevant as the title was not a comparison and Clause 7.3 had not been cited.

Actavis agreed that the title 'Can a single IUS be suitable for so many women?' was a question and one that challenged health professionals who delivered contraceptive services to consider the suitability of a new product, Levosert, to many different types of women. This had been carefully reinforced by the imagery, which sensibly did not portray every type of woman, nor fill the page with lots of women.

Actavis submitted that in its view it had not stated or implied that all women or the majority of them should be prescribed Levosert. The title was a claim and was placed as a question to encourage further thought on this matter and encourage prescribers to consider the suitability of Levosert as a new IUS, for women they might not have originally considered (such as young nulliparous women). Importantly, the claim was in line with the recommendation from the National Institute for Health and Care Excellence (NICE) that an increase in the uptake LARCs would reduce the number of unintended pregnancies.

In terms of substantiation for the claim, Actavis noted that Levosert was studied in a very large IUS study, which included many diverse groups of women including a high percentage of nulliparous women, parous women, women aged between 16–45 years, and with a range of body mass indices (Eisenberg *et al* 2015).

Actavis also noted that an old review article on Mirena stated that its use 'was not generally recommended as the first method of choice for young nulliparous women' (Sitruk-Ware and Inki 2005). Guidance had changed over the years and the young, nulliparous women in the Levosert study were especially important to consider in light of the recommendation from NICE about the uptake of LARCs.

Actavis therefore submitted that the claim 'Can a single IUS be suitable for so many women?' was not misleading, all-embracing or incapable of substantiation and therefore it denied any breach of Clauses 7.2, 7.4 or 7.10.

PANEL RULING

The Panel noted that the title of the leavepiece was 'Can a single IUS be suitable for so many women?'. Above the claim was the stylised drawing of what seemed to be three different head shots of the same young woman. The Panel noted that although the claim was presented as a question, it implied that Levosert was suitable for more women than other IUSs. The Panel noted Actavis's submission that the question prompted health professionals to consider using Levosert. In that regard, the Panel noted that Levosert was indicated for use in fewer women than Mirena in than Levosert was not indicated for protection from endometrial hyperplasia during oestrogen replacement therapy. In terms of its use as a contraceptive, Levosert was contraindicated in more women than Mirena in that it could not be used in those with active or previous severe arterial disease such as stroke or myocardial infarction. Active or previous severe arterial disease, such as stroke or myocardial infarction was only a contraindication when Mirena was used in conjunction with an oestrogen for hormone replacement therapy.

The Panel noted Actavis's reference to a 2005 review of Mirena which stated that the device was generally not recommended as the first method of choice in young, nulliparous women. Further, that the guidance had changed. In its updated clinical guideline on LARC, NICE now stated that all LARC methods were suitable for nulliparous women. Mirena was not contraindicated in nulliparous women.

Overall the Panel considered that the claim implied that Levosert had a broader use than other IUSs which was not so. In the Panel's view the claim was misleading and a breach of Clause 7.2 was ruled. The Panel further considered that the implied claim could not be substantiated and a breach of Clause 7.4 was ruled. The Panel considered that the claim did not encourage the rational use of Levosert. A breach of Clause 7.10 was ruled.

2 Claim 'Levosert is available at a low acquisition cost. 25% saving compared to Mirena'

This claim appeared on page 3 of the leavepiece.

COMPLAINT

Bayer noted that whilst Actavis had agreed to make the licensed duration of use more prominent in its materials, it refuted the need to make it clear that Levosert had a shorter licensed duration when it made claims about cost.

Bayer noted that page three of the leavepiece stated 'All these benefits at a competitive price' and 'Levosert is available at a low acquisition cost. 25% saving compared to Mirena'. Bayer alleged a breach of Clause 7.2 as the supplementary information stated 'Price comparisons, as with any comparison, must be accurate, fair and must not mislead. Valid comparisons can only be made where like is compared with like'. Bayer alleged that Levosert could not be compared with other IUSs and that this comparison with Mirena in particular could mislead by placing undue emphasis on the acquisition cost saving, without clearly stating that it had different licensed indications and duration of use. It was not a like-for-like comparison. The acquisition cost of Mirena was £88 while Levosert cost £66. If used in line with licensed durations of five and three years respectively, Mirena cost £17.60 per year, whereas Levosert cost of £22 per year. For five years Mirena cost less per year than Levosert. Bayer alleged that the claim was thus inaccurate and misleading to prescribers.

RESPONSE

Actavis stated that the claim was clear both in intent and impression; it referred to the 'acquisition cost' alone and did not incorrectly imply costs per year or cost-effectiveness.

Actavis stated that it had taken various PMCPA rulings into account when it created and approved the use of the claim, notably Cases AUTH/2638/9/13 and AUTH/2639/9/13, where the Panel commented that 'comparisons based on acquisition cost alone were not prohibited by the Code'.

Actavis stated that although Bayer asserted that 'Levosert could not be compared with other IUSs', it considered that it was valid to compare costs of Levosert with Mirena as long as this was made on the basis of the equivalent dosage requirement for the same indications. Levosert and Mirena were both IUSs that contained the same total amount of levonorgestrel with a similar release profile and both were licensed for contraception. Further, the claim was on a page entitled 'Effective contraception for so many women'. Therefore it was clear that contraception was the indication being discussed.

Actavis noted Bayer's view that if Levosert and Mirena were 'used in line with licensed durations …' then their respective costs per year differed. This would be true if there was evidence to suggest that all Mirena patients retained their IUS for 5 years. A retrospective analysis of anonymised electronic patient records for patients who had been prescribed Mirena (in 2006/7 and followed longitudinally until 2013), suggested the mean average duration of insertion was 2.82 years; only 1/3 abided to the 5 year licence (34.8%).

Actavis also noted that NICE reported that up to 60% of women stopped using their IUS within 5 years for various reasons. This was not an insignificant number and therefore it was entirely appropriate to compare Levosert and Mirena acquisition costs, so that a health professional could make informed decisions, particularly if they had previous experience of patients retaining their IUS for up to 3 years. The claim was clear in that acquisition costs alone were compared and not costs/year.

Therefore Actavis submitted that the claim 'Levosert is available at a low acquisition cost, 25% saving compared with Mirena' was accurate, not misleading and it denied a breach of Clause 7.2.

PANEL RULING

The Panel noted that comparisons based on acquisition cost alone were not prohibited by the Code. The supplementary information to Clause 7.2 made it clear that, as with any comparison, price comparisons must be accurate, fair and must not mislead. Valid comparisons could only be made where like was compared with like. It followed therefore that a price comparison should be made on the basis of the equivalent dosage requirement for the same indications. For example to compare the cost per ml for topical preparations was likely to mislead unless it could be shown that their usage rates were similar or, where this was not possible, for the comparison to be qualified in such a way as to indicate that usage rates differed.

The Panel noted that the claim at issue, 'Levosert is available at a low acquisition cost. 25% saving compared to Mirena' appeared in a prominent red circle on a white background. Above the circle was the statement 'All these benefits at a competitive price'. The Panel noted that the duration of effect of Levosert was shorter than that of Mirena and so in that regard their 'usage rates' differed. Levosert was effective for three years after which it had to be removed (a new IUS could be inserted if required); Mirena, with which it was compared, was effective for 5 years after which it had to be removed (again, a new IUS could be inserted if required). The cost of Levosert was £66 (£22/year) and the cost of Mirena was £88 (£17.60/year). The Panel noted that Actavis submitted data to show that on average, women only retained Mirena for approximately 2 years and 10 months. From a population of 2,572, 53% of women (n=1,372) retained Mirena for up to 3 years (ie for no longer than they could have retained Levosert). For these women it would have been less expensive if they had been prescribed Levosert. However, 47% of women (n=1,200) retained Mirena for longer than three years and used it for up to eight years. For women who used Mirena for no more than 8 years, it would have been less expensive to prescribe Mirena for the first five years and then switch to Levosert. The cost calculations were not straightforward.

The Panel considered that the claim at issue implied that the cost of contraception with Levosert would always be 25% less than with Mirena, which was not so. In the Panel's view the claim did not provide

enough information for the prescriber to make a well informed decision. The Panel considered that the claim was misleading as alleged and a breach of Clause 7.2 was ruled.

3 Alleged breach of Clause 9.1

COMPLAINT

Bayer alleged that in persisting with the claims referred to above which misled prescribers and other decision makers, Actavis had failed to maintain high standards in breach of Clause 9.1.

RESPONSE

Actavis submitted that compliance with the Code was taken very seriously across the organisation. Clear reasons had been given as to why the Code had not been breached in relation to Bayer's allegations above. It therefore followed that high standards had been maintained and there was no breach of Clause of 9.1.

PANEL RULING

The Panel noted its rulings of breaches of the Code above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **11 September 2015**

Case completed **21 October 2015**