Appeal ASMI Complaints Panel Determination

Dated 4 May 2015

Bayer Australia Ltd ("Bayer")

v

Johnson & Johnson Pacific Pty Ltd ("JJP")

Zyrtec® Advertisements

Hearing – 22 June 2015

Arbiter's Determination

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Bayer Australia Ltd ("Bayer")

v

Johnson & Johnson Pacific Pty Ltd ("JJP")

Zyrtec® Advertisements

1 This is an appeal by Bayer against a determination made by the ASMI Complaints Panel (**the Panel**) on April 23, 2015. Bayer has appealed against a finding by the Panel that a Claim (**Claim 1**) made in print advertisements that Zyrtec® "*starts to work faster than Claratyne® for hay fever relief*" is not misleading and deceptive to the extent that it represents that Zyrtec in conventional tablet form starts to work faster than Claratyne in conventional tablet form.

2 The print advertisement is a display advertisement used at bus stops and pharmacy stores which contain Claim 1 linked to the following disclaimer at the bottom of the advertisement:

"Based on the first dose of cetirizine (Zyrtec®) v loratadine (Claratyne®) tablets" (**the Disclaimer**).

3 The Disclaimer was supported by references to studies by Meltzer[1], Day 1998[2], Day 2001[3] Greisner 2004[4] and Ellis 2013[5] (the Journal Articles).

4 It should be noted that the Panel found that where Claim 1 had been made in television advertisements, the Disclaimer would not have been seen by consumers and that accordingly they would be left with the "*dominant impression*" that Zyrtec, in any form, starts to work faster than Claratyne in any form.[6] The Panel concluded that the journal articles on which JJP relied in the Disclaimer only established that Zyrtec tablets (in conventional form) started to work faster than Claratyne tablets (in conventional form).[7] It therefore found that since viewers of the television advertisement were unlikely to have understood the comparison to be confined to tablets, the television advertisement containing Claim 1 was misleading because it was not confined to Zyrtec tablets as compared with Claratyne tablets.[8] JJP did not appeal that determination.

5 The appeal is limited to the print advertisements. Accordingly, although Bayer submits[9] that *"the key question which the arbiter must answer (leaving aside the disclaimer in the*

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[1] Meltzer et al. J Allergy Clin Immunol 1996.
[2] Day et al. J Allergy Clin Immunol 1998.
[3] Day et al. Asthma Immunol 2001.
[4] Greisner. Allergy and Asthma Proc 2004.
[5] Ellis et al. Allergy, Asthma & Clin Immunol 2013.
[6] Para 57 of the Panel's Determination.
[7] Para 58 of the Panel's Determination.
[8] Para 64 and 67 of the Panel's Determination.
[9] Para 12 of its appeal submissions

advertisements) is whether the data submitted by JJP substantiates a Claim that Zyrtec® "starts to work faster" than Claratyne®", this question is to be answered in the context of the Disclaimer which limits the Claim to a comparison between Zyrtec in conventional tablet form starts and Claratyne in conventional tablet form (i.e. what Bayer has called *"the **Tablet Claim**"*).

6 The main basis for Bayer's contention that the studies relied upon by JJP do not support the Tablet Claim is its assertion that to substantiate a Claim of this type, studies would need to be conducted in which each subject was treated with both Claratyne and Zyrtec at separate times (i.e. a cross over study) and an assessment would have to be made as to the onset of action of, and symptomatic relief afforded by, each drug.

7 Bayer says that the Meltzer, Day 1998 and Day 2001 studies were not cross over studies but compared the onset of cetirizine with its placebo and loratadine with its placebo. In relation to Ellis, it says that the study cannot be relied upon even though it was a cross over study because it didn't take into account factors including but not limited to bulking agents, other excipients and tablet compression which could have had a material effect on the dissolution and absorption rate of the active ingredient.

8 Bayer says further that Greisner 2004, which is a literature review was based largely on the Meltzer and Day studies and accordingly also could not be relied upon by JJP in support of the Tablet Claim.

9 Bayer emphasises that it does not criticise the design or results of the studies relied upon by JJP but says that its key criticism is that they do not substantiate the Tablet Claim.[10]

10 In addition to the study design issue, Bayer says that:

(a) the Meltzer, Day 1998 and Day 2001 studies used encapsulated loratadine (Claratyne®) tablets and therefore cannot be used to substantiate a Claim regarding conventional tablets (**the Encapsulation Argument**)[11]; and

(b) the Journal Articles which are quoted in the Disclaimer do not specify the type of cetirizine and loratadine administered and therefore leave open the possibility that due to differences in formulations and excipients the results of those studies may not reflect the onset of action of the formulations of Claratyne® and Zyrtec® marketed in Australia[12] (**the Formulation Argument**).

Study Design

11 In oral submission on appeal, counsel for JJP referred in detail to the studies relied upon by JJP. In particular, he pointed out that:

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[10] Para 15 of Bayer's appeal submissions.
[11] Para 14.1 of Bayer's appeal submissions.
[12] Para 14.2 of Bayer's appeal submissions.

(a) the stated objective of the Meltzer study was to compare the efficacy duration and onset of action of cetirizine 10mg once daily as compared to that of loratadine 10mg once daily and placebo in a field study of patients with seasonal allergic rhinitis. The study records that:

"This is the first full report of a study ***directly comparing the symptomatic effects of cetirizine and loratadine*** *in patients with seasonal allergic rhinitis in a clinical setting."* (emphasis supplied)

The Meltzer study found that "C*etirizine relieved* rhinitis symptoms more effectively and quickly than loratadine and placebo..."[13]. It also went on to say that *"these findings are consistent with effects observed in several laboratory based studies".*[14] The Meltzer study further found that the onset of action of cetirizine was apparent within two hours of administration compared with five hours with loratadine.[15]

(b) the objective of the Day 1998 study was *"To better categorise the efficacy and onset of action of cetirizine ... compared with loratadine and placebo in patients with symptomatic seasonal allergic rhinitis ...".* The study noted that in the Meltzer study cetirizine had been found to produce significantly greater symptomatic relief when compared with loratadine or placebo and went on to point out that *"this study was designed to further explore the clinical characteristics of cetirizine and loratadine* ***in a rigorously controlled yet clinically relevant setting.***" (emphasis supplied). It found that onset of action was evident within one hour with cetirizine and three hours with loratadine;

(c) the Day 2001 study had as its objective the confirmation of a previous study in the EEU comparing cetirizine, loratadine and placebo. Again, the study found that onset of action with cetirizine occurred at one hour and at three hours with loratadine;

(d) the Greisner study conducted a literature search from 1985 to May 2002 of all clinical studies pertaining to the onset of action for relief of allergic rhinitis symptoms after a singe oral dose of a second generation antihistamine including cetirizine and loratadine. It found that cetirizine had a shorter onset of action than loratadine for all comparisons.

12 Counsel therefore submitted that each of the Meltzer and Day studies had been specifically designed to compare the onset of action of cetirizine against loratadine. Each of those studies had been peer reviewed and were published in well regarded journals. Their results were consistent and supported the Claim made by JJP in the advertisement. Further, although the Ellis study set out to evaluate the onset of action of azelastine nasal spray versus the oral antihistamines loratadine 10mg and cetirizine 10mg in the relief of seasonal allergic rhinitis, its results were consistent with the other studies.

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[13] Page 638 of the Study.
[14] Page 625 of the Study.
[15] Page 622 of the Study.

13 In its written submissions, Bayer says that in coming to the conclusion that the Journal Articles do establish the Tablet Claim, the Panel appears to have accepted JJP's argument that a cross over study is not required to substantiate that Claim because that design is not prescribed by the Code, the TGAC or FDA Guidance.[16] Bayer says that the Code and the TGAC do not and cannot be expected to prescribe the study designs to prove every type of product claim. Moreover it says that the FDA Guidance which does contemplate studies comparing trials which are not identical in design and which are placebo controlled cannot be taken as definitive authority on the adequacy of substantiating data.[17]

14 Bayer further goes on to repeat that because the onset of action in antihistamine products is highly patient specific, only a cross over study in which each patient acts as his or her own control can provide sufficient substantiation as to whether one product has faster action than the other.[18]

Determination on study design

15 In my view, it is clear from their stated objectives that the Meltzer and Day studies were specifically designed to compare the onset of action of cetirizine versus loratadine. They were peer reviewed and published upon the basis that the study designs were clinically acceptable. They made clear findings, none of which have been scientifically challenged by any published article. I note in particular that the Day 1998 study expressly recorded that it was being conducted in a rigorously controlled yet clinically relevant setting. Bayer does not appear to dispute this.

16 The only challenge which is made to their findings is the *"logical"* argument presented by Bayer. It seems to me that where there is published scientific evidence to substantiate a Claim of the nature made in this case, if a party wishes to challenge that evidence, it would be necessary for that party to provide more than an assertion that it is logical that evidence is to be disregarded. This is particularly so in a context in which the study design which is being challenged has been expressly accepted by peer review.

17 In my view, the Panel was correct in accepting that the studies quoted in the Disclaimer were sufficient to support the Tablet Claim. Moreover, the Greisner study conducted a complete literature review on the topic and its findings were consistent with the Tablet Claim. Bayer has not produced any published study to contradict this. In the circumstances, I believe the Panel's Determination should stand on this aspect.

Encapsulation

18 Bayer has criticised the Panel's decision to accept that encapsulation of the loratadine tablets which occurred in the Meltzer and Day studies was unlikely to have a significant effect on time to onset of action and would not have affected the outcome sufficiently to

[16] Para of 58 of the Determination and para 27 of Bayer's submissions.
[17] Para 28 of Bayer's submissions and para 40 of the Panel's Determination.
[18] Para 29 of Bayer's appeal submissions.

overcome the four-hour time difference observed by Meltzer or the two-hour time difference observed in the Day studies.[19]

19 Bayer says that the Panel implicitly accepted JJP's submission that according to Australian Regulatory Guidelines for OTC Medicines (ARGOM) various immediate release oral dosage forms (e.g. tablets, capsules, oral liquids or suspensions) can be considered to be one and the same pharmaceutical form. It says that reliance on this statement in the ARGOM by the Panel is misplaced because although tablets and capsules may be considered to be the same pharmaceutical *"form"* it does not follow that where they contain the same active ingredient they will therefore have the same onset of action.

20 Bayer therefore submitted that because encapsulation could affect the pharmacokinetic profile of a medicine by slowing dissolution and absorption, the use of encapsulated tablets **may** have contributed to the slower onset of action of loratadine observed in the studies relied upon by JJP.[20]

21 In this regard JJP points out that the Panel contains members who are qualified to comment on these issues and that they were correct in finding that encapsulation is a common method used in clinical trials to ensure that tablets cannot be identified. I note that Bayer did not in fact challenge the finding that encapsulation was a common method used in clinical trials to ensure that tablets cannot be identified.

22 The Panel found that encapsulation was unlikely to have such a significant effect that it would cause the differences found by the studies. JJP points out that the Day studies did confirm, based on dissolution times, that the encapsulated loratadine tablet was equivalent to the loratadine tablet alone, i.e. that encapsulation did not affect the onset of action times.[21] In this regard, Counsel for JJP drew my attention to page 640 of the Day 1998 study in which the authors specifically state that *"The dissolution of the encapsulated loratadine tablet was equivalent to that of the loratadine tablet alone"*.

23 In the Day 2001 study the authors state that *"The dissolution of the encapsulated loratadine tablet was demonstrated to be equivalent to that of the loratadine tablet alone."* Thus, both of the Day studies clearly considered the effect of the tablet being encapsulated and found that there was none.

Determination on Encapsulation

24 Bayer has provided no evidence to show that the findings in the two Day studies in relation to the rate of dissolution of the encapsulated tablets was in any way incorrect. It has also produced no evidence to show that encapsulation in the Meltzer study had any real impact on its outcome. It follows in my view therefore that the Panel was correct in accepting that the fact that the loratadine tablet in the Meltzer and Day studies was encapsulated did not impact on the results of those studies in a way which would cast doubt upon their correctness.

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[19] Para 16 of Bayer's appeal submissions.
[20] Para 19 of Bayer's Appeal Submissions (emphasis supplied).
[21] Para 21 – JJP Appeal Response.

25 The fact that Bayer suggests that the encapsulated tablets *"may have"* contributed to the slower onset of action of loratadine is in my view no more than speculation and without any scientific evidence to support it, this is not a basis for overturning the Panel's decision.

Formulation of Products

26 Bayer criticises the Panel for coming to the conclusion that it was satisfied that differences in excipients and formulations would not detract from its conclusion that the Journal Articles substantiate the tablet claim[22]. Again, Bayer's submission is that it is *"unclear"* whether the products used in the studies are bioequivalent to the Australian marketed formulations[23]. It therefore submits that it cannot be assumed that the pharmacokinetic profile of the formulations used in the studies will be the same as or similar to those of the Australian formulations of Zyrtec® and Claratyne®.

27 In response, JJP pointed out that each of the studies compares a 10mg cetirizine tablet with a 10mg loratadine tablet. The tablets sold in Australia are exactly the same dosage. Accordingly, there was no evidence to show that there was any difference in formulation of the Australian product.

Determination on Formulation

28 In my view, Bayer's submission again amounts to no more than speculation as to whether the products available in Australia might hypothetically be different from those which were studied in the Journal Articles. There is no evidence to suggest that the formulation of Zyrtec or Claratyne which was studied in those articles is any different from the formulations which are available in Australia.

29 I have accordingly come to the conclusion that the Panel was correct in determining that the Tablet Claim was not misleading and deceptive and is in fact supported by the Journal Articles to which reference is made in the Disclaimer.

Procedural Error

30 Bayer criticised the Panel's determination on the basis that the Panel merely adopted the arguments advanced by JJP and did not provide a critical analysis and assessment of both parties' submissions. It said this was a procedural error on the part of the Panel.

31 In my view, the Panel's decision clearly sets out the submissions by both Bayer and JJP. There is nothing to suggest that the Panel did not consider Bayer's submissions. The fact that the Panel adopted to some degree the submissions made by JJP does not mean it did so without due consideration or that it did so uncritically.

32 On the contrary, the essence of Bayer's submissions in relation to the matters before the Panel and which are now the subject of the Appeal amount to no more than speculation or to what it believes is a *"logical"* approach to study design. As I have said, Bayer did not seek to support its arguments in this regard with any scientific evidence but merely

[22] Para 62 of the Panel's Determination.
[23] Para 25 of Bayer's Appeal Submissions.

proffered its opinion which it repeatedly stated should be accepted by the Panel. In my view, the Panel was not obliged to go any further in dealing with those submissions than to do so in the way in which it did.

Procedural Fairness – Market Research Report

33 Bayer further submitted on Appeal that it was denied procedural fairness because the Panel refused to consider a Market Research Report which Bayer wished to rely upon but which was not included in its original complaint. The Panel rejected the Market Research Report because it contained new material and that there were no exceptional circumstances as to why it was not included in the original complaint.[24]

34 Bayer submitted[25] that the Market Research Report provided highly probative evidence from actual consumers of their interpretation of the representations in the Advertisements. It requested that I remit the determination to the Panel with a direction that the Panel reconsider Bayer's complaint in the light of the Market Research Report.[26]

35 As JJP pointed out in its response to Bayer's Appeal,[27] the question of how consumers may have perceived or interpreted the Advertisements was not an issue to be determined in the Appeal.

36 In my view, that submission is correct because:

(a) the Panel found that Claim 1, when it was contained in television advertisements, was misleading because consumers would not appreciate the terms of the Disclaimer. There is no Appeal from that determination;[28] and

(b) the Panel dismissed Claim 2 which was the subject of the original complaint because it found that it was not misleading. Bayer did not Appeal that Determination and it does not now suggest that the admissibility of the Market Research Report would have made any difference in relation to Claim 2;

(c) the matters raised by Bayer on this Appeal concerning the Tablet Claim have nothing to do with the perceptions of consumers.

37 Accordingly, the Market Research Report could not be of any assistance either to myself or to the Panel even if I were to remit the matter to it because it cannot go to the issue of whether the Tablet Claim is supported by scientific evidence.

38 It was suggested by Bayer in oral argument before me that the Market Research Report might be relevant to determine whether the sanctions imposed by the Panel in respect of the TV advertisement for Claim 1 were appropriate. However, there is no Appeal on that aspect. I accordingly refuse Bayer's request to remit.

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[24] Para 20 of the Panel's Determination.
[25] Para 36.3 of its appeal submission.
[26] Para 37 of Bayer's Appeal Submission
[27] Para 40
[28] Para 57 of the Panel's Determination

Sanctions

39 JJP submits that Bayer consistently sought to prosecute its complaint in a manner contrary to the intent of the Code and in particular:

(a) sought to submit the Market Research Report after JJP submitted its Formal Response;

(b) sought to include responses to JJP's Formal Response in its Second Formal Complaint dated February 9, 2015; and

(c) now seeks to do so under the guise of this Appeal.

40 JJP submits that Bayer's complaint and its Appeal was therefore submitted for vexatious reasons.

41 The first two matters referred to in paragraph 36(a) and (b) were considered by the Panel in coming to its decision under section 9.4.2.2 of the Code as to the contribution each party should make to ASMI's out of pocket expenses associated with the Determination of the complaint. There was no Cross Appeal by JJP as to the Determination made by the Panel in paragraph 76 that they should contribute two-thirds and that JJP should contribute one-third.

42 Although I have come to the view that Bayer's submissions are based largely upon its own view of the way in which studies comparing the effective onset loratadine and cetirizine should be conducted and its further suggestion that possible encapsulation of tablets and possible differences in formulations, I'm not convinced that Bayer does not genuinely hold those views. Indeed it advanced those views with significant determination both before the Panel and on Appeal.

43 Bayer has already been penalised for its failure to notify JJP of the Market Research Report and for including Responses to JJP's original Response in its proposed Second Formal Complaint by the Panel allocating costs as it did in its Determination. I do not consider that its submissions on Appeal were made for vexatious reasons.

44 I therefore:

(a) confirm the Panel's determination that JJP has shown that conventional Zyrtec tablets start to work faster than conventional Claratyne tablets and that Claim 1 is not misleading and deceptive in the form in which it appears in the print Advertisement which was the subject of the complaint;

(b) I confirm the Panel's sanctions as set out in Paragraphs 73 and 74 of the Determination (against which no Appeal is made); and

(c) I confirm Paragraph 76 of the Panel's Determination that Bayer should contribute two-thirds and that JJP should contribute one-third of ASMI's out of pocket expenses associated with the Determination of Bayer's complaint.

45 I further determine that having regard of the fact that Bayer has been unsuccessful in its Appeal, it should bear ASMI's out of pocket expenses associated with the Determination of the Appeal.

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Harold Werksman – Arbiter

6 July 2015