Federal Court  Cour fédérale

Date: 20140403

Docket: T-1517-13

Citation: 2014 FC 328

Toronto, Ontario, April 3, 2014

PRESENT: Madam Prothonotary Milczynski

BETWEEN:

VIIV HEALTHCARE ULC,
VIIV HEALTHCARE UK LIMITED AND
GLAXO GROUP LIMITED

Applicants

and

TEVA CANADA LIMITED AND
THE MINISTER OF HEALTH

Respondents

REASONS FOR ORDER AND ORDER

Summary of Issue and Disposition

[1] This is a motion brought by the Respondent, Teva Canada Limited ("Teva") for an order pursuant to section 6(5)(a) of the *Patented Medicines (Notice of Compliance) Regulations* ("*PMNOC Regulations*") dismissing the within Application in respect of Canadian Patent No.

2,289,753 (the "753 Patent") on the basis that the 753 Patent is not eligible for inclusion on the Patent Register.

[2] The 753 Patent is listed on the Patent Register in relation to the drug KIVEXA®, a fixed dose dual combination drug containing two medicinal ingredients: abacavir (as the hemisulfate salt, abacavir sulfate) and lamivudine. The Applicant ViiV Healthcare ULC ("ViiV") markets KIVEXA® under a Notice of Compliance ("NOC") first issued by the Minister on July 25, 2005, in respect of ViiV's new drug submission (NDS 087905) for the 600 mg abacavir sulfate/300 mg lamivudine tablet.

[3] Pursuant to section 4(2) of the *PMNOC Regulations*, a patent in relation to a new drug submission is eligible to be added to the patent register maintained by the Office of Patented Medicines and Liaison of Health Canada if the patent contains:

(a) a claim for the medicinal ingredient;

(b) the formulation that contains the medicinal ingredient;

(c) the dosage form; or

(d) a claim for the use of the medicinal ingredient, provided that the medicinal ingredient, formulation, dosage form or use has been approved through the issuance of a NOC in respect of the new or abbreviated new drug submission.

[4] The 753 Patent relates to and claims the medicinal ingredient, hemisulfate salt of abacavir (and solvates thereof). No claim of the 753 Patent specifically claims the combination of abacavir and lamivudine, which are the two medicinal ingredients comprising KIVEXA® as was set out in

the new drug submission for which the NOC was issued. The 753 Patent contemplates pharmaceutical formulations where one or more classes of therapeutic agents may be combined with abacavir, including classes that do not include lamivudine. The 753 Patent does not relate to dosage form or the use of the medicinal ingredient abacavir sulfate.

[5] Although the 753 Patent may encompass lamivudine as a medicinal ingredient, this does not satisfy the requirements for listing under either section 4(2)(a) or section 4(2)(b) of the *PMNOC Regulations*. It is not sufficient for the purposes of listing that a patent identify only one of the two (or more) medicinal ingredients identified in the drug submission in respect of which the NOC was issued. As held by the Federal Court of Appeal in *Gilead Sciences Canada v. Minister of Health*, 2012 FCA 254 ("*Gilead*"), the medicinal ingredient or formulation approved in the NOC must "match up" and be claimed in the patent sought to be listed. A high degree of specificity is required between the patent and the NOC. However, as noted, the NOC for KIVEXA® is for an abacavir sulfate/lamivudine tablet, and the 753 Patent claims only the medicinal ingredient, abacavir sulfate.

[6] Accordingly, and further to the more detailed reasons below, the motion is granted.

Background: Subject-Matter of NOC and Listing of the 753 Patent

[7] On October 31, 2003, GlaxoSmithKline Shire Biochem ("GSK") filed a new drug submission, NDS 087905 seeking approval to market tablets that were formulated with two medicinal ingredients: abacavir sulfate (600 mg) and lamivudine (300 mg), under the brand name "KIVEXA®". The KIVEXA® fixed dosage combination tablet is described as an alternative to the separate administration of each of abacavir sulfate and lamivudine tablets (marketed separately as

ZIAGEN® and 3TC respectively). As noted by the Applicants, from a chemical, scientific, clinical and regulatory standpoint, the medicinal ingredients in one KIVEXA® tablet are identical to two 300 mg ZIAGEN® tablets and one 300 mg tablet administered separately and concomitantly.

[8] A single KIVEXA® tablet, or taken together, two ZIAGEN® tablets (600 mg abacavir sulfate) and one 3TC tablet (300 mg lamivudine), are indicated in antiretroviral combination therapies for the treatment of Human Immunodeficiency Virus ("HIV") infection in adults. The Applicants state that the delivery vehicle of a single tablet in the case of KIVEXA® and fixed dose combination therapies generally, have been shown to be convenient and efficient, overall increasing adherence and satisfaction with the therapeutic regimen prescribed.

[9] The Product Monograph for KIVEXA® states that each KIVEXA® tablet contains 600 mg of abacavir sulfate and 300 mg lamivudine and that KIVEXA® "is one of multiple products containing abacavir".

[10] In addition, the Product Monograph discloses that each tablet contains the following non-medicinal ingredients: hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol 400, polysorbate 80, sodium starch glycolate, titanium dioxide and FD & C Yellow #6 Aluminum Lake.

[11] On July 25, 2005, the Minister of Health issued the Notice of Compliance ("NOC") for KIVEXA®, identifying the "medicinal ingredients" abacavir (supplied as abacavir sulfate) and

lamivudine, indicating the fixed dose: 600 mg abacavir/300 mg lamivudine. The NOC thus identifies two medicinal ingredients.

[12] On May 14, 1998, GSK filed its patent application in respect of the 753 Patent, which is entitled "Carbocyclic Nucleoside Hemisulfate and its Use in Treating Viral Infection", which patent was issued on January 23, 2007. GSK filed a new patent list on February 22, 2007 to list the 753 Patent on the Patent Register in respect of NDS 087905. The 753 Patent was added to the Register in respect of NDS 087905 for KIVEXA® on February 23, 2007.

[13] Subsequently, any generic drug manufacturer seeking a NOC to come to market for its 600 mg abacavir hemisulfate/300 mg lamivudine product would need to address the 753 Patent in the approval process – either waiting until the expiry of the patent after filing its abbreviated new drug submission, or delivering a notice of allegation, asserting the invalidity of the 753 Patent and/or that the 753 Patent would not be infringed. Whether those allegations were justified would then need to be determined by way of application (as in the within case) for an order prohibiting the Minister of Health from issuing the NOC until the 753 Patent's expiry on the grounds that the generic drug manufacturer's allegations of non-infringement and/or invalidity of the 753 Patent are unjustified.

[14] Without listing the 753 Patent on the Patent Register, and leaving aside any other patents that may be listed against the drug, a generic drug manufacturer could receive its NOC and go to market, and the Applicants would enforce their monopoly by way of action for patent infringement.

The 753 Patent

[15] There is no dispute between the parties regarding the proper construction of the 753 Patent. The 753 Patent relates to the hemisulfate salt of abacavir. Claim 1 is a claim to abacavir hemisulfate and solvates thereof. Claim 2 depends on Claim 1, and expressly and exclusively claims abacavir hemisulfate, one of the medicinal ingredients in KIVEXA®. There is no claim of the 753 Patent that specifically claims the combination of abacavir and lamivudine, the two medicinal ingredients in KIVEXA®. Claim 32 of the 753 Patent, however, claims abacavir in combination with another or other medicinal ingredient(s), as follows:

> 32. A pharmaceutical formulation as claimed in any one of claims 25 to 31, additionally comprising one or more therapeutic agents selected from the group consisting of [1] nucleoside reverse transcriptase inhibitors, [2] non-nucleoside reverse transcriptase inhibitors, [3] protease inhibitors, [4] immune modulators and [5] interferons.

[16] The 753 Patent elaborates at page four, that abacavir may be used alone or in combination with a number of these therapeutic agents suitable in the treatment of HIV and HBV infections:

> The compounds of the invention may be administered alone or in combination with other therapeutic agents suitable in the treatment of HIV infections, such as Nucleoside Reverse Transcriptase Inhibitors (NRTIs) for example zidovudine, zalcitabine, lamivudine, didanosine, stavudine, 5-chloro-2',3'-dideoxy-3'-fluorouridine, adefovir and (2R,5S)-5fluoro-1-[2-(hydroxymethyl)-1,3-oxathiolan-5yl]cytosine, lovaride, non-NRTIs for example nevirapine, delavuridine, α-APA, HBY-1293 and efavirenz HIV protease inhibitors for example saquinavir, indinavir, nelfinavir, ritonavir and VX-478, other anti-HIV agents for example soluble CD4, immune modulators for example interleukin II, erthyropoetin, tucaresol, and interferons for example α-interferon. In addition the compound of the invention may be administered in combination with other therapeutic agents suitable in the treatment of HBV infections for example lamivudine, (2R,5S)-5-fluoro-1-[2-(hydroxymethyl)-1,3-oxathiolan-5yl]cytosine, immune modulators, and interferons as described above. Such combinations may be administered together or sequentially providing that any duration between the

> administration of each therapeutic agent does not diminish their additive effect.

[17] Claim 32 thus claims a fixed dose combination of abacavir hemisulfate and one or more of the therapeutic agents selected from the above-noted five defined classes, one of which is the class of nucleoside reverse transcriptase inhibitors, or NRTIs. There are nine specific NRTIs identified, one of which is lamivudine and some twenty-one therapeutic agents in all identified across the five classes (NRTIs, non-NRTIs, protease inhibitors, immune modulators and interferons) that may be selected in combination with abacavir. In other words, claim 32 of the 753 Patent is not limited to a two drug combination with a pharmaceutical formulation comprising abacavir hemisulfate and lamivudine. Claim 32 only includes or encompasses within its scope, a formulation that contains abacavir and another (unspecified) NRTI. Claim 32 contemplates any one or more classes of therapeutic agents that may be combined with abacavir, only one of which is lamivudine.

***PMNOC Regulations* – Eligibility for Listing**

[18] Subsection 4(2) of the *PMNOC Regulations* sets out the applicable patent listing eligibility requirements:

> 4(2) A patent on a patent list in relation to a new drug submission is eligible to be added to the register if the patent contains
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> a. a claim for the medicinal ingredient and the medicinal ingredient has been approved through the issuance of a notice of compliance in respect of the submission;
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> b. a claim for the formulation that contains the medicinal ingredient and the formulation has been approved through the issuance of a notice of compliance in respect of the submission;

> c. a claim for the dosage form and the dosage form has been approved through the issuance of a notice of compliance in respect of the submission; or
>
> d. a claim for the use of the medicinal ingredient, and the use has been approved through the issuance of a notice of compliance in respect of the submission.

[19] Section 2 of the *PMNOC Regulations* defines "claim for the formulation" as "a claim for a substance that is a mixture of medicinal and non-medicinal ingredients in a drug and that is administered to a patient in a particular dosage form". "Claim for the medicinal ingredient" is defined as including:

> A claim in the patent for the medicinal ingredient, whether chemical or biological in nature, when prepared or produced by the methods or processes of manufacture particularly described and claimed in the patent, or by their obvious chemical equivalents, and also includes a claim for different polymorphs of the medicinal ingredient, but does not include different chemical forms of the medicinal ingredient.

[20] As noted earlier above, there is no dispute amongst the parties that the 753 Patent claims abacavir sulfate, one of the approved medicinal ingredients in KIVEXA®. On this basis (the patent claiming "the" or one of the medicinal ingredients), the Applicants and the Minister submit that the 753 Patent is eligible for listing on the Patent Register pursuant to section 4(2)(a) of the *PMNOC Regulations*. Indeed, this approach is set out in Health Canada's 2010 Guidance Document that states that a patent that claims only one medicinal ingredient may be listed against an approved product containing more than one medicinal ingredient:

> Patents claiming a combination of medicinal ingredients are not eligible for listing in respect of a drug that contains only one of the claimed medicinal ingredients. However a patent claiming, as a compound, a single medicinal ingredient will be eligible for listing with respect to a drug that contains the said medicinal ingredient in combination with other medicinal ingredients, notwithstanding that

> the medicinal ingredient on the NOC is the combination of medicinal ingredients.

[21] Both the Applicants and the Minister state that in light of the above, the 753 Patent has the required product specificity for listing under section 4(2)(a) of the *PMNOC Regulations*. The one medicinal ingredient claimed in the patent (abacavir sulfate) is identified in the NOC for KIVEXA® and approved in the drug submission albeit in combination with another medicinal ingredient, namely lamivudine.

[22] The Minister further submits that this approach (requiring less than complete product specificity) should be contrasted with section 4(2)(b) of the *PMNOC Regulations* that deals with formulation claims in a patent that must contain a claim for a particular or specific mixture of medicinal and non-medicinal ingredients actually administered. A formulation that contains multiple compounds or medicinal ingredients must be a different formulation from one which contains a single compound – the formulation claimed in a patent cannot "match" the approved formulation in the NOC unless they both explicitly contain the same medicinal ingredients. If they do match, then the (formulation) patent is eligible for listing under section 4(2)(b) of the *PMNOC Regulations*.

[23] The Minister also relies on *Bayer v. Canada*, 2009 FC 1171, aff'd 2010 FCA 161 (a case concerning eligibility to list under section 4(2)(b) to argue that a different approach must be taken in interpreting section 4(2)(a) of the *PMNOC Regulations* than that taken to interpret section 4(2)(b). In that case, the Minister states that the Court found that the differences between single compound and formulation patents require a different approach when matching the claim(s) in a patent to what

was approved in the NOC for the purposes of determining the requisite degree of specificity for that patent's listing on the Patent Register. The policy rationale for the different approaches is described as one that recognizes that generally, the process of drug development results first in the discovery of a single medicinal ingredient for the treatment of a specific medical condition. After a drug is developed, and that medicinal ingredient is patented, an innovator may seek to combine that medicinal ingredient with other known medicinal ingredients in a formulation. To protect its combination product, an innovator may seek to list the patent claiming the single medicinal ingredient on the Patent Register against the combination product upon the issuance of the NOC for that product, under section 4(2)(a) of the *PMNOC Regulations*.

[24] Thus, according to the Minister and the Applicants, a patent for a compound that claims only abacavir sulfate and another compound patent claiming only lamivudine would each be eligible for listing against KIVEXA® under section 4(2)(a) of the *PMNOC Regulations*. A patent for a formulation containing a claim for a composition containing both abacavir sulfate and lamivudine would also be eligible for listing, under section 4(2)(b) of the *PMNOC Regulations*. According to the Applicants (but not the Minister or Teva), a patent for a formulation containing a claim for a composition that expressly claimed one of the medicinal ingredients, together with another unnamed medicinal ingredient but in a manner that "encompassed" the one identified in the NOC, would also be eligible for listing under section 4(2)(b) of the *PMNOC Regulations*. The issue is thus whether there are different approaches to product specificity as between sections 4(2)(a) and 4(2)(b), and/or whether each provision permits less than a complete match between the NOC and patent to meet the requirement of product specificity for listing.

[25] Teva notes that the *PMNOC Regulations* were amended in 2006 to make product specificity the key requirement for listing a patent on the Patent Register, and that this purpose is reflected in the *Regulatory Impact Analysis Statement* ("RIAS") published with the amendments;

> The amendments reflect this by further entrenching the concepts of product specificity as the key consideration required of the Minister in applying the listing requirements under section 4 of the PM(NOC) Regulations. They do so through more precise language respecting the intended link between the subject matter of a patent on a patent list and the content of the underlying submission for a NOC in relation to which it is submitted. In addition, under the amendments, only certain clearly defined submission types will provide an opportunity to submit a new patent list.

[26] In *Gilead Sciences Canada v. The Minister of Health*, 2012 FCA 254, the Court of Appeal commented on the impact of the RIAS:

> The 2006 revisions also clearly introduced the requirement for product specificity. A plain reading of the version in force prior to the 2006 revisions establishes that if the patent claims were shown to be "relevant to" the approved drug, the submitted patents were generally accepted for listing. In contrast, the revised version introduces a requirement for more detailed information on the product against which the patent is to be listed, including the medicinal ingredient, the brand name, the dosage form, the strength, the route of administration and the use as set out in the NDS. In addition, the categories set out in section 4 are now more detailed and precisely defined. These changes, combined with the greater emphasis on meeting eligibility criteria and being subject to the Minister's determination as noted above, lead to a clear rejection of Gilead's argument for a wide scope of connection between the patent claims and the NOC.

[27] In *Gilead*, Gilead Sciences sought to list on the Patent Register, a patent that claimed tenofovir, emtricitabine and an unidentified non-nucleoside reverse transcriptase inhibitor (NNRTI). The NOC for the drug COMPLERA, however, specified tenofovir, emtricitabine and the NNRTI rilpivirine. Because the patent did not specify the third medicinal ingredient in what was a triple

combination drug that was the subject of the NOC, the Court found that the patent was ineligible for listing:

> The wording of the PM(NOC) Regulations, as well as their object and purpose, suggest that the product specificity requirement sets a high threshold of consistency. Thus in the case at bar, "the" medicinal ingredient, i.e. tenofovir, emtricitabine and rilpirivine, must be set out in the patent claims and the NOC for the patent to be eligible on the register.
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> …the Guidance Document cited by the appellant is useful to clarify the roles of the different actors in the patented medicine system, notably innovators, generic manufacturers, and the Minister. However, it is not a legally binding document. More significantly, where the Guidance Document is inconsistent with, or in conflict with, the PM(NOC) Regulations, the latter takes precedence over the former…At the hearing, the Minister conceded that only the PM(NOC) Regulations are a binding statement of law.
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> I also note that the PM(NOC) Regulations provide no support for the interpretation suggested in the Guidance Document. As noted above, the wording of section 4 is consistent across the four subsections and requires a high degree of specificity between the wording of the claim and the NOC. It would be necessary to read an interpretation into paragraph 4(2)(a) to allow the paragraph to support claims which contain only some of the medicinal ingredients. Such an interpretation goes against the ordinary meaning of the words, the purpose and object of the PM(NOC) Regulations, and the government's position that product specificity is the key consideration in interpreting section 4. As a result, I would not attribute this interpretation to the PM(NOC) Regulations.
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> ****
>
> I would therefore uphold the Judge's conclusion that the patent claims fail the requirement for product specificity because they do not make specific reference to the medicinal ingredient rilpirivine, but only the broad class of compounds [namely NNRTIs].

[28] Similarly, in the case of KIVEXA®, no claim of the 753 Patent specifically claims the combination of the two medicinal ingredients that are the subject of the NOC for KIVEXA®, namely abacavir sulfate and lamivudine. There is nothing in the 753 Patent that requires lamivudine. The 753 Patent claims only abacavir in combination with another unnamed medicinal ingredient. Section 4(2)(a) of the *PMNOC Regulations*, as held in *Gilead*, requires all of the medicinal ingredients identified in the submission that results in the issuance of the NOC to be claimed in the patent for that patent to be listed on the Patent Register. In the same manner, the specific formulation identified in the submission that led to the issuance of the NOC must be claimed in the patent. In the case of the 753 Patent, it is not enough that it encompasses the medicinal ingredient lamivudine (among others) in combination with abacavir for the purposes of section 4(2)(b) of the *Regulations*.

[29] The requisite degree of product specificity is the same for section 4(2)(a) of the *PMNOC Regulations* as it is for each of sections 4(2)(b), (c) and (d). The medicinal ingredient, formulation, dosage form or use of the medicinal ingredient claimed in the patent sought to be listed must match that in the drug submission that was approved through the issuance of the NOC. Different listing requirements in the case of section 4(2)(a) would not be consistent with the purpose and object of the *PMNOC Regulations* to require product specificity, and also contrary to the Federal Court of Appeal's reasons for judgment in *Gilead* (see also: *Purdue Pharma v. The Minister of Health*, 2011 FCA 132, and in the case of subsection 4(2)(b), *Bayer Inc. v. The Minister of Health*, 2009 FCA 161 and *Eli Lilly Canada Inc. v. A.G. of Canada and Minister of Health*, 2014 FC 152). The Court in *Gilead* states at para.39:

> There is no sound reason to adopt different legislative requirements for the paragraphs set out in subsection 4(2). Each paragraph uses the definitive form in referring to both the substance of the claim and the substance in the notice of compliance: "the medicinal ingredient", "the formulation", "the dosage" and "the use" (in French, "l" ingrédient, "la formulation", "la forme posologique", l'utilisation"). The content of each paragraph is otherwise completely consistent.

[30] Applied to the 753 Patent, it is clear that it does not contain:

(i) a claim for the medicinal ingredient, which medicinal ingredient has been approved through the issuance of a notice of compliance in respect of the submission;

(ii) a claim for the formulation that contains the medicinal ingredient and the formulation has been approved through the issuance of a notice of compliance in respect of the submission;

(iii) a claim for the dosage form and the dosage form has been approved through the issuance of a notice of compliance in respect of the submission; or

(iv) a claim for the use of the medicinal ingredient, and the use has been approved through the issuance of a notice of compliance in respect of the submission.

[31] The 753 Patent is not eligible to be listed on the Patent Register against KIVEXA® as it does not claim the medicinal ingredient as required by section 4(2)(a) of the *PMNOC Regulations* or the formulation of abacavir sulfate and lamivudine as required by section 4(2)(b) of the *Regulations*, as approved through the issuance of the NOC in respect of the drug submission for abacavir sulfate (600 mg) and lamivudine (300 mg) KIVEXA® tablets.

ORDER

THIS COURT ORDERS that:

1. The application in respect of Canadian Patent No. 2,289,753 be and is hereby dismissed on the basis that the Patent is not eligible for inclusion on the Patent Register.

2. In the event the parties cannot agree as to the costs of this motion, each may, within 15 days of the date of this Order, file written submissions.

"Martha Milczynski"
Prothonotary

FEDERAL COURT

SOLICITORS OF RECORD

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