NORTON ROSE FULBRIGHT

Pharma in brief - Canada

Federal Court prohibits approval of generic atazanavir: compound patent not obvious

Case:	*Bristol-Myers Squibb Canada Co. v Teva Canada Limited*, 2016 FC 580 (Court File No. T-1364-14)
Drug:	REYATAZ® (atazanavir bisulfate)
Nature of case:	Prohibition application pursuant to section 6 of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 (the ***Regulations***)
Successful party:	Bristol-Myers Squibb Canada Co., Bristol-Myers Squibb Ireland, and Novartis AG (in part)
Date of decision:	June 8, 2016

Summary

Bristol-Myers Squibb Canada Co. (**BMS Canada**) markets atazanavir bisulfate in Canada under the name REYATAZ® for the treatment of HIV. Teva Canada Limited (**Teva**) sought approval to market generic atazanavir capsules and alleged that two patents, listed on the patent register against REYATAZ®, were invalid. BMS Canada, together with Bristol-Myers Squibb Ireland and Novartis AG (collectively, **BMS**), sought an order under the *Regulations* prohibiting the Minister of Health (**Minister**) from approving Teva's generic atazanavir capsules.

The Federal Court held that Teva's anticipation and obviousness allegations regarding Canadian Patent No. 2,250,840 (the **Compound Patent**) were not justified and issued an order prohibiting the Minister from approving Teva's generic atazanavir capsules until the Compound Patent's expiry. The Court dismissed the application in respect of Canadian Patent No. 2,317,736 (the **Salt Patent**) on the basis of Teva's obviousness allegation.

Background

The Compound Patent was filed on April 14, 1997. In this proceeding, BMS asserted two claims: one to atazanavir or a salt thereof and a second to a pharmaceutical composition of the same for treatment of a disease that is responsive to a retroviral protease.

The Salt Patent was filed on December 22, 1998. The Salt Patent contains two claims, both of which were asserted by BMS: one to atazanavir bisulfate and a second to a pharmaceutical dosage form comprising atazanavir bisulfate and a pharmaceutically acceptable carrier.

The Compound Patent claims were not obvious

Teva relied upon two documents for its obviousness allegation regarding the Compound Patent: an Australian patent application and a letter filed in the European Patent Office (**EPO**). Teva's expert testified that among 240 exemplified compounds, the Australian patent application specifically claimed one that would have been a "good starting point" for making atazanavir through routine modification. The promising activity of this compound, he said, was disclosed in the EPO letter.

Justice Mactavish held that Teva did not show either the EPO letter or the relevant claims of the Australian patent application to have been part of the prior art at the relevant date. Justice Mactavish also found that Teva's translation of the EPO letter from German to English was unreliable and that the EPO letter was inadmissible because it was not included in Teva's notice of allegation.

Without either document as a starting point, it would not have been more or less self-evident to a skilled person that the chemical substitutions required to make atazanavir would work, let alone result in the specific combination of advantageous properties that it possesses. Justice Mactavish found that, consistent with the inventors' course of conduct, prolonged and arduous experimentation was required to obtain the invention. It was not obvious.

The Compound Patent claims were not anticipated by a genus of billions of compounds

Teva also argued that asserted claims of the Compound Patent were anticipated by a US genus patent that disclosed billions of compounds, one of which was said to be atazanavir. BMS argued that when properly construed, atazanavir did not fall within the genus. Justice Mactavish agreed with BMS, holding that Teva's construction of the term in dispute was "nothing short of tortured." As a result, atazanavir was not disclosed, nor were its advantageous properties.

Justice Mactavish further held that a claim to a specific chemical such as atazanavir is not anticipated by a prior art reference that only teaches a broad genus of compounds, when the prior art does not provide directions that would inevitably result in the specific compound in issue. The Court also rejected Teva's argument that the Compound Patent was an invalid selection from the US genus patent.

A purposive construction of the Salt Patent

The Salt Patent claims atazanavir bisulfate as a chemical formula. Teva argued that this formula, known as "formula II" in the description, included two crystalline forms of the salt called Type-I and Type-II. Both types were exemplified as embodiments of formula II in the description. BMS argued that as written, the formula only described the Type-I salt. While the Type-I salt has the desired properties described in the Salt Patent, the Type-II salt does not. It was Teva's position that since the claims included the inoperable Type-II salt, they were invalid.

Justice Mactavish agreed with BMS that only the anhydrous Type-I salt was claimed because the formula in the claim did not show the water associated with the Type-II salt, which is a hydrate. In reaching this conclusion, the Court rejected Teva's reliance on foreign jurisprudence to the effect that a claim construction that excludes a preferred embodiment is unlikely to be correct. Although Mactavish J acknowledged it was "puzzling" that the drafters included an embodiment that was not suitable for the intended purpose of the invention, she found that the presence of this example and its reference to "formula II" was not enough to override the text of the claims.

The Salt Patent claims were obvious

On obviousness, the key issue in dispute was the extent to which the skilled person must be able to foresee the results of a "salt screen" in order for a salt to be obvious. BMS argued that before making and testing atazanavir bisulfate, it was impossible to predict whether the salt would be crystalline or have the desired combination of properties. These properties were part of the inventive concept and as a result, BMS said, the salt could not be obvious. Teva disagreed that the advantageous properties of atazanavir bisulfate formed part of the inventive concept and argued that, in any event, obtaining a suitable salt was the result of routine experimentation.

Justice Mactavish agreed with BMS that the inventive concept of the Salt Patent included the advantageous properties of atazanavir bisulfate notwithstanding the lack of supporting data in the patent, which is a question of utility rather than construction. However, the Court held that there was motivation to try to make salts of atazanavir in order to improve its oral bioavailability. The salts made in a "standard salt screen" of atazanavir would have included atazanavir bisulfate, which would then have been characterized by routine means. This was consistent with the inventors' own course of conduct, having synthesized atazanavir bisulfate on the very first day of their salt screen.

As a result the Court found the claims to atazanavir bisulfate obvious even though the salt and its advantageous properties could not have been predicted *a priori*. Teva's allegation was successful and the Court dismissed the application in respect of the Salt Patent.

Appeal

BMS has appealed the dismissal of its application in respect of the Salt Patent (see Court File No. A-191-16).

Link:

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