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Asamura NEWS

Vol. 15
June, 2015

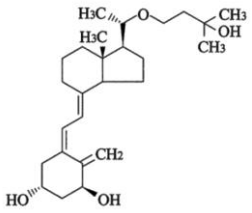
DOE may successfully work to prevent a third party from avoiding the patented process by geometric isomers.

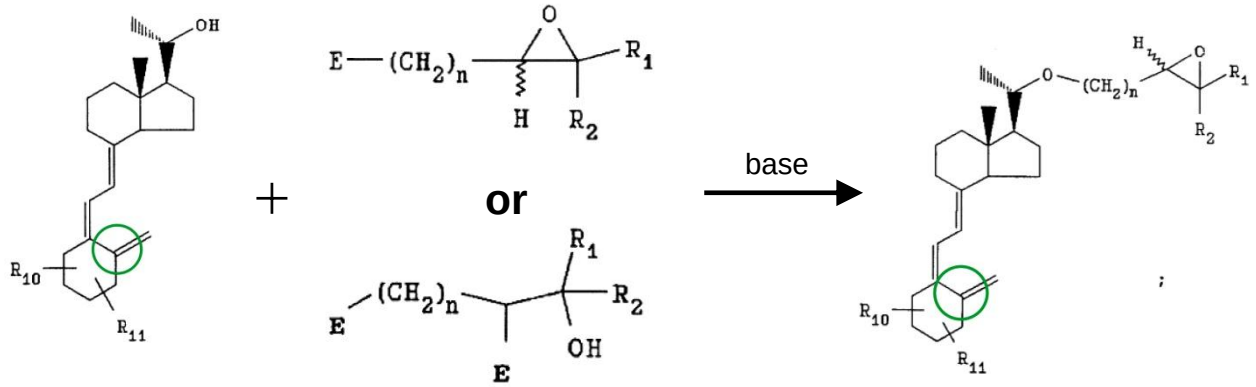
Heisei25(Wa)4040: Tokyo District Court's Decision

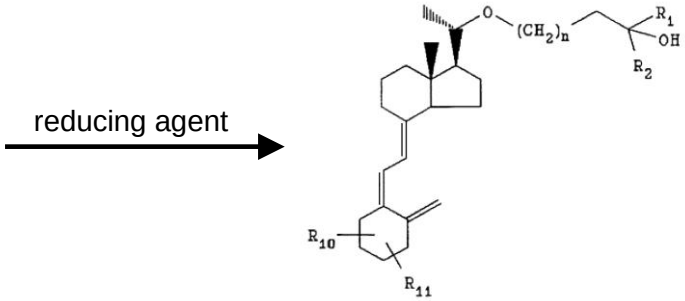
[Summary of Facts]

This reports a patent infringement lawsuit case. The plaintiff is the patentee of Japanese Patent No. 3310301, hereinafter referred to as 301 Patent. This patent relates to a process of manufacturing activity type vitamin D3 derivatives including maxacalcitol. A claim of 301 Patent relates to a process summarized by the following scheme[1*].

maxacalcitol



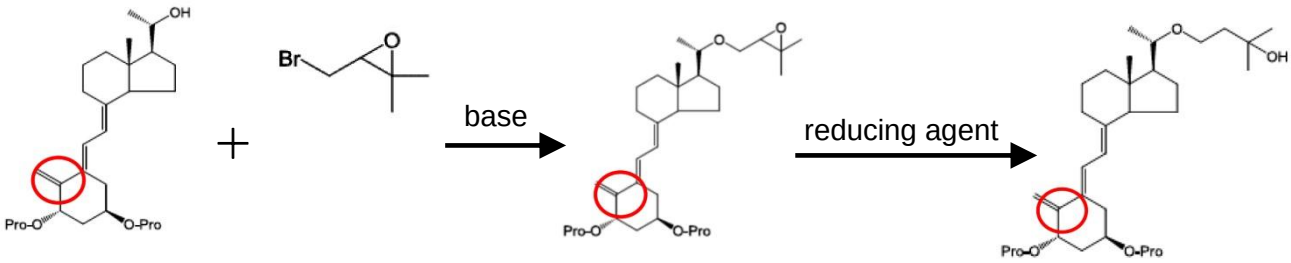


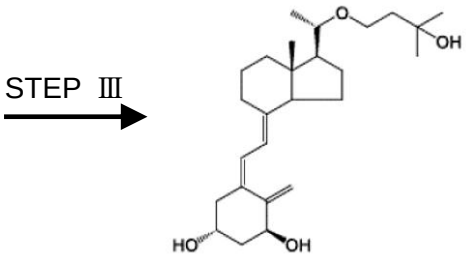


wherein n is 1; each of R_1 and R_2 is methyl; E is an eliminating group; and R_{10} and R_{11} are independently hydrogen, …, or protected hydroxyl.

[1] To simplify, the actual claim is modified.

The plaintiff also owned a patent right which covered maxacalcitol per se, but the term of the patent right expired in December, 2010. The plaintiff has sold a pharmaceutical product for treatment of keratosis containing maxacalcitol as an active substance. The defendants on the other hand received an approval for manufacturing and selling a pharmaceutical product containing maxacalcitol in August 2012 and has imported and sold the product. The accused product has been manufactured by the following process.





Comparing the patented process with the accused process, the latter is different from the former in that the starting material and intermediates have a trans configuration as emphasized by a red circle and in involving a converting step of the trans-form into the corresponding cis-one (STEP III). The plaintiff filed a lawsuit with Tokyo District Court to seek an injunctive order that the defendants ceased and desisted from importing and selling the accused product.

[Summary of Court's Decision]

Tokyo District Court first cited the Supreme Court's decision in Ball Spline Bearing Case, 1994 (O) No. 1083, which ruled that an accused product or process falls under the technical scope of a patented invention under the doctrine of equivalents, DOE, as long as the following five requirements are satisfied: (1) the different part of the product or process claimed in a claim at issue of the patent from the accused one is not essential for the patented invention (Non-essential part); (2) the accused product or process, in which the different part of the claimed product or process is replaced with a corresponding part, accomplishes the same purpose and exhibits the same function and effect as those of the patented invention (Replaceability); (3) a person of ordinary skill in the art could easily conceive the above-mentioned replacement at the time of manufacturing, etc. the accused product or process (Obviousness of replacement); (4) the accused product or process is novel and non-obvious from the prior art at the time of filing patent application (Not falling within public domain); and (5) there are no special circumstances such as intended exclusion of the accused product or process from the technical scope of the claim at issue in the prosecution history (No special circumstances).

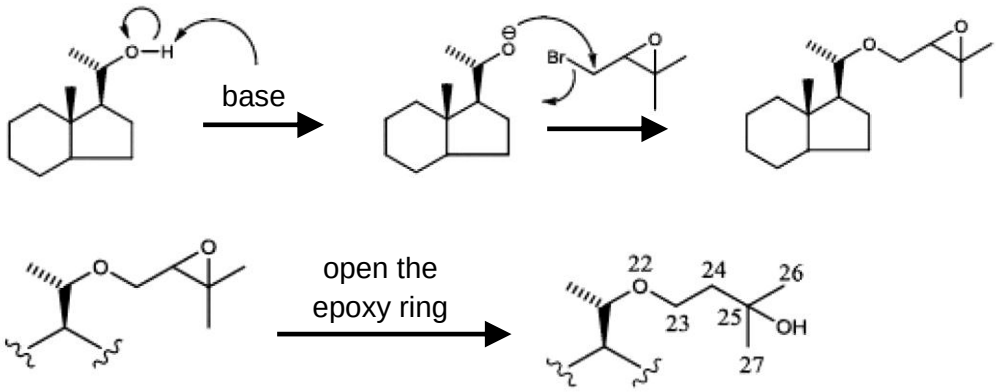
Tokyo District Court then applied the five criteria to this case and concluded that the accused process infringed 301 Patent under DOE as follows.

Req. 1: Non-essential part

An essential part of the patented invention should be, among the constituent elements recited in the claim at issue of the patent, characteristic part which forms a core of a technical concept underlying a unique solution by the claimed invention to a technical problem. In other words, if the replacement of the part with another constituent element substantially changes the technical concept of the patented invention into another one as a whole, the part should be essential for the patented invention.

Considering "Background", "Examples" and others of 301 Patent in a comprehensive manner, the patented invention is deemed to exhibit a unique effect of shortening a process of manufacturing a vitamin D3 derivative including maxacalcitol as compared with the state of the art at the time the patent application was filed. A characteristic part which achieves the unique effect, i.e., an essential part for the patented invention, is deemed to be a methodology of introducing a side chain of interest by reacting a compound having a vitamin D structure with Compound B-2 in the presence of a base to produce an epoxidized compound (1st step), and treating the epoxidized compound with a reducing agent to open the epoxy ring (2nd step).

As shown in the following scheme, regardless of whether the starting material having a vitamin D structure is in a cis-form or trans-form, a side chain which constitutes maxacalcitol can be introduced through an epoxidized compound and epoxy ring-opening.



Consequently, it should not be an essential part whether the starting material and intermediates are in a cis-form or trans-form.

Req. 2: Replaceability

As mentioned above, the accused process can shorten the process as compared with the ordinary processes, through the above-mentioned first and second steps. The accused process can thus accomplish the purpose of the patented invention and exhibit the same function and

effect. The accused process involves an additional step, i.e., STEP III, but it does not affect this conclusion.

Req. 3: Obviousness of replacement

In producing a vitamin D derivative, it was obvious to a person of ordinary skill in the art to introduce a side chain into a starting compound in a trans-form followed by the conversion of the resultant trans-form into the corresponding cis-form. Accordingly, a person skilled in the art could readily conceive the accused process.

Req. 4: Not falling within public domain

The accused process is novel and non-obvious over the prior art submitted by the defendants.

Req. 5: No Special Circumstances

301 Patent only describes a starting material and intermediates having a vitamin D structure in a cis-form. However, 301 Patent is not deemed to intentionally exclude the corresponding compounds in a trans-form. In order to consider an accused product or process to be excluded from the technical scope of the patented invention, it should be required that the patentee has taken such actions as to establish from appearance that the patentee have been clearly aware of a different constitutional element of the accused product or process in the examination procedure or others and then excluded it from the technical scope of the patented invention. The fact that the patentee could easily conceive the constitutional element of the accused product or process in view of the state of the art at the filing of the application but did not draft a claim which recited such element, is not enough to satisfy this requirement. See IPHC decision Heisei17 (Ne) 10047.

[Comments]

In this case, the defendants tried but failed to avoid the patented process by means of geometric isomers and an additional converting step. They have announced that they would stop manufacturing and selling the accused product. The plaintiff has successfully excluded the defendants' generics by the process patent. Meanwhile, circumventing inventions should be taken into consideration in drafting a claim.

(by Hisashi KANAMORI)

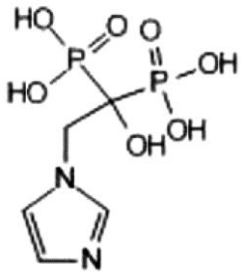
Characteristics in Dosage and Administration may be positively considered in inventive step.

Heisei26(Gyo Ke)10045: Intellectual Property High Court's Decision

[Summary of Facts]

This reports litigation rescinding the trial decision on the inventive step regarding the invention which is characterized by the Dosage and Administration.

The present invention is related to "a treatment agent comprising zoledronic acid or a pharmaceutically acceptable salt thereof as an active ingredient, wherein4mg of zoledronic acid is intravenously administered to a patient in need of said treatment over a period of 15 minutes".



The Appeal Board denied the inventive step of the present invention mainly based on reference 1 which relates to a clinical phase II study of zoledronic acid in view of reference 2 which relates to a clinical phase I study of zoledronic acid and reference 3 which relates to various kinds of Bisphosphonate.

In the Appeal Board Decision, reference 1 was found to disclose a medicament comprising zoledronic acid as active ingredient which was characterized in that 4 mg dose of zoledronic acid was administered by an intravenous drip infusion to a patient of osteolytic diseases such as breast cancer or multiple myeloma over 5 minutes, and it was acknowledged in the Decision that the present invention only differs from the cited invention in the administration time, more specifically, it is "15 minutes" in the present invention, while it is "5 minutes" in the cited invention.

The Appeal Board understood that reference 3 describes adverse events such as renal failure caused by rapid administration of Bisphosphonate can be prevented by administering Bisphosphonate slowly by intravenous drip infusion with large amount of liquid and reference 2 describes serum calcium level was effectively lowered by administration of zoledronic acid intravenous drip infusion for 20 minutes. In conclusion, the Appeal Board judged that it could have been easily carried out to replace the administration time of zoledronic acid for 5 minutes with that for 15 minutes based on premises that adverse events which were not experienced in Phase I and II studies would occur in Phase III study and it well falls within one of ordinary skill in the art to adjust dosage and administration to avoid such predicted adverse events.

The Intellectual Property High Court rescinded the above-mentioned Appeal Board Decision.

[Summary of Court's Decision]

The Intellectual Property High Court states:

According to the results of Phase I and Phase II clinical studies of zoledronic acid described in references 1-2, it is understood that 4 mg dose of zoledronic acid has comparable pharmacological effects of 90mg of pamidronic acid and its safety is established by 5 minutes intravenous drip infusion. Since the results of Phase I and Phase II studies have confirmed

the safety of administration of 4mg for 5 minutes, it is difficult to find any motivation in references 1-2 to further prolong the administration time of 4mg dose of zoledronic acid for 5 minutes intravenous drip infusion in view of convenience and burden reduction for patients.

Reference 3 describes that Bisphosphonate causes a renal failure because it forms solid phase in blood and it is retained in kidney, and thus large dose of Bisphosphonate of intravenous administration should be conducted carefully. Reference 3 also describes that adverse events can be prevented by administering Bisphosphonate slowly by intravenous drip infusion with large amount of liquid. And reference document (Lancet, Vol. 1, 1983, p471) cited in reference 3 states that since renal failure was reported in administration of etidronate (EHDP) and clodronate (C2MDP), daily dose of less than 1g for each of those drugs should be administered slowly and renal function should be monitored. Accordingly it is obvious that reference 3 relates to etidronate (EHDP) and clodronate (C2MDP).

In view of development background for second generation and third generation Bisphosphonate drug and prompt administration result, one of ordinary skill in the art would not understand that finding in adverse events such as renal failure caused by prompt administration of first generation Bisphosphonate drug in reference 3 immediately applies to zoledronic acid which is third generation Bisphosphonate drug. Since zoledronic acid is 100 to 850 times more active than pamidronic acid, and has more potent osteoclastic inhibition activity than incadronic acid and alendronic acid, which makes lower dose administration of zoledronic acid possible, it is difficult to find any motivation in references 1-2 to further prolong the administration time the safety of which was already confirmed in Phase I and Phase II studies from the view point of convenience and burden reduction for patients.

Safety in prompt administration of zoledronic acid was confirmed in Phase I study (reference 2) and subsequent Phase II study (reference 1). Accordingly, there is no doubt in safety for 4mg dose of zoledronic acid for 5 minutes intravenous drip infusion. Furthermore, it is understood that reference 3 does not apply to zoledronic acid which is third generation Bisphosphonate drug. Accordingly, there cannot be found any motivation in references 1-2 to further prolong the administration time of 4mg dose of zoledronic acid for 5 minutes by intravenous drip infusion the safety of which was confirmed in Phase I and Phase II studies.

[Comments]

In the Examination Guideline as revised in October, 2009, characteristics in Dosage and Administration are clearly specified to be considered as a technical feature of the medicinal invention. This revised guideline describes that if efficacy and safety are significantly improved by applying a specific dosage and administration to specific disease, such advantageous effects are considered as grounds for positively acknowledging the inventive step of medicinal invention characterized by its dosage and administration. It is noteworthy that this case judged that there is no motivation in cited references to prolong the administration time the safety of which was already confirmed in preceding clinical studies.

We summarize practices under each of counties listed below with regard to medicinal invention characterized by its dosage and administration.

Novelty and inventive step regarding medicinal invention characterized by its dosage and administration in main countries:

	Are characteristics in dosage and administration taken into amount in the examination for novelty and/or inventive step?	Claim format
JP	Yes	Pharmaceutical composition with its limited use
US	Yes	Method for treatment
EP	Yes	Substance or composition for its limited use
CN	No	Use of a compound in preparing a medicament with its limited use.
KR	No→Yes Korean Supreme Court, for the first time, acknowledged the dosage regime and dose of a known medical use invention as technical features of the invention on May 21, 2015 (2014 (hu) 768).	Pharmaceutical composition or medicament with its limited use

(by Mari YUGE)

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