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Applicant	:	Herriot Tabuteau
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Docket No.	:	1958603.00025 CIP
Customer No.	:	45200
Title	:	COMPOSITIONS FOR ORAL ADMINISTRATION OF ZOLEDRONIC ACID OR RELATED COMPOUNDS FOR TREATING DISEASE

PRELIMINARY AMENDMENT

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The Applicants hereby submit the following Preliminary Amendment in the above referenced patent application.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 7 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-166. (Canceled)

167. (New) A method of enhancing the oral bioavailability of zoledronic acid comprising orally administering a dosage form containing zoledronic acid in the disodium salt form.

168. (New) The method of claim 167, wherein the zoledronic acid in the disodium salt form provides an enhancement to bioavailability, as compared to zoledronic acid in the diacid form, which adds to any enhancement to bioavailability provided by any bioavailability-enhancing agents in the dosage form.

169. (New) The method of claim 167, wherein the zoledronic acid in the disodium salt form is administered to a mammal in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 4 ng•h/mL to about 2000 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

170. (New) The method of claim 169, wherein the zoledronic acid in the disodium salt form is administered at an interval of about 3 to about 4 weeks in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 100 ng•h/mL to about 2000 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

171. (New) The method of claim 169, wherein the zoledronic acid in the disodium salt form is administered weekly, or 3 to 5 times in a month, in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 20 ng•h/mL to about 700 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

172. (New) The method of claim 169, wherein the zoledronic acid in the disodium salt form is administered daily in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 4 ng•h/mL to about 100 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

173. (New) The method of claim 167, wherein the dosage form is a solid.

174. (New) The method of claim 167, wherein the bioavailability of zoledronic acid is improved by at least about 20% as compared to administration of zoledronic acid in the diacid form.

175. (New) The method of claim 167, further comprising administering, on a molar basis, less of the zoledronic acid in the disodium salt form than would be administered of zoledronic acid in the diacid form in order to achieve the same plasma levels of zoledronic acid.

176. (New) The method of claim 175, wherein at least about 10 mole% less of the disodium salt form is administered as compared to the amount of zoledronic acid in the diacid form that would be administered in order to achieve the same plasma levels of zoledronic acid.

177. (New) The method of claim 175, wherein the disodium salt form is administered in an amount, on a molar basis, that has a value of about $0.8n_d$ to about $1.2n_d$, wherein:

$$n_d = (b_a/b_d)(n_a)$$

wherein b_a is the bioavailability of the diacid form, b_d is the bioavailability of the disodium salt form, and n_a is the number of moles of zoledronic acid in the diacid form that would be administered in order to achieve the same plasma levels of zoledronic acid.

178. (New) The method of claim 167, wherein the zoledronic acid is used to treat an inflammatory condition.

179. (New) The method of claim 167, wherein the zoledronic acid is used to treat arthritis or complex regional pain syndrome.

180. (New) The method of claim 167, wherein the zoledronic acid is for the treatment of an inflammatory condition, arthritis, or complex regional pain syndrome, and wherein:

a first oral dosage form is administered; and

a second oral dosage form is administered;

wherein, with respect to the first oral dosage form, the second oral dosage form is administered at 10 x T_{max} or greater, wherein T_{max} is the time of maximum plasma concentration for the first oral dosage form.

181. (New) An oral dosage form comprising zoledronic acid in the disodium salt form, wherein the bioavailability, in a mammal, of zoledronic acid in the disodium salt form is greater than the bioavailability of zoledronic acid in the diacid form would be in the same dosage form.

182. (New) The oral dosage form of claim 181, wherein the dosage form contains an amount of zoledronic acid in the disodium salt form that provides an area under the plasma concentration curve of zoledronic acid of about 100 ng•h/mL to about 2000 ng•h/mL to a human being to which the dosage form is administered.

183. (New) The oral dosage form of claim 181, wherein the dosage form contains an amount of zoledronic acid in the disodium salt form that provides an area under the plasma concentration curve of zoledronic acid of about 20 ng•h/mL to about 700 ng•h/mL to a human being to which the dosage form is administered.

184. (New) The oral dosage form of claim 181, wherein the dosage form contains an amount of zoledronic acid in the disodium salt form that provides an area under the plasma concentration curve of zoledronic acid of about 4 ng•h/mL to about 100 ng•h/mL to a human being to which the dosage form is administered.

185. (New) The oral dosage form of claim 181, wherein the disodium salt form is present in a lower molar amount than would be present if the zoledronic acid were in the diacid form; and wherein the zoledronic acid in the disodium salt form has an improved bioavailability as compared to the zoledronic acid in the diacid form to the extent that the lower molar amount of the disodium salt in the dosage form does not reduce the amount of zoledronic acid delivered to the plasma of a mammal.

186. (New) The oral dosage form of claim 185, containing at least about 20 mole% less of the disodium salt form as compared to the amount of the zoledronic acid in the diacid form that would be present if the zoledronic acid were in the diacid form.

187. (New) The oral dosage form of claim 185, wherein the disodium salt form is present in an amount, on a molar basis, that has a value of about $0.9n_d$ to about $1.1n_d$, wherein:

$$n_d = (b_a/b_d)(n_a)$$

wherein b_a is the bioavailability of the diacid form, b_d is the bioavailability of the disodium salt form, and n_a is the number of moles of the diacid form that would be present if the zoledronic acid were in the diacid form.

188. (New) The oral dosage form of claim 187, wherein the disodium salt is administered in an amount that has a value of about n_d.

189. (New) The oral dosage form of claim 181, wherein the dosage form is a solid.

190. (New) The oral dosage form of claim 181, wherein the bioavailability of zoledronic acid in the disodium salt form is improved by at least about 10% as compared to an otherwise identical dosage form containing zoledronic acid in the diacid form.

191. (New) The method of claim 167, wherein the zoledronic acid is for the treatment of an inflammatory condition, arthritis, or complex regional pain syndrome, and wherein:

only a single oral dosage form is administered; or

a first oral dosage form is administered, and a second oral dosage form is administered after the first oral dosage form;

wherein the second oral dosage form is administered before the maximum pain relieving effect of the first oral dosage form is achieved, or the second oral dosage form is administered before an observable pain relieving effect is achieved.

192. (New) The method of claim 191 wherein the second oral dosage form is administered before an observable pain relieving effect is achieved.

193. (New) The method of claim 167, wherein the zoledronic acid is for the treatment of an inflammatory condition, arthritis, or complex regional pain syndrome, and

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