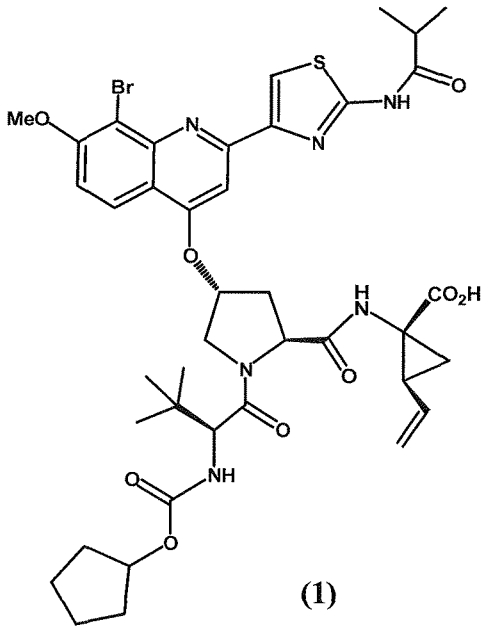
BRIEF SUMMARY

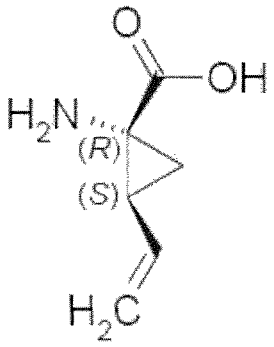
The present application is directed to various methods for controlling the level of the degradation product Compound X in liquid pharmacueutical compositions comprising Compound (1), or a pharmaceutically acceptable salt thereof, and to the resulting stabilized pharmacueutical compositions.

In a first aspect, there is provided a liquid pharmaceutical composition having an internal apparent pH of greater than 7 and a water content of less than 3.0 % w/w comprising a compound of formula (1):



(1)

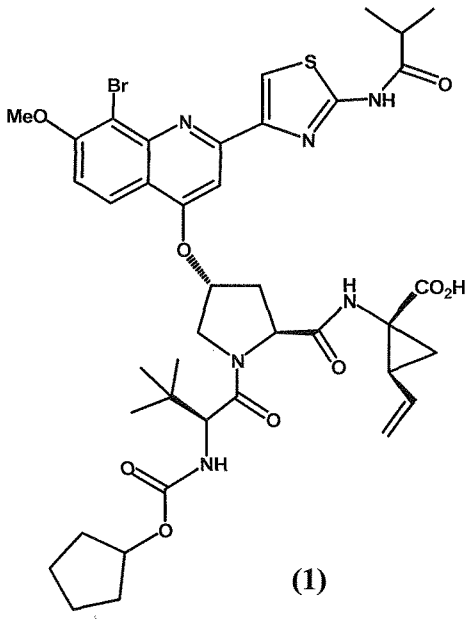
or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient, wherein after 24 months of storage at a temperature of between 2 and 8 degrees Celsius the amount of degradation product Compound X:



X

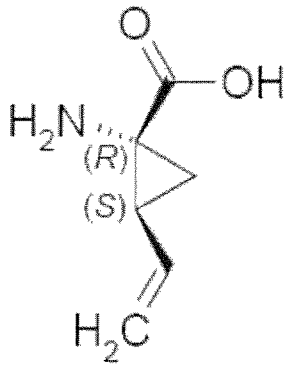
CLAIMS

1. A liquid pharmaceutical composition having an internal apparent pH of greater than 7 and a water content of less than 3.0 % w/w comprising a compound of formula (1):



(1)

or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient, wherein after 24 months of storage at a temperature of between 2 and 8 degrees Celsius the amount of degradation product Compound X:



X

in the composition is below a level of 400 µg.

~~2. A liquid pharmaceutical composition according to claim 1, wherein the composition has one or more of the following properties:~~

~~(a) a water content of less than 3.0 % w/w;~~

~~(b) an internal temperature of between 2 and 8 degrees Celsius~~

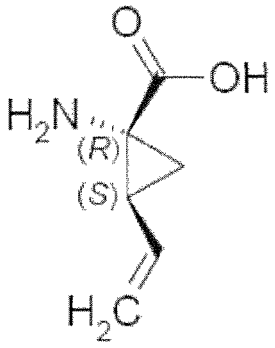
~~.~~

~~3~~2. A liquid pharmaceutical composition according to claim 1, wherein the liquid pharmaceutical composition is contained within a capsule shell material free of citric acid.

43. A liquid pharmaceutical composition according to any of claims 1 to ~~3~~2, wherein the composition contains a fatty acid excipient.

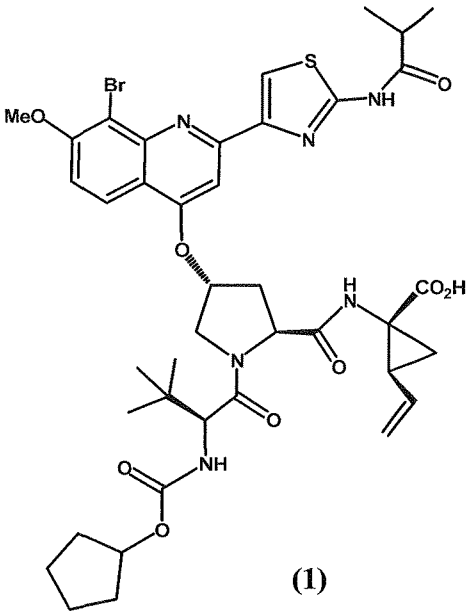
54. A liquid pharmaceutical composition according to claim 2, wherein the composition is a water-containing solution ~~stored at a temperature of between 2 and 8 degrees Celsius~~.

65. A method for controlling the level of degradation product Compound X:



X

in a liquid pharmaceutical composition comprising a compound of formula (1):



(1)

or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient, said method comprising adding a basifier to said composition to achieve an internal apparent pH of greater than 7.

~~7~~6. A method according to claim ~~6~~5, wherein the method further comprises one or more of the following:

(a) drying said composition such that it has a water content of less than 3.0 % w/w and storing the composition under conditions sufficient to maintain a water content of less than 3.0 % w/w;

(b) storing said composition at a temperature of between 2 and 8 degrees Celsius; or

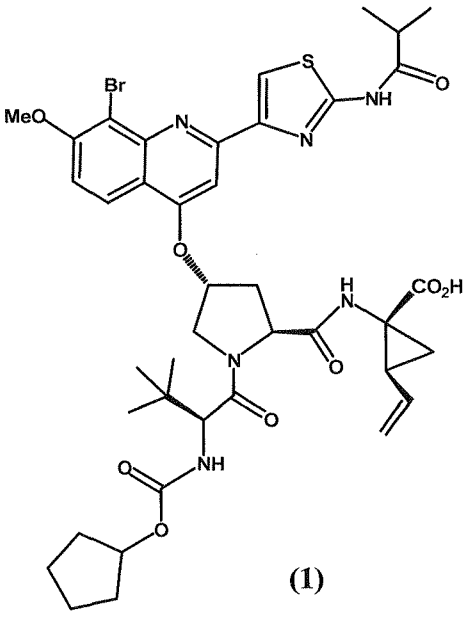
(c) if the liquid pharmaceutical composition is to contain water as an excipient material, first preparing a first formulation pre-mixture comprising only Compound (1), or pharmaceutically acceptable salt thereof, and non-aqueous based excipients and a second formulation pre-mixture comprising water as an excipient, and then mixing the first and second formulation pre-mixtures to prepare the final composition just prior to patient use.

87. A method according to claim 76, wherein the liquid pharmaceutical composition is contained within a capsule and one or both of the following methods are applied to the capsule: (a) it is dried such that it has a water content of less than 3.0 % w/w and stored under conditions sufficient to maintain a water content of less than 3.0 % w/w; and/or (b) it is stored in at a temperature of between 2 and 8 degrees Celsius.

~~98~~. A method according to any of claims ~~6~~ 5 to ~~8~~7, wherein the composition contains a fatty acid excipient.

~~109~~. A kit comprising:

(a) a first formulation pre-mixture comprising a compound of formula (1):



(1)

or a pharmaceutically acceptable salt thereof, and one or more non-aqueous based excipients; and

(b) a second formulation pre-mixture comprising water as an excipient, and optionally one or more additional excipients.