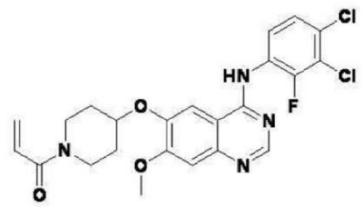
[13] With respect to a pharmaceutical preparation comprising Chemical Formula 1 above, it is intended to provide a pharmaceutical preparation having high productivity due to improved tableting properties, friability and mass uniformity, and high stability due to low generated amount of impurities even under severe conditions.

Summary

[13a] In one aspect, the present disclosure refers to a pharmaceutical preparation comprising a granule comprising a compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof and a diluent to be mixed with the granule:

[Chemical Formula 1]



.

[13b] In another aspect, the present disclosure refers to a method of preparing the pharmaceutical preparation as disclosed herein, the method comprising the steps of:

1) mixing a compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable additive and then performing granulation to prepare a granule;

2) mixing the granule with a pharmaceutically acceptable additive and then adding a diluent to prepare a mixed granule; and

3) formulating the mixed granules.

[13c] In another aspect, the present disclosure refers to a pharmaceutical product in which the pharmaceutical preparation as disclosed herein is packaged in a packaging material.

[13d] In another aspect, the method of improving stability of a pharmaceutical preparation by reducing the formation of impurities comprising preparing the pharmaceutical preparation as disclosed herein, the method comprising the steps of:

1) mixing a compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable additive and then performing granulation to prepare a granule;

2) mixing the granule with a pharmaceutically acceptable additive and then adding a diluent to prepare a mixed granule, wherein the diluent is a mixture of mannitol and microcrystalline cellulose in a weight ratio of 0.50:1 to 3.2:1; and

3) formulating the mixed granules.

[13e] In yet another aspect, the present disclosure refers to the use of the pharmaceutical preparation as disclosed herein in the manufacture of a medicament for treating cancer in a subject, wherein the subject has one or more EGFR or HER2 activating mutations.

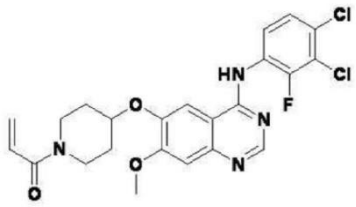
Solution to Problem

[14] The present invention addresses the shortcomings in the prior art.

[15] According to a first aspect of the present invention,

[16] The present invention provides a pharmaceutical preparation comprising a granule comprising a compound of following Chemical Formula 1 or a pharmaceutically acceptable salt thereof, and a diluent:

[17] [Chemical Formula 1]

[18] 

[19] In one embodiment of the present invention, the compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof is included in the pharmaceutical preparation in an amount of 2.0% or more and less than 20% by weight based on the total weight of the pharmaceutical preparation.

[20] In one embodiment of the present invention, the diluent is included in the pharmaceutical preparation in an amount of 20% to 50% by weight based on the total weight of the pharmaceutical preparation.

[21] In one embodiment of the present invention, the diluent is mannitol, microcrystalline cellulose, or a mixture thereof.

[22] In one embodiment of the present invention, the diluent is a mixture of mannitol and microcrystalline cellulose in a weight ratio of 0.50:1 to 3.2:1.

[23] In one embodiment of the present invention, the pharmaceutical preparation further comprises a glidant.

[24] In one embodiment of the present invention, the glidant is selected from the group consisting of calcium stearate, magnesium stearate, sodium lauryl sulfate, zinc stearate, sodium benzoate, and mixtures thereof.

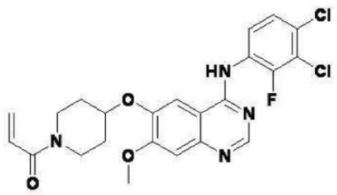
[25] In one embodiment of the present invention, the glidant is included in the pharmaceutical preparation in an amount of 0.5% to 1.5% by weight based on the total weight of the pharmaceutical preparation.

【CLAIMS】

【Claim 1】

A pharmaceutical preparation comprising a granule comprising a compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof and a diluent to be mixed with the granule:

[Chemical Formula 1]



【Claim 2】

The pharmaceutical preparation according to claim 1, wherein the compound of Chemical Formula 1 or the pharmaceutically acceptable salt thereof is included in the pharmaceutical preparation in an amount of 2.0% or more and less than 20% by weight based on the total weight of the pharmaceutical preparation.

【Claim 3】

The pharmaceutical preparation according to claim 1, wherein the diluent is included in the pharmaceutical preparation in an amount of 20% to 50% by weight based on the total weight of the pharmaceutical preparation.

【Claim 4】

The pharmaceutical preparation according to claim 1, wherein the diluent is mannitol, microcrystalline cellulose, or a mixture thereof.

【Claim 5】

The pharmaceutical preparation according to claim 4, wherein the diluent is a mixture of mannitol and microcrystalline cellulose in a weight ratio of 0.50:1 to 3.2:1.

【Claim 6】

The pharmaceutical preparation according to claim 1, wherein the pharmaceutical preparation further comprises a glidant.

【Claim 7】

The pharmaceutical preparation according to claim 6, wherein the glidant is selected from the group consisting of calcium stearate, magnesium stearate, sodium lauryl sulfate, zinc stearate, sodium benzoate, and mixtures thereof.

【Claim 8】

The pharmaceutical preparation according to claim 6, wherein the glidant is included in the pharmaceutical preparation in an amount of 0.5% to 1.5% by weight based on the total weight of the pharmaceutical preparation.

【Claim 9】

A method of preparing the pharmaceutical preparation according to claim 1, the method comprising the steps of:

1) mixing a compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable additive and then performing granulation to prepare a granule;

2) mixing the granule with a pharmaceutically acceptable additive and then adding a diluent to prepare a mixed granule; and

3) formulating the mixed granules.

【Claim 10】

A pharmaceutical product in which the pharmaceutical preparation according to claim 1 is packaged in a packaging material.

【Claim 11】

The pharmaceutical product according to claim 10, wherein the material of the packaging material is selected from the group consisting of glass, high density polyethylene (HDPE), polypropylene (PP), polyvinyl chloride (PVC), polyvinylidene chloride (PVDC), polychlorotrifluoroethylene (PCTFE), cycloolefin polymer (COP), cycloolefin copolymer (COC), polyolefin (PO), aluminum (Al), and combinations thereof, and the shape of the packaging material is selected from the group consisting of bottles, blisters, and pouches.

【Claim 12】

The pharmaceutical product according to claim 10, wherein the packaging material comprises a moisture absorbent.

【Claim 13】

The pharmaceutical product according to claim 12, wherein the moisture absorbent is calcium oxide or silica gel.

【Claim 14】

The pharmaceutical product according to claim 13, wherein the silica gel is included in the packaging material in an amount of 2 to 5 g based on a 125 ml HDPE bottle.

【Claim 15】

A method of improving stability of a pharmaceutical preparation by reducing the formation of impurities comprising preparing the pharmaceutical preparation according to claim 1, the method comprising the steps of:

1) mixing a compound of Chemical Formula 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable additive and then performing granulation to prepare a granule;

2) mixing the granule with a pharmaceutically acceptable additive and then adding a diluent to prepare a mixed granule, wherein the diluent is a mixture of mannitol and microcrystalline cellulose in a weight ratio of 0.50:1 to 3.2:1; and

3) formulating the mixed granules.

【Claim 16】

Use of the pharmaceutical preparation of claim 1 in the manufacture of a medicament for ~~A method of~~ treating cancer in a subject ~~comprising administering a therapeutically effective amount of pharmaceutical preparation of claim 1~~, wherein the subject has ~~been determined to have~~ one or more EGFR or HER2 activating mutations.

【Claim 17】

The ~~method~~ use of claim 16, wherein the subject has ~~been determined to have~~ one or more HER2 activating mutations selected from the group consisting of S310F/Y, I655V, V659E, R678Q, V697L, T733I, L755X, I767M, D769H/N/Y, V773M, V777L/M, L786V, V842I, and L869R.

【Claim 18】

The ~~method~~ use of claim 16, wherein the subject has one or more EGFR activating mutations selected from the group consisting of EGFRvIII, R108K, R222C, A289T, P596L, G598V, Exon 20 insertion, E709K, G719X, V742I, E746_A750del, S768I, V769M, V774M, R831C, R831H, L858R, L861Q, and A864V.