CLAIMS

1.- Concentrated liquid aqueous pharmaceutical composition comprising the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof and a cyclodextrin.

2. Concentrated liquid aqueous pharmaceutical composition according to claim 1, wherein the cyclodextrin is a sulfobutylether-beta-cyclodextrin sodium.

3. Concentrated liquid aqueous pharmaceutical composition according to claim 1 or 2, wherein the cyclodextrin concentration is from 10 to 50 % w/v, typically around 40 % w/v.

4. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 3, the pH of which is from 2.5 to 4.0, typically from 2.5 to 3.5.

5. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 4, wherein the concentration of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof is from 5 to 20 mg/mL, such as 10 mg/mL or 15 mg/mL.

6. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 5, comprising :

- 10 mg/mL of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof
- 40% w/v of sulfobutylether-beta-cyclodextrin sodium,

and having a pH of 3.0.

7. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 5, comprising :

- 15 mg/mL of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea,, or a pharmaceutically acceptable salt thereof
- 40% w/v of sulfobutylether-beta-cyclodextrin sodium,

and having a pH of 3.0.

8. Diluted liquid aqueous pharmaceutical composition comprising the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof, a cyclodextrin and an infusion media, such as an aqueous sodium chloride solution or a dextrose solution.

9. Diluted liquid aqueous pharmaceutical composition according to claim 8, wherein the weight ratio of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea / cyclodextrin is 1/40.

10. Diluted liquid aqueous pharmaceutical composition according to claim 8 or 9, wherein the weight ratio of compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea / cyclodextrin is 1/26.7.

11. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 7, for its use for the treatment of cancer.

12. Diluted liquid aqueous pharmaceutical composition according to anyone of claims 8 to 10, for its use for the treatment of cancer.

13. Compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or a pharmaceutically acceptable salt thereof for its use in the treatment of cancer at a dose of the compound comprised from 25 to 960 mg/m^2, typically at a dose selected from the following doses: 25, 50, 75, 100, 150, 200, 250, 260, 300, 340, 350, 400, 440, 450, 570, 500, 550, 600, 650, 700, 740, 750, 800, 850, 900, 950 and 960 mg/m^2, for example selected from the following doses: 260, 340, 440, 570, 740 and 960 mg/m^2.

14. The compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or a pharmaceutically acceptable salt thereof for its use according to claim 13, wherein the dose of the compound is of 570 mg/m^2.

15. The compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or a pharmaceutically acceptable salt thereof for its use according to claim 13, wherein the dose of the compound is of 440 mg/m^2.

16. Compound for its use according to claim 13, 14 or 15, wherein the cancer is an advanced solid tumor, typically a MET-gene amplified tumor.

17. Compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or a pharmaceutically acceptable salt thereof for its use for the treatment of advanced solid tumors, typically a MET-gene amplified tumor.

18. Compound for its use according to anyone of claims 13 to 17, wherein the compound is parenterally administered, typically by intravenous infusion.

19. Compound for its use according to anyone of claims 13 to 18, wherein the compound is formulated as the concentrated liquid aqueous pharmaceutical composition according to claims 1 to 7.

20. Compound for its use according to claim 19, wherein the treatment comprises the steps consisting of:

a) diluting the concentrated liquid aqueous pharmaceutical composition as defined in anyone of claims 1 to 7 with an infusion media, such as an aqueous sodium chloride solution or a dextrose solution, in order to obtain the diluted liquid aqueous pharmaceutical composition as defined in anyone of claims 8 to 10,

b) administrating the obtained diluted liquid aqueous pharmaceutical composition as defined in anyone of claims 8 to 10 to the patient.

21. Compound for its use according to anyone of claims 13 to 20, wherein the compound is administered once a week.

CLAIMS

1.- Concentrated liquid aqueous pharmaceutical composition comprising the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof and a cyclodextrin.

2. Concentrated liquid aqueous pharmaceutical composition according to claim 1, wherein the cyclodextrin is a sulfobutylether-beta-cyclodextrin sodium.

3. Concentrated liquid aqueous pharmaceutical composition according to claim 1 or 2, wherein the cyclodextrin concentration is from 10 to 50 % w/v, typically around 40 % w/v.

4. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 3, the pH of which is from 2.5 to 4.0, typically from 2.5 to 3.5.

5. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 4, wherein the concentration of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof is from 5 to 20 mg/mL, such as 10 mg/mL or 15 mg/mL.

6. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 5, comprising :

- 10 mg/mL of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof
- 40% w/v of sulfobutylether-beta-cyclodextrin sodium,

and having a pH of 3.0.

7. Concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 5, comprising :

- 15 mg/mL of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea,, or a pharmaceutically acceptable salt thereof
- 40% w/v of sulfobutylether-beta-cyclodextrin sodium,

and having a pH of 3.0.

8. Diluted liquid aqueous pharmaceutical composition comprising the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea, or a pharmaceutically acceptable salt thereof, a cyclodextrin and an infusion media, such as an aqueous sodium chloride solution or a dextrose solution.

9. Diluted liquid aqueous pharmaceutical composition according to claim 8, wherein the weight ratio of the compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea / cyclodextrin is 1/40.

10. Diluted liquid aqueous pharmaceutical composition according to claim 8 or 9, wherein the weight ratio of compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea / cyclodextrin is 1/26.7.

11. Use of the concentrated liquid aqueous pharmaceutical composition according to anyone of claims 1 to 7, for the preparation of a medicine for the treatment of cancer.

12. Use of the diluted liquid aqueous pharmaceutical composition according to anyone of claims 8 to 10, for the preparation of a medicine for the treatment of cancer.

13. Use of compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or of a pharmaceutically acceptable salt thereof for its use for the preparation of a medicine for the treatment of cancer at a dose of the compound comprised from 25 to 960 mg/m^2, typically at a dose selected from the following doses: 25, 50, 75, 100, 150, 200, 250, 260, 300, 340, 350, 400, 440, 450, 570, 500, 550, 600, 650, 700, 740, 750, 800, 850, 900, 950 and 960 mg/m^2, for example selected from the following doses: 260, 340, 440, 570, 740 and 960 mg/m^2, wherein the compound is formulated as the concentrated liquid aqueous pharmaceutical composition according to claims 1 to 7.

14. Use of compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or of a pharmaceutically acceptable salt thereof according to claim 13, wherein the dose of the compound is of 570 mg/m^2.

15. Use of compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or of a pharmaceutically acceptable salt thereof according to claim 13, wherein the dose of the compound is of 440 mg/m^2.

16. Use according to claim 13, 14 or 15, wherein the cancer is an advanced solid tumor, typically a MET-gene amplified tumor.

17. Use of compound 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulfanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea or of a pharmaceutically acceptable salt thereof for the preparation of a medicine for the treatment of advanced solid tumors, typically a MET-gene amplified tumor, wherein the compound is formulated as the concentrated liquid aqueous pharmaceutical composition according to claims 1 to 7.

18. Use according to anyone of claims 13 to 17, wherein the compound is parenterally administered, typically by intravenous infusion.

19. Use according to anyone of claims 13 to 18, wherein the treatment comprises the steps consisting of:
a) diluting the concentrated liquid aqueous pharmaceutical composition as defined in anyone of claims 1 to 7 with an infusion media, such as an aqueous sodium chloride solution or a dextrose solution, in order to obtain the diluted liquid aqueous pharmaceutical composition as defined in anyone of claims 8 to 10,
b) administrating the obtained diluted liquid aqueous pharmaceutical composition as defined in anyone of claims 8 to 10 to the patient.

20. Use according to anyone of claims 13 to 19, wherein the compound is administered once a week.