Claims

1. A pharmaceutical composition comprising a labeling moiety-anti-human antibody Fab fragment conjugate, a buffering agent, a stabilizer and a nonionic surfactant and having a pH of 6.5 to 7.5, wherein

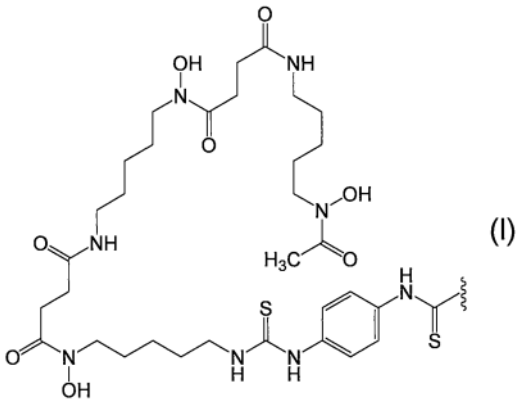
the anti-human antibody Fab fragment is one or more selected from the group consisting of the following (a) and (b):

(a) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 2 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4; and

(b) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment derived from a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 2 by the modification of glutamic acid at amino acid position 1 of SEQ ID NO: 2 into pyroglutamic acid, and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4.,

the labeling moiety is a group represented by the following formula (I):

[Chemical Formula 1]



(I)

wherein the wavy line represents binding to the anti-human CEACAM5 antibody Fab fragment, where the anti-human CEACAM5 antibody Fab fragment is bound to the carbon atom of a labeling moiety terminal C(=S) group via an amino group in the anti-human CEACAM5 antibody Fab fragment,

the nonionic surfactant comprises Polysorbate 80,

the concentration of the nonionic surfactant is 0.02 to 0.2 w/v%,

the buffering agent comprises citric acid, ~~phosphoric acid, 2-[4-(2-hydroxyethyl)-1-~~

piperazinyl]ethanesulfonic acid or trishydroxymethyl aminomethane, and

the concentration of the buffering agent is 10 to 30 mmol/L,

the stabilizer comprises sucrose or glycerin,

the concentration of the stabilizer is 5 to 30 w/v%.

2 The pharmaceutical composition according to claim 1, wherein

the anti-human antibody Fab fragment is one or more selected from the group consisting of the following (a) and (b):

(a) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 2 and a light chain comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 112 of SEQ ID NO: 4; and

(b) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment comprising a heavy chain variable region derived from a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 2 by the modification of glutamic acid at amino acid position 1 of SEQ ID NO: 2 into pyroglutamic acid, and a light chain comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 112 of SEQ ID NO: 4, and

the labeling moiety is a group represented by the following formula (I):

[Chemical Formula 1]

wherein the wavy line represents binding to the anti-human CEACAM5 antibody Fab fragment, where the anti-human CEACAM5 antibody Fab fragment is bound to the carbon atom of a labeling moiety terminal C(=S) group via an amino group in the anti-human CEACAM5 antibody Fab fragment.

3. The pharmaceutical composition according to claim 2, wherein the anti-human antibody Fab fragment is one or more selected from the group consisting of the following (a) and (b):

(a) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 2 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4; and

~~(b) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment derived from a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 2 by the modification of glutamic acid at amino acid position 1 of SEQ ID NO: 2 into pyroglutamic acid, and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4.~~

~~4~~2. A pharmaceutical composition comprising a labeling moiety-anti-human antibody Fab fragment conjugate, a buffering agent, a stabilizer and a nonionic surfactant and having a pH of 6.5 to 7.0~~The pharmaceutical composition according to claim 1~~, wherein

the anti-human antibody Fab fragment is one or more selected from the group consisting of the following (a) and (b):

(a) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 6 or SEQ ID NO: 8 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 10; and

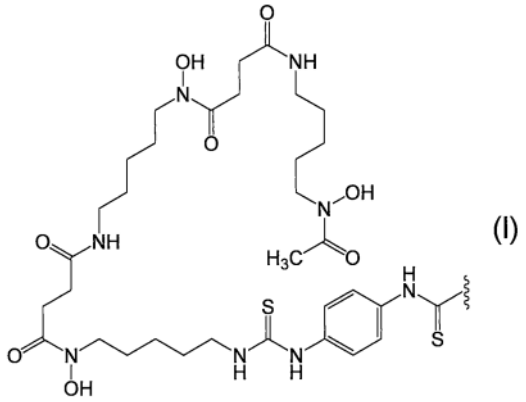
(b) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment derived from a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 6 or SEQ ID NO: 8 by the modification of glutamine at amino acid position 1 of SEQ ID NO: 6 or SEQ ID NO: 8 into pyroglutamic acid, and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 10,

~~(a) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment comprising a heavy chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 12 or SEQ ID NO: 14 and a light chain comprising a light chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 16; and~~

~~(b) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment comprising a heavy chain variable region derived from a heavy chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 12 or SEQ ID NO: 14 by the modification of glutamine at amino acid position 1 of SEQ ID NO: 12 or SEQ ID NO: 14 into pyroglutamic acid, and a light chain comprising a light chain variable region consisting of the amino acid sequence represented by SEQ ID NO: 16, and~~

the labeling moiety is a group represented by the following formula (I):

[Chemical Formula 2]



(I)

wherein the wavy line represents binding to the anti-human MUC1 antibody Fab fragment, where the anti-human MUC1 antibody Fab fragment is bound to the carbon atom of a labeling moiety terminal C(=S) group via an amino group in the anti-human MUC1 antibody Fab fragment.

the nonionic surfactant comprises Polysorbate 80,

the concentration of the nonionic surfactant is 0.02 to 0.2 w/v%,

the buffering agent comprises citric acid,

the concentration of the buffering agent is 10 to 30 mmol/L,

the stabilizer comprises sucrose,

the concentration of the stabilizer is 5 to 30 w/v%.

~~5. The pharmaceutical composition according to claim 4, wherein the anti-human antibody Fab fragment is one or more selected from the group consisting of the following (a) and (b):~~

~~(a) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 6 or SEQ ID NO: 8 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 10; and~~

~~(b) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment derived from a heavy chain fragment consisting of the amino acid sequence represented by SEQ ID NO: 6 or SEQ ID NO: 8 by the modification of glutamine at amino acid position 1 of SEQ ID NO: 6 or SEQ ID NO: 8 into pyroglutamic acid, and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 10.~~

~~6. The pharmaceutical composition according to any one of claims 1 to 5, wherein the~~

~~nonionic surfactant comprises Polysorbate 80.~~

3. The pharmaceutical composition according to claim 1, wherein
the stabilizer comprises sucrose, and
the range of pH is 6.5 to 7.0.

4. The pharmaceutical composition according to any one of claims 1 to 3, wherein
the concentration of the labeling moiety-anti-human antibody Fab fragment conjugate is 5 to 20 mg/mL,
the concentration of the nonionic surfactant is 0.04 to 0.1 w/v%, and
the concentration of the buffering agent is 15 to 25 mmol/L.

5. The pharmaceutical composition according to claim 4, wherein
the range of pH is 6.7.

6. The pharmaceutical composition according to claim 1 or 2, wherein
the concentration of the labeling moiety-anti-human antibody Fab fragment conjugate is 10 mg/mL,
the pH is 6.7,
the concentration of the nonionic surfactant is 0.05 w/v%,
the concentration of the buffering agent is 20 mmol/L,
the stabilizer comprises sucrose, and
the concentration of the stabilizer is 10 w/v%.

7. The pharmaceutical composition according to claim 1, wherein
the concentration of the labeling moiety-anti-human antibody Fab fragment conjugate is 10 mg/mL,
the pH is 6.7,
the concentration of the nonionic surfactant is 0.05 w/v%,
the concentration of the buffering agent is 20 mmol/L,
the stabilizer comprises glycerin, and
the concentration of the stabilizer is 30 w/v%.

87. The pharmaceutical composition according to any one of claims 12 to 76, wherein the labeling moiety-anti-human antibody Fab fragment conjugate further comprises ^{89}Zr.

98. The pharmaceutical composition according to claim 87 for use in the diagnosis of colorectal cancer or a cancer resulting from the metastasis of colorectal cancer.

109. The pharmaceutical composition according to claim 7 8- for use in the diagnosis of breast cancer or a cancer resulting from the metastasis of breast cancer.

17. The pharmaceutical composition according to any one of claims 1 to 16, wherein the concentration of the nonionic surfactant is 0.02 to 0.2 w/v%.

1118. The pharmaceutical composition according to any one of claims 1 to 1017, which is a liquid formulation, a frozen formulation or a lyophilized formulation.

1219. A method for producing thea pharmaceutical composition according to claim1comprising a labeling moiety-anti-human antibody Fab fragment conjugate, comprising the steps of:
(a) producing and adding the labeling moiety-anti-human antibody Fab fragment conjugate;
(b) adding citric acid at 10 to 30 mmol/L, phosphoric acid, 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid or trishydroxymethyl aminomethane as a buffering agent;
(c) adding sucrose or glycerin at 5 to 30 w/v% as a stabilizer;
(d) adding Polysorbate 80 at 0.02 to 0.2 w/v% as a nonionic surfactant; and
(e) adjusting the pH to 6.5 to 7.5.

13. A method for producing the pharmaceutical composition according to claim 2, comprising the steps of:
(a) producing and adding the labeling moiety-anti-human antibody Fab fragment conjugate;
(b) adding citric acid at 10 to 30 mmol/L as a buffering agent;
(c) adding sucrose at 5 to 30 w/v% as a stabilizer;
(d) adding Polysorbate 80 at 0.02 to 0.2 w/v% as a nonionic surfactant; and
(e) adjusting the pH to 6.5 to 7.0.

1420. A method for stably preserving a labeling moiety-anti-human antibody Fab fragment conjugate contained in the pharmaceutical composition according to claim 1, comprising the steps of:

(a) adding citric acid at 10 to 30 mmol/L~~, phosphoric acid, 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid or trishydroxymethyl aminomethane~~ as a buffering agent to a solution containing the labeling moiety-anti-human antibody Fab fragment conjugate;

(b) adding sucrose or glycerin at 5 to 30 w/v% as a stabilizer to the solution containing the labeling moiety-anti-human antibody Fab fragment conjugate;

(c) adding Polysorbate 80 at 0.02 to 0.2 w/v% as a nonionic surfactant to the solution containing the labeling moiety-anti-human antibody Fab fragment conjugate; and

(d) adjusting the pH of the solution containing the labeling moiety-anti-human antibody Fab fragment conjugate to 6.5 to 7.5.

15. A method for stably preserving a labeling moiety-anti-human antibody Fab fragment conjugate contained in the pharmaceutical composition according to claim 2, comprising the steps of:

(a) adding citric acid at 10 to 30 mmol/L as a buffering agent to a solution containing the labeling moiety-anti-human antibody Fab fragment conjugate;

(b) adding sucrose at 5 to 30 w/v% as a stabilizer to the solution containing the labeling moiety-anti-human antibody Fab fragment conjugate;

(c) adding Polysorbate 80 at 0.02 to 0.2 w/v% as a nonionic surfactant to the solution containing the labeling moiety-anti-human antibody Fab fragment conjugate; and

(d) adjusting the pH of the solution containing the labeling moiety-anti-human antibody Fab fragment conjugate to 6.5 to 7.0.