

CLAIMS

1. Use of fitusiran in the manufacture of a medicament for A method of prophylactic treatment of hemophilia A or B in a patient ~~with hemophilia A or B~~ with or without inhibitors, comprising:

(a) wherein the medicament is to be subcutaneously ~~administering~~ administered to the patient in need thereof ~~fitusiran~~ at a starting dose amount at a selected dosing frequency;

(b) wherein ~~obtaining~~ a measurement of an antithrombin (AT) level is to be obtained in the patient; and

(c) ~~wherein performing one of the following steps:~~

(i) if the AT level is 15-35%, the medicament is to be further administered according to repeating step (a),

(ii) if the AT level is >35%, the medicament is to be further subcutaneously ~~administering~~ administered to the patient ~~fitusiran~~ at a higher dose amount at the selected dosing frequency, or at the starting dose amount at a higher dosing frequency, or

(iii) if the AT level is <15%, ~~discontinuing or pausing fitusiran the~~ treatment is to be discontinued or paused.

2. ~~—The use of claim 1, wherein the A method of reducing~~ thrombotic risk in ~~a the~~ patient is reduced. ~~receiving fitusiran for prophylactic treatment of hemophilia A or B with or without inhibitors, comprising:~~

~~—(a) subcutaneously administering to the patient in need thereof fitusiran at a starting dose amount at a selected dosing frequency;~~

~~—(b) obtaining a measurement of an antithrombin (AT) level in the patient; and~~

~~—(c) performing one of the following steps:~~

~~—(i) if the AT level is 15-35%, repeating step (a);~~

~~—(ii) if the AT level is >35%, subcutaneously administering to the patient fitusiran at a higher dose amount at the selected dosing frequency, or at the starting dose amount at a higher dosing frequency, or~~

3.2. ~~—(iii) if the AT level is <15%, discontinuing or pausing fitusiran treatment.~~

4.3. The ~~method-use~~ of claim 1 or 2, wherein the starting dose amount of fitusiran is selected from about 10 mg to about 50 mg.

5.4. The ~~method-use~~ of any one of claims 1-3, wherein the selected dosing frequency is about every two months (Q2M) or about every eight weeks (Q8W), optionally wherein the higher dosing frequency is about every month (QM) or about every four weeks (Q4W).

6.5. The ~~method-use~~ of claim 4, wherein the starting dose amount is about 20 mg and the selected dosing frequency is about Q2M or about Q8W.

7.6. The ~~method-use~~ of claim 4, wherein the starting dose amount is about 50 mg and the selected dosing frequency is about Q2M or about Q8W, optionally wherein
step-the medicament is to be administered according to (c)(ii) is performed if two measurements of the AT level are >35%, or

step-the treatment is to be discontinued or paused according to (c)(iii) is performed if more than one measurement, optionally two measurements, of the AT level is <15%.

8.7. The ~~method-use~~ of claim 6, wherein step-according to (c)(ii) the medicament is to be administered ~~comprises~~ subcutaneously administering to the patient ~~fitusiran~~ at a dose of about 50 mg fitusiran about QM.

9.8. The ~~method-use~~ of claim 7, wherein the medicament is to be administered subcutaneously to the patient at a dose of comprising, after step (c)(ii), subcutaneously administering to the patient fitusiran at about 80 mg fitusiran about QM if the AT level in the patient after following treatment according to step (c)(ii) is >35%, optionally according to two measurements.

10.9. The ~~method-use~~ of any one of claims 6-8, comprising wherein, after step-discontinuing or pausing treatment according to (c)(iii):

(A) the medicament is to be administered to the patient subcutaneously administering ~~fitusiran to the patient~~ at a dose of about 20 mg of fitusiran about Q2M; and

(B) if the AT level of the patient treated according to after step (A) is
<15%, optionally according to more than measurement, ~~discontinuing~~ fitusiran
treatment is to be discontinued,
15-35%, ~~repeating step the medicament is to be further administered according to~~ (A),
or _____
>35%, optionally according to two measurements, the medicament is to be
administered subcutaneously ~~administering~~ to the patient ~~fitusiran~~ at a dose of about 20 mg
fitusiran about QM.

~~11.10.~~ The ~~method-use~~ of any one of the preceding claims, ~~further wherein the medicament is to~~
~~be administered comprising~~ subcutaneously ~~administering fitusiran~~ to the patient at a dose
amount and a dosing frequency sufficient to maintain the AT level in the patient at 15-35%,
optionally ~~comprising wherein the medicament is to be administered~~ subcutaneously
~~administering fitusiran~~ at a dose of:

about 10 mg fitusiran about QM or about Q4W,
about 20 mg fitusiran about QM or about Q4W,
about 20 mg fitusiran about Q2M or about Q8W,
about 50 mg fitusiran about QM or about Q4W,
about 50 mg fitusiran about Q2M or about Q8W, or
about 80 mg fitusiran about QM or about Q4W.

~~12.11.~~ The ~~method-use~~ of any one of the preceding claims, wherein each AT level measurement
is to be obtained after the patient has received at least two doses of ~~fitusiran the medicament~~ at a
given dose amount.

~~13.12.~~ Use of fitusiran in the manufacture of a medicament for ~~A method of~~ prophylactic
treatment of hemophilia A or B in a patient ~~with hemophilia A or B~~ with or without inhibitors,
~~comprising wherein the medicament is to be administered~~ subcutaneously ~~administering~~ to the
patient in need thereof at a dose of about 50 or about 80 mg of fitusiran about every two months
or about every eight weeks.

~~14.13.~~ Use of fitusiran in the manufacture of a medicament for ~~A method of~~ prophylactic treatment of hemophilia A or B in a patient with ~~hemophilia A or B with~~ or without inhibitors, ~~comprising wherein the medicament is to be administered~~ subcutaneously ~~administering~~ to the patient in need thereof at a dose of about 20 mg of fitusiran about every month or about every four weeks, or about every two months or about every eight weeks.

~~15.14.~~ Use of fitusiran in the manufacture of a medicament for ~~A method of~~ prophylactic treatment of hemophilia A or B in a patient with ~~hemophilia A or B with~~ or without inhibitors, ~~comprising wherein the medicament is to be administered~~ subcutaneously ~~administering~~ to the patient in need thereof at a dose of about 10 mg of fitusiran about every month or about every four weeks.

~~16.15.~~ The ~~method-use~~ of any one of the preceding claims, ~~comprising wherein obtaining a~~ measurement of an AT level in the patient is to be obtained about every four weeks, about every eight weeks, about every month, about every two months, about every four months, about every six months, or about every 12 months.

~~17.16.~~ The ~~method-use~~ of any one of claims 1-15, wherein the patient is twelve years of age or older.

~~18.17.~~ The ~~method-use~~ of any one of claims 1-16, wherein fitusiran is provided in a phosphate-buffered saline (PBS) at about 50-200 mg/mL, optionally about 100 mg/mL, and optionally wherein the PBS has a pH of about 7.

~~19.~~ ~~Fitusiran for use in a method of any one of claims 1-17.~~

~~20.1.~~ ~~An article of manufacture for use in a method of any one of claims 1-17, optionally wherein the article of manufacture is a kit.~~

~~21.18.~~ ~~The~~ An article of manufacture ~~for use of claim 19~~, wherein the article of manufacture is a container containing one or more doses of fitusiran, each dose being about 80 mg, about 50 mg, about 20 mg, or about 10 mg,

optionally wherein

the about 80 mg of fitusiran is in about 0.8 mL of a phosphate-buffered saline (PBS),
the about 50 mg of fitusiran is in about 0.5 mL of a PBS,
the about 20 mg of fitusiran is in about 0.2 mL of a PBS, or
the about 10 mg of fitusiran is in about 0.1 mL of a PBS, and
optionally wherein the PBS has a pH of about 7.

19. ~~An~~ The article of manufacture ~~for use in a method of any one of claims 1-17~~ of claim 18,
~~optionally wherein the article of manufacture is a kit.~~

~~22.20.~~ The article of manufacture ~~for use of claim 20~~ of claim 18 or 19, wherein the container is a single-use, single-dose prefilled syringe.

~~23. Use of fitusiran for the manufacture of a medicament to treat hemophilia A or B with or without inhibitors in a method of any one of claims 1-17.~~