TITLE

Prefilled Autoinfusion Device

TECHNICAL FIELD

[0001] The present disclosure generally relates to a prefilled autoinfusion device for delivery of a medicament.

BACKGROUND

[0002] Current autoinfusion devices like syringe pumps are limited to extremely low flow rates, limiting their usefulness for delivery of high volumes. Current biologics typically can have dose volumes of 5-50 mL. Higher flow rates are required to make use of an autoinfusion device practical for doses of larger volumes.

SUMMARY

[0003] In one aspect, the present disclosure provides a use of a hyaluronidase PH20 enzyme formulation formulated for subcutaneous administration in the manufacture of a medicament for the treatment of a disease or disorder in a subject in need thereof, wherein the formulation comprises recombinant human hyaluronidase PH20 enzyme comprising a sequence having at least 95% amino acid sequence identity to an amino acid sequence selected from any of SEQ ID NO: 1 through 7 or 15, and having an activity of 500 U/mL to 5,000 U/mL, and an active ingredient selected from a small molecule, a peptide fragment, a biologic, a nanoparticle, an antibody, an antibody fragment, and a small molecule antiviral; wherein the formulation is to be administered via subcutaneous administration at a volume of 3 mL to 50 mL and the subcutaneous administration is facilitated by a prefilled autoinjection or autoinfusion device comprising:

a delivery apparatus comprising:

a housing having a proximal end and a distal end opposite the proximal end;

a medicament container at least partially disposed within the housing containing a volume of a medicament;

an outlet on the distal end of the housing in fluid communication with the medicament container;

an energy source disposed within the housing configured to interact with the medicament container to expel the medicament from the outlet; and

a trigger mechanism coupled to the housing and engageable with the energy source and configured to activate the energy source in response to a user input;

a port having a user engagement surface, and an injection apparatus extending from the user engagement surface; and

a conduit removably coupled to the outlet and the port and fluidly connecting the delivery apparatus and the port when coupled therebetween.

[0003a] In another aspect, the present disclosure provides a use of a hyaluronidase PH20 enzyme formulation formulated for subcutaneous administration in the manufacture of a medicament for the treatment of a disease or disorder in a subject in need thereof, wherein the formulation comprises recombinant human hyaluronidase PH20 enzyme comprising a sequence having at least 95% amino acid sequence identity to an amino acid sequence selected from any of SEQ ID NO: 1 through 7 or 15, and having an activity of 500 U/mL to 5,000 U/mL, and an active ingredient selected from a small molecule, a peptide fragment, a biologic, a nanoparticle, an antibody, an antibody fragment, and a small molecule antiviral; wherein the subcutaneous administration is facilitated by a prefilled autoinjection or autoinfusion device comprising:

a delivery apparatus comprising:

a housing having a proximal end and a distal end opposite the proximal end;

a medicament container at least partially disposed within the housing containing a volume of at least 10 mL of a medicament;

an outlet on the distal end of the housing in fluid communication with the medicament container;

an energy source disposed within the housing configured to interact with the medicament container to expel the medicament from the outlet; and

a trigger mechanism coupled to the housing and engageable with the energy source and configured to activate the energy source in response to a user input;

a port comprising:

a user engagement surface; and

a needle extending from the user engagement surface; and

a flexible tube removably coupled to the outlet and the port and fluidly connecting the delivery apparatus and the port when coupled therebetween,

wherein the delivery apparatus is not resettable.

[0003b] In another aspect, the present disclosure provides a use of a hyaluronidase PH20 enzyme formulation formulated for subcutaneous administration in the manufacture of a medicament for delivering a formulation to a subject in need thereof, wherein the formulation comprises recombinant human hyaluronidase PH20 enzyme comprising a sequence having at least 95% amino acid sequence identity to an amino acid sequence selected from any of SEQ ID NO: 1 through 7 or 15, and having an activity of 500 U/mL to 5,000 U/mL, and an active ingredient selected from a small molecule, a peptide fragment, a biologic, a nanoparticle, an antibody, an antibody fragment, and a small molecule antiviral, wherein the formulation is to be administered via subcutaneous administration at a volume of 3 mL to 50 mL into a patient with a delivery apparatus comprising a prefilled medicament container containing a volume of the formulation, an energy source configured to interact with the medicament container to expel the formulation and a trigger mechanism configured to activate the energy source in response to a user input, wherein:

the delivery apparatus is coupled to a first end of a conduit, the conduit in fluid communication with the prefilled medicament container;

a second end of the conduit is coupled to a port comprising an injection apparatus extending therefrom, the injection apparatus in fluid communication with the prefilled medicament container;

the injection apparatus is configured for insertion into an injection site on a patient; and

the trigger mechanism is configured for manipulation to allow the energy source to expel the formulation from the prefilled medicament container;

a port having a user engagement surface, and an injection apparatus extending from the user engagement surface; and

a conduit removably coupled to the outlet and the port and fluidly connecting the delivery apparatus and the port when coupled therebetween;

wherein the energy source urges the volume of the formulation through the injection apparatus during the injection.

[0003c] In one example, the present disclosure provides a method of treating a disease or disorder in a subject in need thereof, the method comprising administering to the subject via subcutaneous administration about 3 mL to about 50 mL of a formulation comprising a

therapeutically effective amount of an active ingredient selected from a small molecule, a peptide fragment, a biologic, a nanoparticle, an antibody, an antibody fragment, and a small molecule antiviral, wherein the subcutaneous administration occurs via a high-volume autoinfusion device with a starting delivery force of about 5 lbf to about 50 lbf, an ending delivery force of about 3 lbf to about 20 lbf, a starting pressure of about 50 psi to about 200 psi, and/or an ending pressure of about 20 psi to about 75 psi. In one example, the formulation further comprises a hyaluronidase enzyme. In one example, the hyaluronidase enzyme is a recombinant human hyaluronidase enzyme. In one example, the hyaluronidase enzyme is a recombinant human hyaluronidase PH20 enzyme. In one example, the hyaluronidase enzyme has an activity of about 150 U/mL to about 150 kU/mL. In one example, the hyaluronidase enzyme has an activity of about 500 U/mL to about 5,000 U/mL. In one example, the hyaluronidase enzyme has an activity of about 1,500 U/mL to about 10,000 U/mL. In one example, the active ingredient is a small molecule, a peptide fragment, a biologic, or a nanoparticle. In one example, the active ingredient is an antibody, an antibody fragment, or a small molecule antiviral. In one example, the method comprises administering to the subject about 10 mL to about 20 mL of the formulation. In one

example, the method comprises administering to the subject about 3 mL to about 15 mL of the formulation. In one example, the method comprises administering to the subject about 3 mL, about 3.1 mL, about 3.2 mL, about 3.4 mL, about 3.5 mL, about 3.6 mL, about 3.7 mL, about 3.8 mL, about 3.9 mL, about 4 mL, about 4.1 mL, about 4.2 mL, about 4.3 mL, about 4.4 mL, about 4.5 mL, about 5 mL, about 5.1 mL, about 5.2 mL, about 5.3 mL, about 5.4 mL, about 5.5 mL, about 5.6 mL, about 5.7 mL, about 5.8 mL, about 5.9 mL, about 6 mL, about 6.1 mL, about 6.2 mL, about 6.3 mL, about 6.4 mL, about 6.5 mL, about 6.6 mL, about 6.7 mL, about 6.8 mL, about 6.9 mL, about 7 mL, about 7.1 mL, about 7.2 mL, about 7.3 mL, about 7.4 mL, about 7.5 mL, about 7.6 mL, about 7.7 mL, about 7.8 mL, about 7.9 mL, about 8 mL, about 8.1 mL, about 8.2 mL, about 8.3 mL, about 8.4 mL, about 8.5 mL, about 8.6 mL, about 8.7 mL, about 8.8 mL, about 8.9 mL, about 9 mL, about 9.1 mL, about 9.2 mL, about 9.3 mL, about 9.4 mL, about 9.5 mL, about 9.6 mL, about 9.7 mL, about 9.8 mL, about 9.9 mL, about 10 mL, about 10.1 mL, about 10.2 mL, about 10.3 mL, about 10.4 mL, about 10.5 mL, about 10.6 mL, about 10.7 mL, about 10.8 mL, about 10.9 mL, about 11 mL, about 11.1 mL, about 11.2 mL, about 11.3 mL, about 11.4 mL, about 11.5 mL, about 11.6 mL, about 11.7 mL, about 11.8 mL, about 11.9 mL, about 12 mL, about 12.1 mL, about 12.2 mL, about 12.3 mL, about 12.4 mL, about 12.5 mL, about 12.6 mL, about 12.7 mL, about 12.8 mL, about 12.9 mL, about 13 mL, about 13.1 mL, about 13.2 mL, about 13.3 mL, about 13.4 mL, about 13.5 mL, about 13.6 mL, about 13.7 mL, about 13.8 mL, about 13.9 mL, about 14 mL, about 14.1 mL, about 14.2 mL, about 14.3 mL, about 14.4 mL, about 14.5 mL, about 14.6 mL, about 14.7 mL, about 14.8 mL, about 14.9 mL, about 15 mL, about 15.1 mL, about 15.2 mL, about 15.3 mL, about 15.4 mL, about 15.5 mL, about 15.6 mL, about 15.7 mL, about 15.8 mL, about 15.9 mL, about 16 mL, about 16.1 mL, about 16.2 mL, about 16.3 mL, about 16.4 mL, about 16.5 mL, about 16.6 mL, about 16.7 mL, about 16.8 mL, about 16.9 mL about 17 mL, about 17.1 mL, about 17.2 mL, about 17.3 mL, about 17.4 mL, about 17.5 mL, about 17.6 mL, about 17.7 mL, about 17.8 mL, about 17.9 mL, about 18 mL, about 18.1 mL, about 18.2 mL, about 18.3 mL, about 18.4 mL, about 18.5 mL, about 18.6 mL, about 18.7 mL, about 18.8 mL, about 18.9 mL, about 19 mL, about 19.1 mL, about 19.2 mL, about 19.3 mL, about 19.4 mL, about 19.5 mL, about 19.6 mL, about 19.7 mL, about 19.8 mL, about 19.9 mL, about 20 mL, about 20.1 mL, about 20.2 mL, about 20.3 mL, about 20.4 mL, about 20.5 mL, about 20.6 mL, about 20.7 mL, about 20.8 mL, about 20.9 mL, about 21 mL, about 21.1 mL, about 21.2 mL, about 21.3 mL, about 21.4 mL, about 21.5 mL, about 21.6 mL, about 21.7 mL, about 21.8 mL, about 21.9 mL, about 22 mL, about 22.1 mL, about 22.2 mL, about 22.3 mL, about 22.4 mL, about 22.5 mL, about 22.6 mL, about 22.7 mL, about 22.8 mL, about 22.9 mL, about 23 mL, about 23.1 mL, about 23.2 mL, about 23.3 mL, about 23.4 mL, about 23.5 mL, about 23.6 mL,

about 23.7 mL, about 23.8 mL, about 23.9 mL, about 24 mL, about 24.1 mL, about 24.2 mL, about 24.3 mL, about 24.4 mL, about 24.5 mL, about 24.6 mL, about 24.7 mL, about 24.8 mL, about 24.9 mL, or about 25 mL. In another example, the method comprises administering to the subject, about 26 mL, about 27 mL, about 28 mL, about 29 mL, about 30 mL, about 31 mL, about 32 mL, about 33 mL, about 34 mL, about 35 mL, about 36 mL, about 37 mL, about 38 mL, about 39 mL, about 40 mL, about 41 mL, about 42 mL, about 43 mL, about 44 mL, about 45 mL, about 46 mL, about 47 mL, about 48 mL, about 49 mL, or about 50 mL. In one example, the method comprises administering the formulation using a high-volume autoinfusion device. In one example, the method comprises administering the formulation with a starting delivery force of about 3 lbf to about 50 lbf using a high-volume autoinfusion device. In one example, the method comprises administering the formulation with an ending delivery force of about 5 lbf to about 20 lbf using a high-volume autoinfusion device. In one example, the method comprises administering the formulation with a starting pressure of about 50 psi to about 200 psi using a high-volume autoinfusion device. In one example, the method comprises administering the formulation with an ending pressure of about 20 psi to about 75 psi using a high-volume autoinfusion device. In one example, the formulation is in a prefilled syringe. In one example, the prefilled syringe contains about 3 mL, about 3.1 mL, about 3.2 mL, about 3.4 mL, about 3.5 mL, about 3.6 mL, about 3.7 mL, about 3.8 mL, about 3.9 mL, about 4 mL, about 4.1 mL, about 4.2 mL, about 4.3 mL, about 4.4 mL, about 4.5 mL, about 5 mL, about 5.1 mL, about 5.2 mL, about 5.3 mL, about 5.4 mL, about 5.5 mL, about 5.6 mL, about 5.7 mL, about 5.8 mL, about 5.9 mL, about 6 mL, about 6.1 mL, about 6.2 mL, about 6.3 mL, about 6.4 mL, about 6.5 mL, about 6.6 mL, about 6.7 mL, about 6.8 mL, about 6.9 mL, about 7 mL, about 7.1 mL, about 7.2 mL, about 7.3 mL, about 7.4 mL, about 7.5 mL, about 7.6 mL, about 7.7 mL, about 7.8 mL, about 7.9 mL, about 8 mL, about 8.1 mL, about 8.2 mL, about 8.3 mL, about 8.4 mL, about 8.5 mL, about 8.6 mL, about 8.7 mL, about 8.8 mL, about 8.9 mL, about 9 mL, about 9.1 mL, about 9.2 mL, about 9.3 mL, about 9.4 mL, about 9.5 mL, about 9.6 mL, about 9.7 mL, about 9.8 mL, about 9.9 mL, about 10 mL, about 10.1 mL, about 10.2 mL, about 10.3 mL, about 10.4 mL, about 10.5 mL, about 10.6 mL, about 10.7 mL, about 10.8 mL, about 10.9 mL, about 11 mL, about 11.1 mL, about 11.2 mL, about 11.3 mL, about 11.4 mL, about 11.5 mL, about 11.6 mL, about 11.7 mL, about 11.8 mL, about 11.9 mL, about 12 mL, about 12.1 mL, about 12.2 mL, about 12.3 mL, about 12.4 mL, about 12.5 mL, about 12.6 mL, about 12.7 mL, about 12.8 mL, about 12.9 mL, about 13 mL, about 13.1 mL, about 13.2 mL, about 13.3 mL, about 13.4 mL, about 13.5 mL, about 13.6 mL, about 13.7 mL, about 13.8 mL, about 13.9 mL, about 14 mL, about 14.1 mL, about 14.2 mL, about 14.3 mL, about 14.4 mL,

about 14.5 mL, about 14.6 mL, about 14.7 mL, about 14.8 mL, about 14.9 mL, about 15 mL, about 15.1 mL, about 15.2 mL, about 15.3 mL, about 15.4 mL, about 15.5 mL, about 15.6 mL, about 15.7 mL, about 15.8 mL, about 15.9 mL, about 16 mL, about 16.1 mL, about 16.2 mL, about 16.3 mL, about 16.4 mL, about 16.5 mL, about 16.6 mL, about 16.7 mL, about 16.8 mL, about 16.9 mL, about 17 mL, about 17.1 mL, about 17.2 mL, about 17.3 mL, about 17.4 mL, about 17.5 mL, about 17.6 mL, about 17.7 mL, about 17.8 mL, about 17.9 mL, about 18 mL, about 18.1 mL, about 18.2 mL, about 18.3 mL, about 18.4 mL, about 18.5 mL, about 18.6 mL, about 18.7 mL, about 18.8 mL, about 18.9 mL, about 19 mL, about 19.1 mL, about 19.2 mL, about 19.3 mL, about 19.4 mL, about 19.5 mL, about 19.6 mL, about 19.7 mL, about 19.8 mL, about 19.9 mL, about 20 mL, about 20.1 mL, about 20.2 mL, about 20.3 mL, about 20.4 mL, about 20.5 mL, about 20.6 mL, about 20.7 mL, about 20.8 mL, about 20.9 mL, about 21 mL, about 21.1 mL, about 21.2 mL, about 21.3 mL, about 21.4 mL, about 21.5 mL, about 21.6 mL, about 21.7 mL, about 21.8 mL, about 21.9 mL, about 22 mL, about 22.1 mL, about 22.2 mL, about 22.3 mL, about 22.4 mL, about 22.5 mL, about 22.6 mL, about 22.7 mL, about 22.8 mL, about 22.9 mL, about 23 mL, about 23.1 mL, about 23.2 mL, about 23.3 mL, about 23.4 mL, about 23.5 mL, about 23.6 mL, about 23.7 mL, about 23.8 mL, about 23.9 mL, about 24 mL, about 24.1 mL, about 24.2 mL, about 24.3 mL, about 24.4 mL, about 24.5 mL, about 24.6 mL, about 24.7 mL, about 24.8 mL, about 24.9 mL, or about 25 mL of the formulation. In another example, the prefilled syringe contains about 26 mL, about 27 mL, about 28 mL, about 29 mL, about 30 mL, about 31 mL, about 32 mL, about 33 mL, about 34 mL, about 35 mL, about 36 mL, about 37 mL, about 38 mL, about 39 mL, about 40 mL, about 41 mL, about 42 mL, about 43 mL, about 44 mL, about 45 mL, about 46 mL, about 47 mL, about 48 mL, about 49 mL, or about 50 mL of the formulation. In one example, the prefilled syringe comprises a needle having a gauge of about 20 to about 33. In one example, the prefilled syringe comprises a 20-gauge needle, a 21-gauge needle, a 22-gauge needle, a 23-gauge needle, a 24-gauge needle, a 25-gauge needle, a 26-gauge needle, a 27-gauge needle, a 28-gauge needle, a 29-gauge needle, a 30-gauge needle, a 31-gauge needle, a 32-gauge needle, or a 33-gauge needle. In one example, the method comprises administering the formulation at a rate of about 4 to about 21 mL/min. In one example, the method comprises administering the formulation at a rate of at least about 5 to about 20 mL/min. In one example, the method comprises administering the formulation at a rate of at least or faster than about 10 to about 15 mL/min. In one example, the administration takes about 30 seconds to about 360 seconds. In one example, the administration takes at least about 60 seconds to about 300 seconds. In one example, the administration takes at least or less than about 120 seconds to about 240 seconds. In one example, the administration takes about 15

seconds to about 30 seconds. In one example, the administration takes at least about 60 seconds to about 180 seconds. In one example, the administration takes at least or less than about 120 seconds to about 240 seconds. In one example, the method comprises administering about 5 mL of the formulation at a rate of about 4 mL/min to about 21 mL/min. In one example, the method comprises administering about 10 mL of the formulation at a rate of about 4 mL/min to about 21 mL/min. In one example, the formulation has a viscosity of about 1 cP to about 50 cP. In one example, administration of the formulation requires less applied force when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, the method comprises administering about 5 mL of the formulation at a rate of about 4 mL/min to about 21 mL/min with an applied force of about 10 N to about 45 N. In one example, the method comprises administering the formulation to the subject using a prefilled syringe comprising a 25-gauge needle. In one example, the method comprises administering about 10 mL of the formulation to the subject at a rate of about 4 mL/min to about 21 mL/min with an applied force of about 25 N to about 50 N. In one example, the method comprises administering the formulation to the subject using a prefilled syringe comprising a 25-gauge needle. In one example, administration of the formulation is faster when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, administration of the formulation causes fewer side effects in the subject when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, administration of the formulation causes less pain and discomfort in the subject when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, administration of the formulation causes less back leakage at the injection site when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, the back leakage at the injection site is about 100% to about 30% less when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, administration of the formulation causes less swelling volume and/or swelling height at the injection site when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, the formulation causes about 35% to about 1% less swelling and/or swelling height at the injection site when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, administration of the formulation yields a lower bleb swelling size, less bleb induration, and/or quicker bleb resolution when compared to a similar formulation that does not comprise a hyaluronidase enzyme. In one example, the subject is human. In one example, the administering comprises the subject self-administering the formulation. In one example, the administering comprises a healthcare

provider or a caregiver administering the formulation to the subject. In one example, the subcutaneous administration comprises a single injection. In one example, the subcutaneous administration comprises two or more injections. In one example, the subcutaneous administration is delivered via an on-body device.

BRIEF DESCRIPTION OF THE DRAWINGS

[0004] The following detailed description of embodiments of the prefilled autoinfusion device will be better understood when read in conjunction with the appended drawings of exemplary embodiments. It should be understood, however, that the invention is not limited to the precise arrangements and instrumentalities shown.

[0005] Fig. 1 is a side perspective view of a prefilled autoinfusion device in accordance with an exemplary embodiment of the present invention.

[0006] Fig. 2 is a side cross-section view of a delivery apparatus in accordance with a second exemplary embodiment of the present invention.

[0007] Fig. 3 is a top view of a conduit and port of the prefilled autoinfusion device of Fig. 1.

[0008] Fig. 4 is a partial magnified view of a first end of the conduit and a distal end of the delivery apparatus of the prefilled autoinfusion device of Fig. 1.

[0009] Fig. 5 is a side perspective view of the delivery apparatus of Fig. 2 with a conduit connected thereto.

[0010] Fig. 6 is a graph of HVAI injection times (mean ± SEM).

[0011] Fig. 7 shows mean (mg ± SEM) and individual weights of back-leakage.

[0012] Fig. 8 shows individual swelling volumes (mL) after SC injection of Ig-120 and Ig-120 + rHuPH20 taken by caliper measurement at T0.

[0013] Fig. 9 shows individual swelling area (cm^2) after SC injection of Ig-120 and Ig-120 + rHuPH20 taken by caliper measurement at T0.

[0014] Fig. 10 shows individual swelling height (mm) after SC injection of Ig-120 and Ig-120 + rHuPH20 taken by caliper measurement at T0.

[0015] Fig. 11 is a graph of swelling volume (mL ± SEM) taken by caliper measurement over time (T0-T15-T30).

[0016] Fig. 12 is a graph of swelling area (cm^2 ± SEM) taken by caliper measurement over time (T0-T15-T30).