US 20130096534A1

(19) **United States**

(12) **Patent Application Publication**

Orilla et al.

(10) **Pub. No.: US 2013/0096534 A1**

(43) **Pub. Date: Apr. 18, 2013**

(54) **DRUG DELIVERY SYSTEMS AND METHODS**

(71) Applicant: **Allergan, Inc**, Irvine, CA (US)

(72) Inventors: **Werhner C. Orilla**, Anaheim, CA (US); **James A. Burke**, Santa Ana, CA (US)

(73) Assignee: **ALLERGAN, INC**, Irvine, CA (US)

(21) Appl. No.: **13/706,594**

(22) Filed: **Dec. 6, 2012**

Related U.S. Application Data

(63) Continuation of application No. 11/934,218, filed on Nov. 2, 2007, now Pat. No. 8,353,862.

Publication Classification

(51) **Int. Cl.**

A61F 9/007 (2006.01)

A61M 5/315 (2006.01)

(52) **U.S. Cl.**

CPC ***A61F 9/00736*** (2013.01); ***A61M 5/31515*** (2013.01); ***A61F 9/007*** (2013.01)

USPC **604/506**; 604/60

(57) **ABSTRACT**

A delivery system includes a housing along with a tip connected to one end of the housing. A first cannula extending from the tip is provided for inserting a rod implant into tissue. A second cannula, concentrically disposed within the first cannula, is utilized to force the rod implant from the first cannula and for ejecting a fluid behind the inserted rod implant in the tissue.

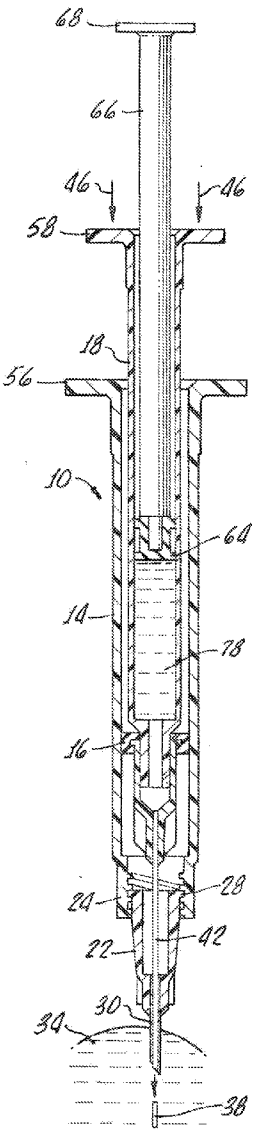
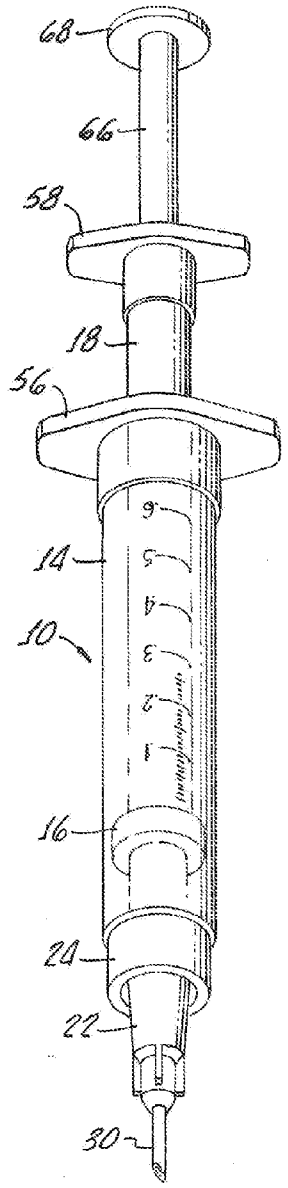


FIG. 1.



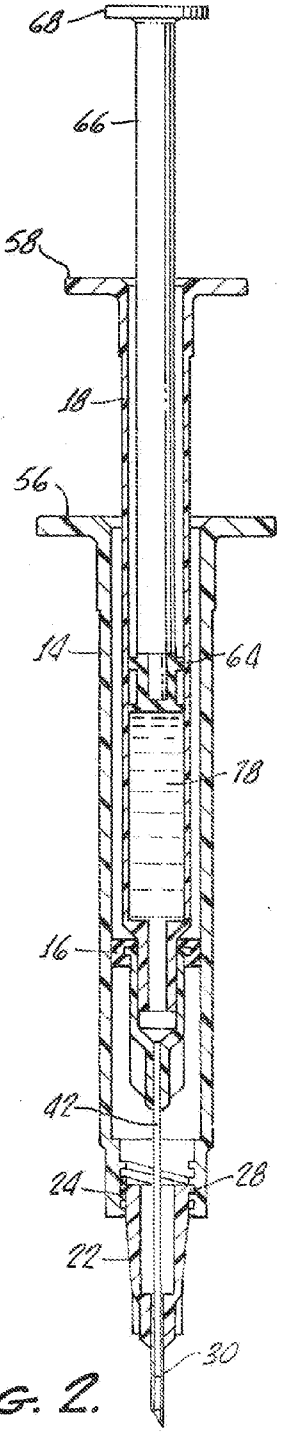


FIG. 2.

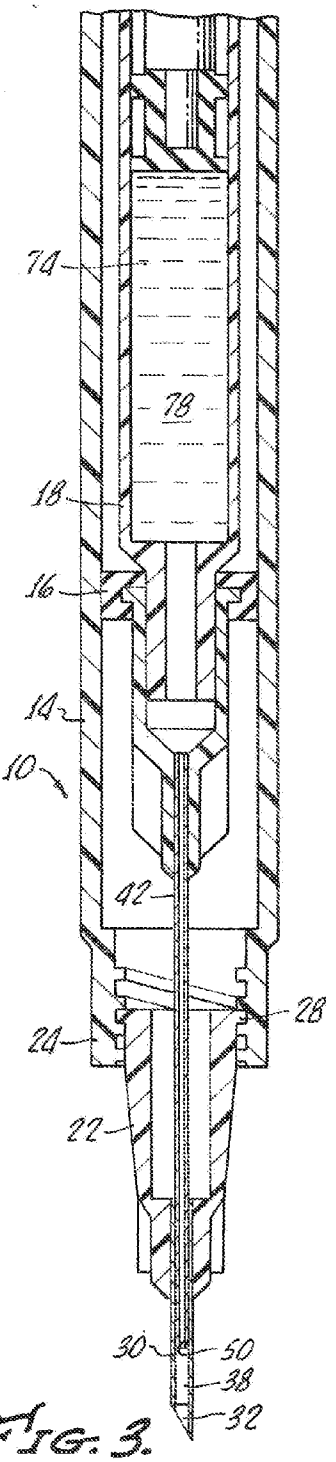


FIG. 3.

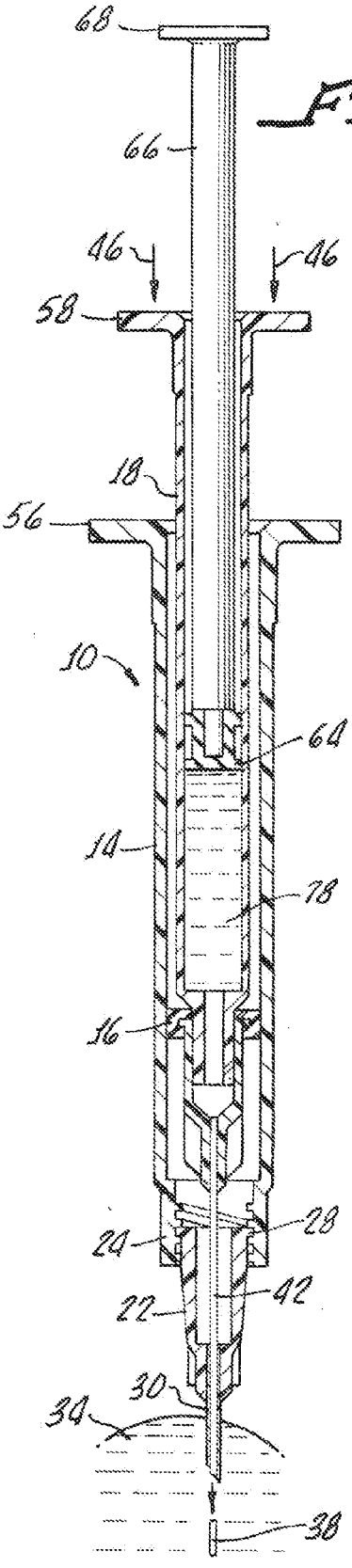

68
66
46
46
58
18
56
10
60
14
78
16
24
28
22
42
30
34
38

FIG. 4.

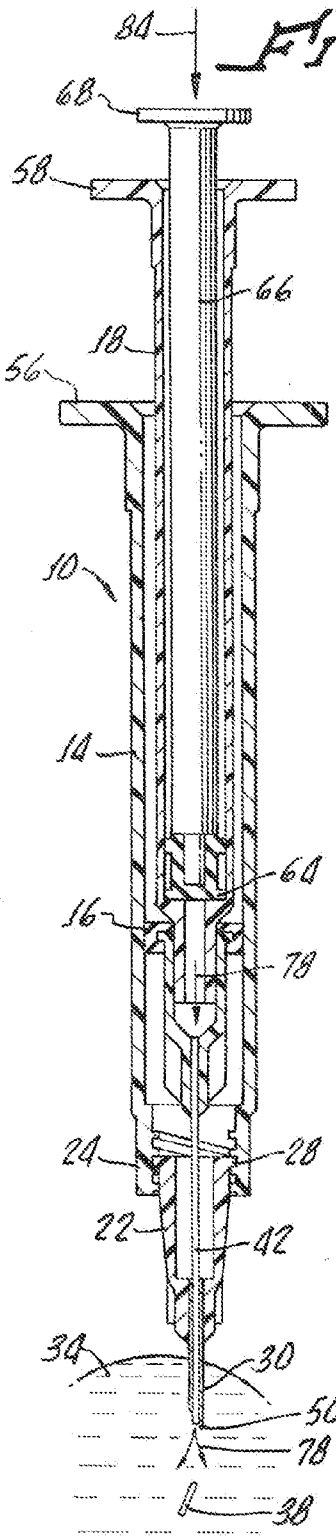

80
68
58
66
18
56
10
14
60
16
78
24
28
22
42
34
30
50
78
38

FIG. 5.

DRUG DELIVERY SYSTEMS AND METHODS

[0001] The present invention relates to methods and apparatus for delivering solid or semi-solid materials into the eye. Specifically, the present invention relates to a drug delivery system and methods that can be used to introduce implants containing therapeutic or active agents, including bioerodible implants, into various locations within the eye, including into the vitreous of the eye.

[0002] A primary difficulty in treating diseases of the eye is the inability to introduce drugs or therapeutic agents into the eye and maintain these drugs or agents at a therapeutically effective concentration in the eye for the necessary duration. Systemic administration may not be an ideal solution because, often, unacceptably high levels of systemic dosing is needed to achieve effective intraocular concentrations, with the increased incidence of unacceptable side effects of the drugs. Simple ocular instillation or application is not an acceptable alternative in many cases because the drug may be quickly washed out by tear-action or is otherwise depleted from within the eye into the general circulation. Suprachoroidal injections of drug solutions have also been performed, but again the drug availability is short-lived. Such methods make it difficult to maintain therapeutic levels of drug for adequate time periods.

[0003] Efforts to address this problem have lead to the development of drug delivery devices, or implants, which can be implanted into the eye such that a controlled amount of desired drug can be released constantly over a period of several days, or weeks, or even months. Many such devices have been previously reported. See, for example, U.S. Pat. No. 4,853,224, which discloses biocompatible implants for introduction into an anterior segment or posterior segment of an eye for the treatment of an ocular condition. U.S. Pat. No. 5,164,188 discloses a method of treating an ocular condition by introduction of a biodegradable implant comprising drugs of interest into the suprachoroidal space or pars plana of the eye. See also U.S. Pat. Nos. 5,824,072, 5,476,511, 4,997,652, 4,959,217, 4,668,506, and 4,144,317. Other method includes anchoring a plug or tack containing a drug into the sclera of the eye (see, e.g. U.S. Pat. No. 5,466,233).

[0004] Various sites exist in the eye for implantation of a drug delivery device or implant, such as the vitreous of the eye, anterior or posterior chambers of the eye, or other areas of the eye including intraretinal, subretinal, intrachoroidal, suprachoroidal, intrascleral, episcleral, subconjuctival, intracorneal or epicorneal spaces. Wherever the desired location of implantation, typical methods of implantation all require relatively invasive surgical procedures, pose a risk of excessive trauma to the eye, and require excessive handling of the implant. For example, in a typical method for placement in the vitreous, an incision is made through the sclera, and the implant is inserted into and deposited at the desired location in the vitreous, using forceps or other like manual grasping device. Once deposited, the forceps (or grasping device) is removed, and the incision is sutured closed. Alternatively, an incision can be made through the sclera, a trocar can be advanced through the incision and then the implant can be delivered through the trocar. Similar methods can be employed to deliver implants to other locations, e.g., implantation in the anterior chamber of the eye through an incision in the cornea.

[0005] The drawbacks of such techniques for implant delivery are many-fold. Extensive handling of the implant is necessary in these techniques, creating a risk that the implant will be damaged in the process. Many such implants are polymer-based and are relatively fragile. If portions of such plants are damaged and broken-off, the effective therapeutic dose delivered by the implant once placed will be significantly altered. In addition, it becomes inherently difficult using these methods to achieve reproducible placement from patient to patient. Also of import is that fact that all such techniques require an incision or puncture in the eye large enough to require suturing. Thus, such techniques are typically performed in a surgical setting.

[0006] U.S. Pat. No. 6,899,717 provides for an ergonomically designed apparatus in which a simple manual depression of an actuator produces proportional movement of a linkage that causes an implant or micro-implant (Drug Delivery System, DDS) to be ejected through an applicator cannula and disposed at the desired location in the eye. Small gauge cannulas are provided for self-sealing methods of delivery.

[0007] However, it has been found that a DDS deposited at a desired location in the vitreous does not remain at the desired location but may track back with the applicator cannula during withdrawal of the cannula. It has been concluded that the viscous property of the vitreous humor appears to be the cause of the attraction between the DDS and the application cannula.

[0008] The present invention overcomes this problem with two mechanisms.

[0009] The first mechanism provides a stylet that pushes the DDS out from a needle into the vitreous and the second mechanism provides for the injection of a viscous material from the same stylet. The viscous material plugs up the channel of the needle in the vitreous and accordingly prevents the DDS from tracking back with the applicator cannula during withdrawal.

SUMMARY OF THE INVENTION

[0010] An embodiment of delivery system for intraocular (such as intravitreal) administration of one or more solid or semi-solid implants to the eye of a patient in accordance with the present invention may include a housing with a tip connected to one end of the housing along with a first cannula extending from the tip for inserting a rod implant into tissue.

[0011] A second cannula may be concentrically disposed within said first cannula for forcing said rod implant out of the first cannula and for ejecting a fluid behind the insertion rod implant in said tissue.

[0012] A rod implant may also be part of the present invention along with a fluid which may be a viscous material or have a viscous inducing component such as for example a polymeric high molecular weight hyaluronic acid, carbomers, polyacrylic acid, cellulosic derivatives, polycarbophil, polyvinylpyrrolidone, gelatin, dextrin, polysaccharides, polyacrylamide, polyvinyl alcohol, polyvinyl acetate, derivatives thereof and mixtures thereof.

[0013] A first piston may be provided and slidably disposed within the housing along with a first plunger fixed to the first piston and also slidably disposed within the housing for ejecting the rod implant, disposed in the first cannula lumen, from the first cannula lumen by movement of the first plunger and first piston toward the tip.

[0014] A second cannula may be provided which extends from the first piston and is concentrically disposed within the first cannula and extendable through the first cannula lumen for forcing the rod implant out of the first cannula lumen as the first plunger is moved toward the tip.

[0015] A second piston may be provided and slidably disposed within the first plunger and a chamber is defined between the first piston and second piston within the first plunger. The second cannula is in fluid communication with the chamber and a second plunger, fixed to the second piston, is provided for ejecting the fluid, disposed in the chamber, through the second cannula by movement of the second plunger and the second piston toward the tip.

[0016] Preferably, the first cannula has an angulated end for facilitating penetration of tissue and the second cannula has a blunt end to facilitate engagement with the implant rod. The fluid comprises a viscous material for stabilizing the ejected rod implant.

[0017] A method in accordance with the present invention for implanting a drug delivery system rod into the vitreous of an eye generally includes disposing a drug delivery system rod into the vitreous of an eye and stabilizing a position of the rod in the vitreous by a viscous material. More particularly, the rod may be implanted through a first cannula lumen and the viscous material is ejected into the vitreous proximate the rod by a second cannula.

[0018] The method further includes using a second cannula to push the rod out of the first cannula lumen and such action is performed before ejecting the viscous material proximate the rod which may not only stabilize the rod within the viscous but also further push the rod into the vitreous.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The advantages and features of the present invention will be better understood by the following detailed description when considered in connection with the accompanying drawings, in which:

[0020] FIG. **1** is a perspective view of an applicator in accordance with the present invention generally showing a housing, a tip connected to one end of the housing, first and second pistons, first and second cannulas, and first and second plungers;

[0021] FIG. **2** is a cross sectional view of the applicator shown in FIG. **1**;

[0022] FIG. **3** is an enlarged cross sectional view of the applicator tip and cannulas illustrated in FIGS. **1** and **2**;

[0023] FIG. **4** is a cross sectional view illustrating the use of the applicator in injecting a rod implant into tissue; and

[0024] FIG. **5** is a view similar to FIG. **4** illustrating the stabilization of the rod within the tissue by a viscous material.

DETAILED DESCRIPTION

[0025] With reference to FIGS. **1-5**, there is shown a syringe needle stylet drug delivery system intravitreal implant applicator **10** in accordance with the present invention which generally includes a housing **14** which may be formed from any suitable material and is preferably transparent in order to visualize the position of a first piston **16** and plunger **18** therein. A tip **22** is connected to one end **24** of the housing **14** by means of threads **28**, or the like, (See FIG. **2**) and a first cannula **30** extends from the tip **22** which includes a lumen **32** therethrough, as most clearly seen in FIG. **3**. Preferably, the first cannula **30** is angulated for facilitating a penetration of vitreous **34** illustrated in FIGS. **4** and **5**.

[0026] With continued reference to FIG. **3**, a rod implant **38**, disposed within the first lumen **32**, is ejected therefrom by a second cannula **42** which extends through the first cannula lumen **32** and forces the rod implant **38** out of the first cannula lumen **32** as the first piston **16** and plunger **18** is moved toward the tip **22**. This is illustrated in FIG. **4** by the arrows **46**. Suitable rod implants and method of manufacturing same is set forth in U.S. patent application Ser. No. 11/859,627, filed Sep. 21, 2007 and entitled "Steroid Containing Drug Delivery Systems". This patent is to be incorporated herein in its entirety by this specific reference thereto.

[0027] Providing the second cannula **42** with a blunt end **50** facilitates ejection of the rod **38**. The rod **38** and may be an intravitreal drug delivery system (DDS) such as Posurdex and the Brimonidine. A housing handle **56** and a first plunger handle **58** facilitate the manual movement of the first plunger **18** and the first piston **16** for ejecting the DDS rod **38** through the first cannula **30**.

[0028] A second piston **64** is disposed within the first plunger **18** and interconnected to a second plunger **66** and handle **68**. Initially defined between the first piston **16** and second piston **64** is a chamber **74** for containing any biocompatible viscous material, such as, for example, Healon.

[0029] Alternatively, the fluid may include any suitable viscosity inducing component such as, for example, but are not limited to, a polymeric high molecular weight hyaluronic acid, carbomers, polyacrylic acid, cellulosic derivatives, polycarbophil, polyvinylpyrrolidone, gelatin, dextrin, polysaccharides, polyacrylamide, polyvinyl alcohol, polyvinyl acetate, derivatives thereof and mixtures thereof.

[0030] The viscosity-inducing component may be a polymeric hyaluronate component, for example, a metal hyaluronate component, preferably selected from alkali metal hyaluronates, alkaline earth metal hyaluronates and mixtures thereof, and still more preferably selected from sodium hyaluronates, and mixtures thereof. Such components are described and set forth in U.S. Ser. No. 11/859,621 hereinabove referenced and incorporated herein.

[0031] In addition, the delivery of an active agent or implant described in U.S. Ser. Nos. 10/966,764, 11/741,366, 11/039,192, 11/116,698, 11/695,527; 60/939,659 and 11/742,350 which are to be incorporated herein in their entirety by this specific reference thereto.

[0032] As illustrated, the second cannula **42** is in fluid communication with the chamber **74** for enabling ejection of the fluid, or viscous material, **78** through the second cannula **42** by movement of the second plunger **66** and second piston **64** toward the tip **22** as illustrated by the arrow **84**.

[0033] As shown in FIG. **5** the viscous material **78**, forced from the second cannula **42** behind the rod **38**, both stabilizes the rod **38** and prevents movement thereof as the applicator **10** with cannulas **30** and **42** are withdrawn from the vitreous **34**. In addition, the viscous material **78** may further force the rod **38** into the viscous **34** to a desired location.

[0034] FIGS. **4** and **5** further illustrate a method of implanting a drug delivery system rod into the vitreous of an eye in accordance with the present invention. This method generally includes disposing a drug delivery system rod into the vitreous of an eye and stabilizing a position of the rod in the vitreous by a viscous material. The rod is implanted through a first cannula lumen **32** through the use of the second cannula **42** for pushing the rod **38** out of the first cannula lumen **32**.

[0035] As illustrated in FIG. **5**, the viscous material **78** is injected into the vitreous **34** proximate the rod **38** via the second cannula **42**. Further pushing of the rod **38** in the vitreous **34** may be accomplished by continued movement of the second piston **64** and second plunger to force more of the

viscous material **78** behind the rod **38**. After injecting of the viscous material **78** the applicator **10** is removed from the viscous **34**.

[0036] Although there has been hereinabove described a specific drug delivery system and methods in accordance with the present invention for the purpose of illustrating the manner in which the invention may be used to advantage, it should be appreciated that the invention is not limited thereto. That is, the present invention may suitably comprise, consist of, or consist essentially of the recited elements. Further, the invention illustratively disclosed herein suitably may be practiced in the absence of any element which is not specifically disclosed herein. Accordingly, any and all modifications, variations or equivalent arrangements which may occur to those skilled in the art, should be considered to be within the scope of the present invention as defined in the appended claims.

1.-**9**. (canceled)

10. A drug delivery system for introducing a bioerodible implant into the vitreous of an eye, the system comprising:

a housing;

a tip connected to one end of said housing;

a first piston slideably disposed within said housing;

a first cannula extending from said tip and having a lumen extending therethrough;

a bioerodible implant disposed within the first cannula lumen;

a first plunger fixed to said first piston and slideably disposed within said housing for ejecting said implant from the first cannula lumen as the first plunger is moved toward said tip;

a second cannula extending from said first piston and concentrically disposed within said first cannula and extendable through the first cannula lumen for forcing said implant out of the first cannula lumen as the first plunger is moved forward;

a second piston slideably disposed within said first plunger;

a chamber within said first plunger, said chamber being defined between said first piston and said second piston, said second cannula being in fluid communication with said chamber;

a rod stabilizing fluid, disposed in said chamber, for preventing movement of the ejected implant in the vitreous as the first and second cannulas are withdrawn from the vitreous; and

a second plunger fixed to said second piston for ejecting the rod stabilizing fluid through said second cannula and behind the ejected implant by movement of said second plunger and second piston toward said tip;

wherein the rod stabilizing fluid includes a sodium hyaluronate.

11. The drug delivery system according to claim **10**, wherein said first cannula has an angulated end for facilitating penetration of the vitreous of an eye and said second cannula has a blunt end to facilitate engagement with said implant.

12.-**14**. (canceled)

15. A method of introducing a bioerodible implant into the vitreous of an eye, said method comprising:

introducing a bioerodible implant into the vitreous of an eye using the drug delivery system of claim **10** or **11**; and

stabilizing a position of the implant in the vitreous by ejection of the rod stabilizing fluid.

16.-**23**. (canceled)

* * * * *