In practice, due to manufacturing and assembly tolerances radial position of the piston rod 10 and/or the bearing disc 12 may vary within certain limits. Hence, a piston rod 10 and/or a bearing disc 12 can be radially displaced with respect to the center of the piston 16. If not properly aligned, it may occur, that the force provided by the piston rod 10 and the bearing disc 12 is non-centrically transferred to the piston 16. Such radial offset may in turn lead to a cant or tilt of the piston 16, which is flexibly deformable to a certain extent. As a consequence, a displacement force required for distally displacing the piston 16 may substantially rise. Additionally, also the dosing accuracy may decrease when a distally directed driving force is non-centrally transferred to the piston 16.

Also, since the distance elements 14 protrude from the proximal end face of the piston 16, thrust being applied to the piston 16 is entirely received by the distance elements 14, which, as a consequence may become squeezed. However, such point stresses and squeezing effects may further have a negative impact on the dosing accuracy of the drug delivery device and its drive mechanism.

Objects of the Invention

It is therefore an object of the present invention to provide an improved piston for a cartridge as well as an improved plunger of a drug delivery device interacting with such pistons. In particular, the invention focuses on the plunger-piston interface of cartridges and drive mechanisms of drug delivery devices, preferably of pen-injector type. It is a further aim of the present invention to prevent non-centrally directed force transmission towards a cartridge's piston. As a further object, the invention aims to provide an improved dosing accuracy.

Summary ~~of the Invention~~

In one aspect, there is provided a drug delivery device for dispensing of a pre-defined amount of a liquid drug comprising a drive mechanism having a plunger (10, 32) and being adapted to receive a cartridge (33), wherein the cartridge (24) comprises a cylindrical cartridge body (24) providing a drug receiving volume being at least partially filled with a medicament and being sealed by means of a piston (36), the piston comprising:

- a body (36) comprising natural or synthetic rubber,

- at least one annular sealing surface (35) to radially abut against an inner side wall (24) of a cartridge (33),

- a distal surface (42) to confine a drug receiving volume of the cartridge (33),

- a thrust receiving surface (40) adapted to receive a thrust exerting plunger (10, 32) of a drug delivery device for displacing the piston in a distal direction relative to the side wall (24),

- wherein the thrust receiving surface (40) comprises numerous knob-like centering elements (34) protruding from the thrust receiving surface (40) towards the plunger (10, 32) and wherein the centering elements (34) comprise an outer shape and geometry that matches with a corresponding receptacle (38) of the plunger (10, 32), and wherein the centering elements (34) are arranged and aligned on the circumference of an imaginary annular or circular structure, and

- wherein the plunger comprises a bearing disc (32) with a circumferential groove (38) to entirely receive the centering elements (34) such that the distal end face (44) of the bearing disc (32) directly abuts against the thrust receiving surface (40) of the piston and wherein the shape and geometry of the groove (38) matches with the shape and

geometry of the piston's centering elements (34), such that the end face (44) almost entirely buts against the thrust receiving surface (40) of the piston (36).

The present disclosure~~invention~~ provides a piston for a cartridge for a drug delivery device, wherein the piston comprises at least one annular sealing surface to radially abut against an inner side wall of a cartridge, being typically of cylindrical shape. The piston is adapted to be slidably disposed in the cartridge and to provide a durable and leak-

The centering elements are arranged and aligned on the circumference of an imaginary annular or circular structure in the plane of the thrust receiving surface.

The circular structure may be circular-symmetric but may also be oval or elliptical. By making use of such a circular arrangement, mutual centering and alignment of piston and plunger can be easily attained when the circular structure is inherently symmetric to the centre of the thrust receiving surface.

In a preferred embodiment, the centering elements and/or the circular structure corresponds with a circular shape of the receptacle of the plunger. In this way, not only the structure and shape of numerous centering elements but also their mutual distance and alignment matches with the receptacle of the plunger.

In this embodiment, the at least one centering element may also comprise a rectangular and/or arcuate shape in a plane parallel to the thrust receiving surface. Further, it is of particular benefit, when various centering elements are arranged at a distance with respect to each other on the circumference of said imaginary circular or annular structure.

Each of the centering elements may for instance comprise a somewhat rectangular shape, wherein each centering element is slightly bended according to the radius and circumference of the imaginary circular structure.

By having a circular shaped receptacle or groove on the plunger and by having numerous centering elements distributed along the circumference of the imaginary circle, a mutual radial centering of piston and plunger as well as a mutual orientation in the transverse plane can be achieved irrespective on the orientation of the piston and its centering elements in the plane of the thrust receiving surface.

Furthermore, and according to another preferred embodiment~~aspect~~, the centering elements comprise an arcuate shape in a plane parallel to the thrust receiving surface. Hence, the shape of at least some, preferably of all centering elements matches with the shape and geometry of the ring-like or annular receptacle of the plunger. This way, when plunger and piston are arranged with a slight lateral offset, almost

all available centering elements contribute in a rather similar way to a mutual alignment and centering of piston and plunger.

According to another preferred embodiment of the disclosure~~invention~~, the at least one centering element is integrally formed with a body of the piston. Typically, the piston is manufactured by injection moulding. It may comprise thermoplastic materials and/or natural or synthetic rubber. At least one of the centering elements may further act as a spacer or distance element that serves to prevent mutual adhering of pistons in the course of a mass production process. Said at least one particular centering element comprises a knob-like shape.

In a further preferred embodiment, at least one centering element is tapered in direction towards the plunger. Accordingly, also the receptacle provided in the plunger comprises a corresponding tapered cross-section, which allows to entirely receive the centering element therein.

In a further preferred embodiment, the at least one centering element comprises a bevelled lateral surface. Since the receptacle is correspondingly shaped, by way of such bevelled surfaces, a radial adjustment of piston and plunger can be attained when mutually corresponding bevelled surfaces of receptacle and centering element get in contact in the course of an axially and distally directed displacement of the plunger.

Preferably, the bevelled lateral surface of the at least one centering element is oriented at an angle of 20° to 80° with respect to the plane of the thrust receiving surface. More preferably, the bevelled lateral surface of the centering element is oriented at an angle between 30° to 60°, most preferably, the angle is around 45°.

Furthermore, it is beneficial, when at least one centering element is substantially triangular or convex in shape in a plane perpendicular to the thrust receiving surface. Hence, the bevelled lateral surface does not necessarily have to be rectilinear. It can be bended, such as to facilitate mutual radial alignment of piston and plunger in the course of a distally directed movement of the plunger.

According to another preferred embodiment of the disclosure~~invention~~, the ratio of at least one centering element's axial extension, that is the extension substantially perpendicular to the thrust receiving surface, versus its radial expansion, that is the expansion parallel to the plane of the thrust receiving surface, is larger or equal than 0.6. Such a ratio is particularly beneficial for the purpose of radially centering plunger and piston or cartridge in the course of a distally directed movement of the plunger towards the piston.

In another independent embodiment~~aspect~~, the disclosure~~invention~~ further relates to a plunger of a drive mechanism of a drug delivery device, such as a pen-type injector. The plunger comprises an end face adapted to but against a thrust receiving surface of a piston being slidably disposed in a drug containing cartridge. The end face of the plunger facing towards the piston comprises at least one receptacle being adapted to receive a centering element that protrudes from the thrust receiving surface of the piston.

The receptacle of the sface as well as the centering element protruding from the piston's thrust receiving surface mutually match in size, shape and geometry. Also, the receptacle comprises a somewhat circular or annular shape that corresponds with the position and/or alignment of the centering element provided on the thrust receiving surface. In this way, an eventual radial offset in position or orientation of plunger and/or piston or cartridge can be compensated in the course of bringing plunger and piston in a mutual abutment configuration.

When shape and geometry of the receptacle matches with the shape and geometry and/or alignment of the piston's centering element, the end face of the plunger may almost entirely but against the thrust receiving surface of the piston. In this way, thrust provided by the plunger can be evenly distributed across the plunger-piston-interface. Also, point stresses as they are arising in the prior art and their negative impact on dosing accuracy can be effectively reduced.

In preferable embodiments, the receptacle disposed on the end face of the plunger comprises a substantially U- or V-shaped groove of circular geometry in the plane of the end face. By having a circular symmetric receptacle, a plurality of centering elements spaced apart from each other and being arranged on an imaginary circumference of a

corresponding circle can be inserted into said receptacle, irrespective of the orientation of the piston in the plane of its thrust receiving surface.

According to still another preferred embodiment, the plunger comprises an axially displaceable piston rod and a radially extending bearing disc. The bearing disc is rotatably supported at a distal end portion of the piston rod. Preferably, the bearing disc comprises the receptacle at its end face pointing towards the piston, when the drug delivery device is finally assembled.

In a further independent embodiment~~aspect~~ the disclosure~~invention~~ also refers to a cartridge for a drug delivery device that comprises a substantially cylindrical cartridge body providing a drug receiving volume at least partially filled with a medicament and being sealed by means of a piston as described above. The medicament is typically intended for injection into biological tissue of a patient.

Moreover, the disclosure~~invention~~ also refers to a drug delivery device for dispensing a pre-defined amount of a liquid drug and being further adapted to receive a cartridge having a piston as described above. The drug delivery device further comprises a drive mechanism having a plunger comprising at least one receptacle being adapted to receive a centering element protruding from a thrust receiving surface of the piston of said cartridge.

The term „medicament", as used herein, means a pharmaceutical formulation containing at least one pharmaceutically active compound,

wherein in one embodiment the pharmaceutically active compound has a molecular weight up to 1500 Da and/or is a peptide, a proteine, a polysaccharide, a vaccine, a DNA, a RNA, a antibody, an enzyme, an antibody, a hormone or an oligonucleotide, or a mixture of the above-mentioned pharmaceutically active compound,

wherein in a further embodiment the pharmaceutically active compound is useful for the treatment and/or prophylaxis of diabetes mellitus or complications associated with diabetes mellitus such as diabetic retinopathy, thromboembolism disorders such as deep vein or pulmonary thromboembolism, acute coronary syndrome (ACS), angina,

pharmaceutically acceptable salt of a poly-sulphated low molecular weight heparin is enoxaparin sodium.

Pharmaceutically acceptable salts are for example acid addition salts and basic salts. Acid addition salts are e.g. HCl or HBr salts. Basic salts are e.g. salts having a cation selected from alkali or alkaline, e.g. Na+, or K+, or Ca2+, or an ammonium ion N+(R1)(R2)(R3)(R4), wherein R1 to R4 independently of each other mean: hydrogen, an optionally substituted C1-C6-alkyl group, an optionally substituted C2-C6-alkenyl group, an optionally substituted C6-C10-aryl group, or an optionally substituted C6-C10-heteroaryl group. Further examples of pharmaceutically acceptable salts are described in "Remington's Pharmaceutical Sciences" 17. ed. Alfonso R. Gennaro (Ed.), Mark Publishing Company, Easton, Pa., U.S.A., 1985 and in Encyclopedia of Pharmaceutical Technology.

Pharmaceutically acceptable solvates are for example hydrates.

It will be apparent to those skilled in the art that various modifications and variations can be made to the present disclosure~~invention~~ without departing from its spirit and scope. Further, it is to be noted, that any reference signs used in the appended claims are not to be construed as limiting the scope of the present disclosure~~invention~~.

Brief Description of the Drawings

Without limitation, the present invention will be explained in greater detail below in connection with preferred embodiments and with reference to the drawings in which:

Figure 1 illustrates a cross-section of a plunger-piston-interface region inside a pen-type injector according to the prior art,

Figure 2 illustrates a top view of the piston according to Figure 1,

Figure 3 shows a cross section of a plunger-piston-interface region according to the present invention,