



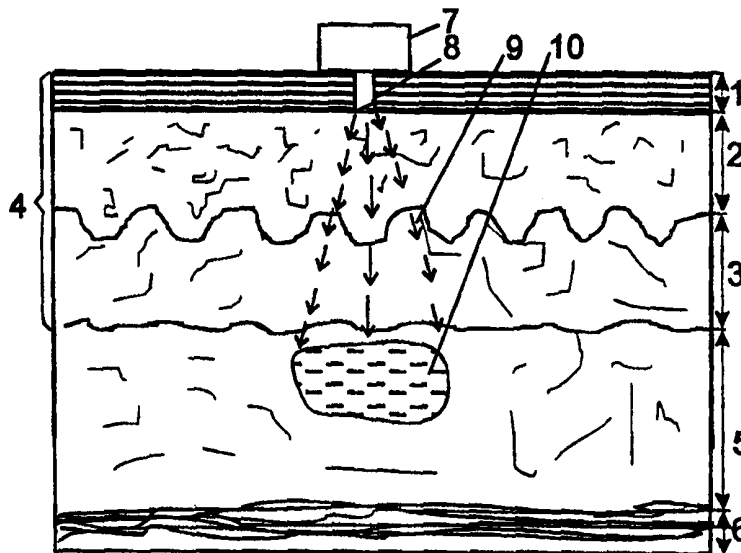
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/DK98/00292 (22) International Filing Date: 1 July 1998 (01.07.98) (30) Priority Data: 0861/97 14 July 1997 (14.07.97) DK 60/053,496 23 July 1997 (23.07.97) US (71) Applicant: NOVO NORDISK A/S [DK/DK]; Novo Allé, DK-2880 Bagsværd (DK). (72) Inventor: SMEDEGAARD, Jørgen, K.; Bernhard Bangs Allé 22, DK-2000 Frederiksberg (DK).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>	

(54) Title: INJECTION MEMBER

(57) Abstract

An injection member for a jet spray injection device through which device a dose of medicine is administered for subcutaneous or intramuscular injection has a jet nozzle designed as a needle having a length of 0,05 - 0,3 mm enabling it just to penetrate the stratum corneum.



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Injection member

- 5 The invention relates to an injection member for a jet spray injection device through which device a dose of medicine is administered for subcutaneous or intramuscular injection.

It is often wanted to perform a subcutaneous injection of a medicine dose. The medicine is deposited in the subcutis tissue from where it subsequently finds its way to the blood. Especially diabetics have to frequently inject themselves with insulin to keep their blood glucose content under control. For this purpose more kinds of injection devices exist.

A classic injection device comprises a syringe which is provided with a needle which has a length enabling it to penetrate cutis and enter subcutis where a dose of medicine is deposited by being pressed from the syringe out through the needle.

However, many people are reluctant to prick themselves with needles and although needles are made very thin and short an injection may still happen to nourish the above mentioned reluctance which may promote a user to cut down the number of injections to a level beyond the warrantable.

To overcome this needle phobia of the patient and to further reduce pain, various jet injection systems have been developed. Such jet injection systems have no needle but a spray nozzle through which the medicine is sprayed to give the medicine a speed enabling it to penetrate the cutis and be dispersed in the subcutis. However, dosing is difficult, in part due to the anatomical condition of the skin (cutis) where the first layer (stratum corneum) consists of dead, keratinised cells. The layer is much more resistant to water penetration than to lipid penetration, and it forms a strong mechanical barrier, especially considering the thickness of the layer, which has a mean of 0.1 mm on the most of the body (thin skin). The stratum corneum is enlarged in a few specific areas (thick skin): e. g. the hand and the foot sole, areas where injection normally is avoided. Beneath stratum corneum follows the various other layers of epidermis, with living skin cells, blood vessels, sensory nerve endings ect. Epidermis is followed by dermis which is mainly connective tissue. Then follows subcutis (mostly adipose tissue and connective tissue), the size of subcutis is very variable in the in-

dividual person and between persons. By the spray injection it is difficult to estimate how much of the medicine glances off from the dead cells at the skin surface and how much actually reaches the subcutis.

- 5 It is an object of the invention to provide an injection member for a jet spray injection device by which injection member the above mentioned draw-backs are overcome.

An injection member according to the invention is characterised in that it comprises a jet nozzle designed as a needle having a length in the range from 0,05mm to 6 mm combined
10 with the jet spray nozzle.

The use of the injection member according to the invention will reduce the risk of damaging the often very large medicine molecules during the passage of the skin. Furthermore, less injection force need to be applied and a more precise definition of the injection depth is possible so that superficial or too profound deposits is avoided. The size of the pointer or the
15 needle may be so small that it does not cause pain but is, if at all, felt as a small pressure on the skin. The risk for bleeding due to needle trauma is also reduced to almost zero.

According to the invention the needle or pointer may have a length in the range 0.05 mm to
20 4 mm, preferably between 0.3 mm and 2 mm. Such needles will be too short for conventional injection but may be used for jet injection to ensure that the jet has not to penetrate the stratum corneum.

In a preferred embodiment of the injection member according to the invention the nozzle
25 may be designed as a pointer having a length from 0.05 mm to 0.3 mm, more preferred 0.1 mm to 0.2 mm. With this length the pointer is long enough to weaken or penetrate the stratum corneum but not long enough to cause significant contact with the layer of living cells beneath stratum corneum and insertion in subcutis is impossible. Neither will the pointer be able to get in contact with the sensory nerve endings located in cutis. Medicine delivered as
30 a jet through the pointer will not partly glance off from the keratine layer, thus the injected dose will be more accurate. Moreover the risk of pain release as seen with conventional subcutaneous needles will be minimised to that of the jet stream.

The shape of the pointer may be that of a conventional needle , but it may have other forms and the peripheral end may be sharp or blunted. The inner diameter of the pointer may be from 0.1 mm to 3 mm.

- 5 According to the invention the injection member may appropriately be a changeable unit which can be mounted on a jet injection syringe. This will allow the injection member to be changed each time an injection has been made. Also the needle may at each injection be chosen to have a length suited for the user and the intended point of injection.
- 10 By a number of measurement it is found that the thickness of the cutis and subcutis lies in the intervals described in the following table. The mean values may be seen as the values valid for the preferred injection zones.

	<u>Females</u>			<u>Males</u>		
	min	max	mean	min	max	mean
cutis	1,1	3,6	1,7	1,2	4,1	2,3
subcutis	4,5	30,8	12,1	2,3	26,9	7,2
sum	5,6	34,4	13,8	3,5	31,0	9,5

15

According to the invention the injection member may be provided with an array of short needles. Hereby a better distribution of the injected liquid is ensured .

20 In the following the invention is described in further details with references to the drawing, wherein

Figure 1 schematically shows a sectional view of the skin during the injection of a liquid in a jet from an injection member according to the invention, and

25 Figure 2 shows schematically a sectional view of the skin during injection of a liquid in multiple jets from another embodiment of the injection member according to the invention.

In figure 1 a keratin layer 1, stratum corneum, overlies the epidermal 2 and dermal layer 3. These three layers forms cutis, the skin, 4. Beneath this is subcutis 5 followed by a muscle 6 in its fascia.

5 An injection member 7 is pressed against the upper surface of the skin so that a pointer 8 penetrates the keratin layer 1. From this position a jet 9 is expelled from the pointer 8 at a speed allowing it to penetrate the remaining part of cutis and to intrude the subcutis 5 where it forms a deposit 10 which subsequently is taken up by the blood/lymph system. During its passage into subcutis 5 the jet 9 is decelerated so it will not penetrate the muscle fascia 6.

10

As the pointer helps the jet to pass the cutis the jet need not be expelled with as high an energy content as needs a jet which must pierce the surface of the cutis. If an intramuscular injection is wanted the velocity and the pressure by which the jet is expelled must be correspondingly higher so that the liquid is not decelerated to an extent disabling its penetration ability until it has passed the muscle membrane 3.

15

In figure 2 elements corresponding to elements shown in figure 1 are given the same reference numbers. The injection member may be equipped with a number of needles or pointers. In the embodiment shown in figure 2 an injection member with three needles 8 are shown. By this dividing into more jets 9 a better distribution of the liquid in the subcutis is obtained. As the jets do not have to perform the initial penetration of the cutis surface a lower energy content in each jet will do and the output energy which may be supplied by an injector can be distributed to more jets.

20

25 Figure 3 shows an injection member 7 mounted on a cartridge 12 in a housing 13 of an injection device. The cartridge 12 is closed by a rubber membrane 14 which is by a metal cap 16 clamped sealingly to a flange 15 forming an integral part of the cartridge 12. The injection member is clicked onto the ampoule by circular hook edge 17 gripping behind the flange 15. A needle element 18 penetrates the membrane to establish communication between the inside of the cartridge and a nozzle 19 which is surrounded by a ring shaped or tubular pointer 8. The injection member may be released from the ampoule by breaking the hook edge out of engagement with the flange, and the member may be replaced by a new injection member.

30

Claims

1. An injection member for a jet spray injection device through which device a dose of medicine is administered for subcutaneous or intramuscular injection characterised in that it comprises a jet nozzle designed as a needle having a length in the range from 0,05mm to 6 mm combined with the jet spray nozzle.
- 5
2. An injection member according to claim 1, characterized in the that the needle has a length in the range 0.05 mm to 4 mm, preferably between 0.3 mm and 2 mm.
- 10
3. An injection member according to claim 1, characterised in that the needle has a length in the range 0.05 mm to 0.3 mm, preferably 0.1 mm to 0.2 mm.
4. An injection member according to claim 1, 2 or 3, characterised in that the member is a changeable unit which can be mounted on a jet injection syringe.
- 15
5. An injection member according to anyone of the preceding claims, characterised in that it comprises an array of needles
- 20
- 25
- 30

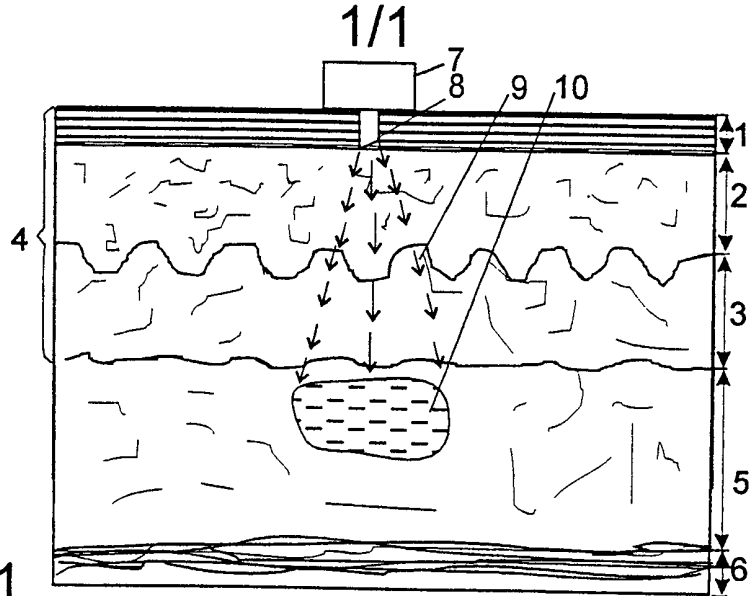


Fig. 1

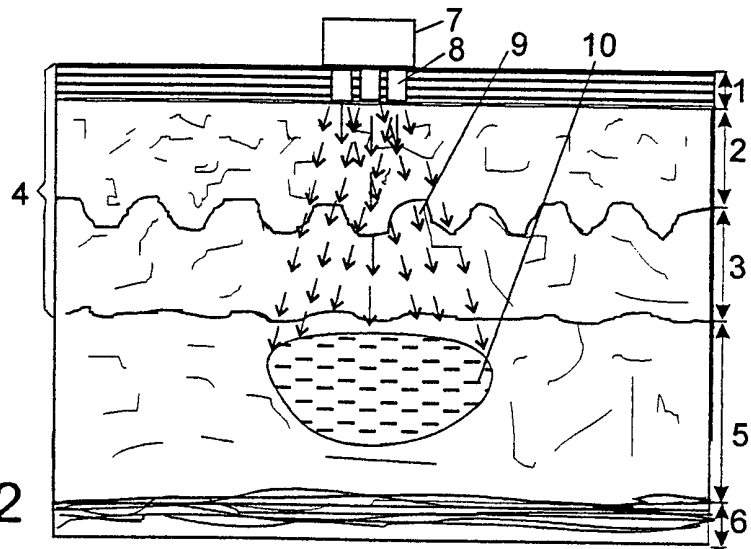


Fig. 2

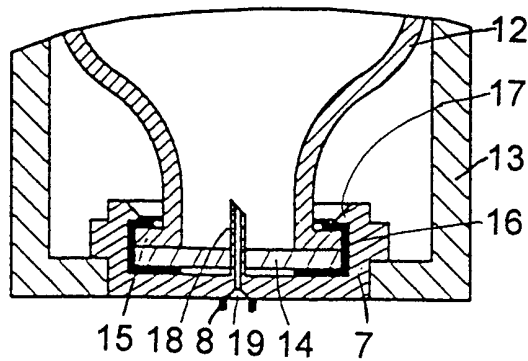


Fig. 3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/DK 98/00292

A. CLASSIFICATION OF SUBJECT MATTER		
IPC6: A61M 5/30, A61M 5/158 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
IPC6: A61M		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
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C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5304128 A (T.M.HABER ET AL), 19 April 1994 (19.04.94), column 2, line 29 - line 31	1-4
Y	column 2, line 23 - line 25 --	5
Y	EP 0205915 A1 (ALUIGI,MARIO ET AL), 30 December 1986 (30.12.86), figure 1, abstract -- -----	5
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Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5304128 A	19/04/94	WO 9406493 A	31/03/94
EP 0205915 A1	30/12/86	CA 1275215 A	16/10/90
		JP 62026075 A	04/02/87