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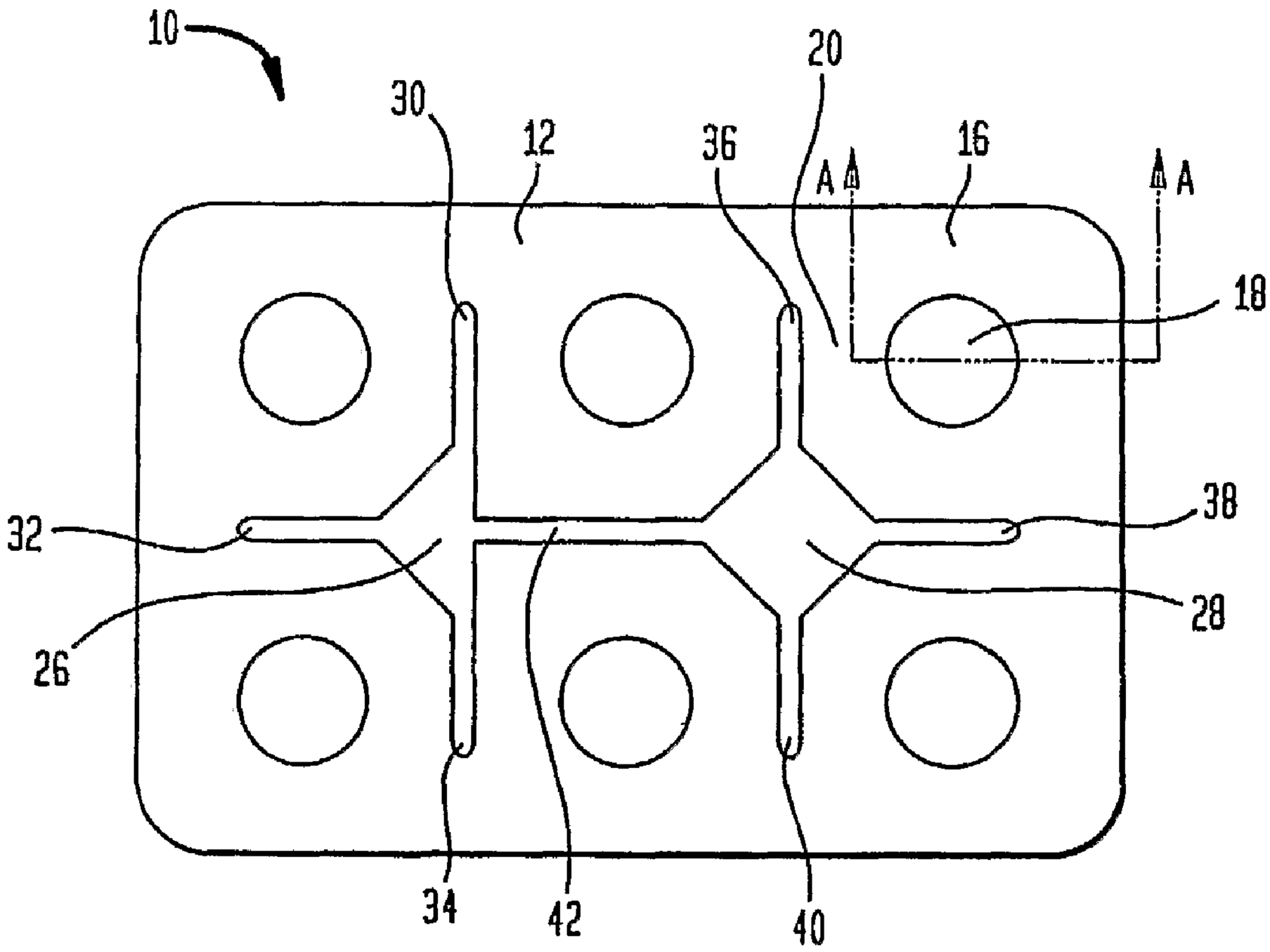
(54) Title: NON-TEARABLE CHILD RESISTANT BLISTER PACKAGE



(57) Abrégé/Abstract:
A non-tearable child resistant blister package (10) and method of utilizing same are disclosed. The package (10) may include a unitary blister sheet (12) and a unitary sheet of lidding material (14). The lidding sheet (14) is preferably peelably sealed to the blister sheet (12), and includes unsealed areas (26) for facilitating the peeling of the lidding material (14) from the blister sheet (12). These unsealed areas (26) are only accessible by cutting at least a portion of the blister package (14).

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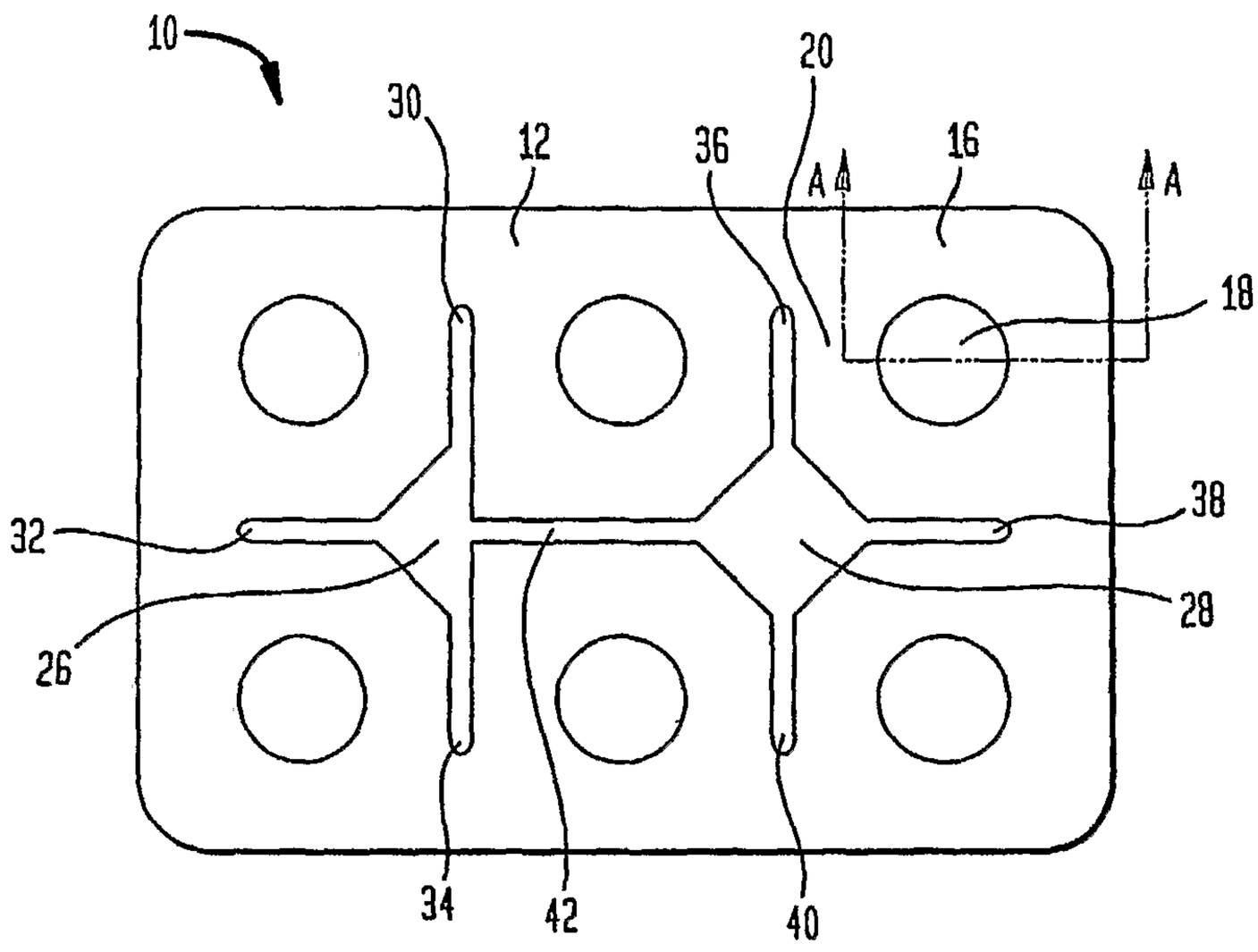
(54) Title: NON-TEARABLE CHILD RESISTANT BLISTER PACKAGE



(57) Abstract: A non-tearable child resistant blister package (10) and method of utilizing same are disclosed. The package (10) may include a unitary blister sheet (12) and a unitary sheet of lidding material (14). The lidding sheet (14) is preferably peelably sealed to the blister sheet (12), and includes unsealed areas (26) for facilitating the peeling of the lidding material (14) from the blister sheet (12). These unsealed areas (26) are only accessible by cutting at least a portion of the blister package (14).

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NON-TEARABLE CHILD RESISTANT BLISTER PACKAGE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of the filing date of United States Provisional Patent Application No. 60/644,263 filed January 14, 2005, the disclosure of which is hereby incorporated herein by reference

[0002] Many people, as part of their daily routine, take various types of medication. Some may take several different types of pharmaceutical dosage forms in a given period. These pharmaceutical dosage forms may include pills, capsules, tablets, liquids and the like. As with many industries for which a tangible product is offered for sale, packaging is an issue. Often times, the manner in which a product is offered is a deciding factor in whether or not a purchase is made. This situation is no different in the pharmaceutical field. But other concerns may also drive the style of packaging in the pharmaceutical industry.

[0003] One packaging concern is the nature of the dosage form. Some tablets, for example, are frangible, friable or breakable (used synonymously). Such dosage forms may be easily damaged both during transport of the package and by a user upon opening. The disclosures of commonly assigned U.S. Pat. Nos. 5,178,878 and 5,223,264, which are hereby incorporated by reference herein, describe relatively soft tablets which are susceptible to this type of damage. Tablets which fall into this category tend to have a low hardness and may include very soft tablets with a hardness below about 15 Newtons.

[0004] Standard dosage forms are typically packaged in blister packages, which are comprised of multi-layered sheets of material having pockets, blisters or wells for containing the dosage forms. One type of conventional blister packages include packages having a foil layer through which a user of the package must push the tablet, thereby breaking the foil. An example of such a conventional blister package is shown in

U.S. Pat. No. 4,158,411 to Hall et al., the disclosure of which is hereby incorporated by reference herein. While this type of package is sufficient for packaging standard dosage forms, packaging of frangible dosage forms in such a package would cause damage to the frangible dosage form when attempting to push it through the foil layer. These types of packages are also generally not child proof.

[0005] Another concern with the packaging of pharmaceutical dosage forms relates to safety. Child proof or child resistant packaging is often very desirable for the packaging of dosage forms. Clearly, a big concern with having medication in the home is the possibility of a child gaining access to it. For example, certain medications would be deadly to a child if consumed, even in small quantities. For this reason, packaging is often rated based upon the number of children who can gain access to the drug in five minutes. One example of testing procedure standards for achieving ratings such as this are set forth in 16 C.F.R. § 1700.20.

[0006] Therefore, there exists a need for a package, and in particular, a frangible or friable dosage package that is child proof, while still being configured to prevent damage of the dosage that the package is designed to store.

SUMMARY OF THE INVENTION

[0007] The present invention relates to packages including but not limited to packages for frangible pharmaceutical dosage forms or tablets, more particularly, the packages invented are non-tearable child resistant packages that require the cutting of the package with a scissor to expose a flap allowing for the package to be opened and its contents removed.

[0008] A first aspect of the present invention is a non-tearable blister package for frangible or non-frangible pharmaceutical dosage forms. The package preferably includes a unitary blister sheet defining a plurality of unit package regions, each unit package region including a recess having an

open top and a flange surrounding the recess. Each recess may accommodate one or more dosage forms. The package also includes a unitary sheet of lidding material peelably sealed to the flanges. The blister sheet and the sheet of lidding material define unsealed areas for facilitating peeling of the lidding material from the blister sheet. The unsealed areas are only accessible by cutting at least a portion of the blister package. In a preferred embodiment, the blister package is constituted of materials and configured to retard access through tearing or chewing, especially by children. In another aspect, the blister sheet and/or lidding material includes indicia indicating that the blister must be cut with a scissors or other similar devices.

[0009] In a particularly preferred embodiment, the blister package is designed to reduce breakage of a frangible or friable tablet housed therein. The frangible dosage forms disposed in each recess of the preferred blisters preferably engages the walls of each recess so that the walls hold the dosage form away from the bottom of the recess and adjacent the lidding material. This aspect protects the dosage form from damage by preventing shifting of the dosage form during transport. An empty space between each dosage form and the bottom of the recess in which the dosage form is disposed cushions the dosage form from impact when the package is dropped. The recesses of the package and the dosage forms disposed in the recesses may have essentially any shape. For example, the dosage forms may be disk-shaped tablets, oblong capsules or square-shaped pills. Similarly, shapes for recesses include circular, oblong, polygonal or star shapes in the plane of the blister sheet.

[0010] Furthermore, the walls and bottom of the recesses may define a shape in the form of a surface of revolution, about a vertical axis normal to the flange surrounding each of the recesses. For example, the recesses may have a curved, cup-

like shape. Where the dosage forms are disc-shaped, they may each have an edge which contacts the walls of the recess in which each dosage form is disposed. The edge and walls preferably define an annular region of contact coaxial with the vertical axis of the recess. The edge of such a disc-shaped dosage form may comprise a bevel which contacts the walls of the recess. This annular region of contact may prevent shifting of the dosage form within the blister and the damage to the dosage form associated with such shifting.

[0011] In certain embodiments of the present invention, the packaging can be rated as a highly child resistant package such as packages generally referred to in the industry as "F4", "F3", "F2" or "F1". These monikers are given to packages that pass certain tests relating to how many children can gain access to the dosage forms housed in the packages in a certain amount of time. Typically, the number following the "F" refers to the number of tablets that would cause serious personal injury or serious illness to a twenty five pound child if ingested. For example, one such test begins with a base of fifty children, their goal being to access the dosage form housed in the package. The children are first given the packages without instructions to access the dosage forms, and are given five minutes to attempt to gain access. After the five minutes expires, the children are asked to stop, at which point they are shown the proper steps to take in order to gain access to the dosage forms. Thereafter, the children are given an additional five minutes to work with the package. According to this one test, an F1 package would be one in which no more than five children can gain access to one pill during the ten minute period. A package would be given the F2 label if no more than five children can gain access to two pills. And, an F3 package would be one in which no more than five children can gain access to three pills in the ten minute period. While the above described test is one well known test utilized by the

packaging industry, there are clearly many different tests that can be conducted in order to properly rate packages. These tests are generally done in accordance with 16 C.F.R. § 1700.00 - 1700.20.

[0012] Another aspect of the present invention is a method of removing a dosage form from a blister package. The method according to this aspect includes providing a blister package having a blister sheet defining a plurality of unit package regions, each unit package region including a recess having an open top and a flange surrounding the recess and a unitary sheet of lidding material peelably sealed to the flanges, the blister sheet and the sheet of lidding material defining unsealed areas for facilitating peeling of the lidding material from the blister sheet, where the unsealed areas are only accessible by cutting at least a portion of the blister package. The method also includes the steps of cutting at least a portion of the blister package to reveal at least one of the unsealed areas, peeling away at least a portion of the lidding material to reveal at least one dosage form disposed in the recess, and removing the at least one dosage form from the recess. In a preferred embodiment, the blister package is constructed of materials and configured to retard access through tearing, chewing, puncture, etc. especially by children. In another aspect, the blister sheet and/or lidding material includes indicia indicating that the blister must be cut with a scissors or other similar device. In a particularly preferred embodiment, the blister package is designed to reduce breakage of a frangible or friable tablet housed therein.

[0013] Another embodiment of the present invention is another method of removing a dosage form from a blister package. The method according to this embodiment includes providing a blister sheet including unit package regions and a lidding sheet for sealing the unit package regions, the lidding sheet including peelable and non-peelable areas, the non-

peelable areas surrounding the package periphery. The method also may include the step of accessing the peelable areas with a cutting instrument, such as scissors.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] FIG. 1 is a bottom plan view of the blister package according to the present invention.

[0015] FIG. 2 is top a plan view of the blister package of FIG. 1.

[0016] FIG. 3 is a cross-sectional side view of a unit package region of the blister package taken along line A-A of FIG. 1.

[0017] FIG. 4 is a top plan view of the blister package according to another embodiment of the present invention.

[0018] FIG. 5 is a bottom plan view of the blister package according to yet another embodiment of the present invention.

DETAILED DESCRIPTION

[0019] A non-tearable child resistant blister package 10 in accordance with an embodiment of the present invention is shown in FIGS. 1-3. The blister package 10 shown is non-tearable, to create a child resistant container for tablets that requires the cutting of specific portions in order to access the dosage forms contained therein. Blister package 10 includes a blister sheet 12 and a lidding material sheet 14. It is contemplated that blister package 10 can be designed so that the cutting may be performed with the use of ordinary scissors, or other common cutting devices.

[0020] The overall design of blister package 10 prevents easy access of often highly dangerous and poisonous dosage forms, by children or the like. To reduce the ability to tear the package, at least one of the blister sheet 12 or the lidding sheet 14 will not include a structure at its edge (the periphery of the package), which facilitate tearing such as indentations, cuts, scores or the like. On the contrary, the edge may be thickened or reinforced to retard tearing. In

other words, at least one of the lidding material or the blister sheet may be composed of materials that will be difficult to tear. The thickness of the lidding material or the blister sheet may also play a role. For example, in certain preferred embodiments, blister sheet 12 may be constructed of material supplied by Alcan Pharma Center of Shelbyville, KY ("Alcan") and offered as PCS technical and material specification no. 92011 ("the 92011 material") having a thickness of approximately 205 μm. The 92011 material includes several different individual layers, for example, approximately 60 μm of PVC film, approximately 25 μm of polyamide film, approximately 60 μm of aluminum foil and approximately 60 μm of additional PVC film, which are preferably at least joined together by suitable adhesives. Lidding material sheet 14, on the other hand, may be constructed of PCS technical and material specification nos. 15144 having a thickness of approximately 37 μm or 15127 having a thickness of approximately 37 μm. Both of these materials are also supplied by Alcan, and preferably include a paper layer, an approximately 12 μm thick polyester film, an approximately 25 μm thick aluminum foil layer and a heat seal coating. Using Alcan adhesive supplied under the No. 4516, one can obtain a so-called "F1" package using the construction illustrated in Figure 5 and the materials described above. It is noted that in certain preferred embodiments, the package depicted in Figure 5 may have a length of approximately of one hundred (100) mm, and most preferably 104 mm, and a width of approximately sixty (60) mm, and most preferably 68 mm. However, it is noted that certain materials may be tearable if they are thin enough. Other materials, which would be expected to be tearable, may not be if thick enough or if properly reinforced. Moreover, if one of these two layers is tear resistant, it is not required that the other be tear resistant. Although, neither layer would preferably permit easy puncture

with a finger or allow pressing the tablet out by rupture; the upper limit of thickness is generally not important so long as it is not so thick so as to be difficult to cut by an adult using an ordinary household scissor, or other common cutting devices.

[0021] Non-tearable blister package 10 is formed by blister sheet 12 and lidding material sheet 14 shown in FIGS. 1 and 2, respectively. Blister sheet 12 includes a plurality of unit package regions 16, each unit package region including a recess 18 and a flange 20 surrounding the recess (shown in FIGS. 1 and 3). Blister sheet 12 includes six package regions 16, although any number of package regions 16 can be included. As shown in FIG. 3, each recess 18 is dimensioned and configured to house a tablet 1, and includes an open top 22 and a closed bottom 24. Preferably, recesses in accordance with the present invention will be circular and one (1) inch in diameter or less, preferably three quarters (3/4) of an inch or less, more preferably eleven sixteenths (11/16) of an inch or less, and most preferably one half (1/2) of an inch are less. However, while larger recesses are indeed possible, such larger recesses may make rupture by biting or puncture easier.

[0022] Blister sheet 12 also includes raised areas 26 and 28. Raised and/or unsealed area 26 further includes raised finger sections 30, 32, and 34, and raised and/or unsealed area 28 further includes raised finger sections 36, 38, and 40. The terms raised and unsealed are used interchangeably throughout. Raised connection section 42 connects raised areas 26 and 28 together, thereby creating a continuous raised section between each of the raised areas and their respective finger sections. In the embodiment shown in FIGS. 1-3, none of the raised areas and/or finger sections extends to any of the edges of blister sheet 12. This creates a blister package 10 that is non-tearable. It is contemplated that the particular size and/or shape of the same may vary in different embodiments. These

raised areas will be discussed further below in the discussion relating to removing lidding material.

[0023] Lidding material sheet 14 is a unitary sheet that overlies recesses 18 and is peelably attached to flanges 20, thereby covering tablets 1 housed in the recesses. It is contemplated that lidding material sheet 14 may be attached to flanges 20 through the use of an adhesive, for example, certain embodiments utilize adhesive supplied by Alcan under the number 4563 or the aforementioned 4516. However, it is also contemplated that other modes of attaching lidding material sheet 14 to flanges 20 can be utilized, and that the strength of the attachment mode can be varied to determine the difficulty required to remove the lidding material. Cut lines 44 may also be welded indicia and are designed to instruct a user on where to cut in order to create individual lidding sections 46. These individual lidding sections 46 are configured so that they correspond to unit package regions 16. Cutting along cut lines 44, creates a separated unit package region 16 with a corresponding lidding section 46 attached thereto, as is best shown in FIG. 3. Lidding material sheet 14 may further include cutting indicia 48, which along with cut lines 44, instructs a user on how and where make the various cuts. The indicia may be written instructions or symbols. Lidding sheet may also include peeling indicia 50 that instructs a user where and how to peel away lidding section 46 from its corresponding unit package region 16. Finally, blister package 10 may include reinforced areas 60 cut on adjacent edges thereof to provide further tear resistance. These may be regions of increased thickness, embossed or glued on structures and the like.

[0024] As best shown in FIG. 3, the cutting and subsequent separation of individual unit package regions 16 and their corresponding individual lidding sections 46, allows the aforementioned raised areas to become accessible by a user.

FIG. 3 depicts raised area 26, however, it is noted that the separation of other unit package regions 16 from the other unit package regions 16 may allow for any raised area or section to become accessible. As shown in FIG. 3, raised area 26 creates a non-attached region between blister sheet 12 and lidding material sheet 14. Essentially, the raised areas prevent peelable attachment of lidding sheet 14 to blister sheet 12 along the entire area of the given raised areas, and thus create areas where a user can grasp the lidding material and peel it away. The aforementioned raised finger sections provide additional unsealed areas that may allow for the easier pealing away of the lidding material along different lengths of the unit package region. The fact that none of the raised areas or raised finger sections extends to any of the edges of blister sheet 12, forces a user to cut at least a portion of blister package 10 in order to access these unsealed sections.

[0025] The embodiment shown in FIGS. 1 and 2 is configured so that the cutting of individual unit package regions 16 and corresponding lidding sections 46 away from blister package 10 may allow for the easy accessibility to dosage forms stored in more than a single recess 18. In other words, the embodiment depicted in FIGS. 1 and 2 might allow for the easy grasping and peeling away of more that one lidding section 46 upon the cutting away of a single unit package region. However, other embodiments are envisioned in which the removal of a unit package region only allows for a single lidding section to be peeled away from its corresponding unit package region. For example, as shown in FIG. 4, blister package 110 is provided having a different configuration from that of blister package 10. Blister package 110 may include a blister sheet similarly configured to that of blister package 10. However, as shown in FIG. 4, lidding sheet 114 includes differently arranged cut lines 144, thus creating differently arranged lidding sections 146. Lidding sheet 114 may also include cutting indicia 148

and peeling indicia 150, similar to that of blister sheet 14.

[0026] Cut lines 144 are arranged so that the cutting away of a single unit package region only allows for the peeling away of the lidding section 146 corresponding to that particular unit package region. As shown in FIG. 4, cutting away of the individual unit package regions leaves a remainder section 152. In certain embodiments, remainder sections 152 extend around the raised fingers of blister sheet 12. This, in turn, prevents the peeling away of other lidding sections 146, as after cutting away the unit package region, only a portion of the raised area, and none of the raised finger, is accessible to a user. However, it is contemplated that other embodiments may include blister sheets that are configured in such a manner so as to allow for both a raised area and a finger area to be accessed upon the removal of the lidding section 146. Essentially, these blister sheets would provide a configuration that compliments lidding sheet 114.

[0027] It is contemplated that the design of blister package 10 may also provide protection for frangible dosage forms by including recesses 18 that cooperate with such dosage forms to prevent shifting of the frangible dosage forms during transport and/or cushioning in the event of impact from the dropping of the package. Commonly assigned U.S. Patent No. 6,155,423 to Katzner et al. ("the '423 patent"), the disclosure of which is hereby incorporated by reference herein, teaches one solution to this problem. The '423 patent discloses a blister package having a peelable layer which when pealed away allows for access to the dosage form. Therefore, the '423 patent provides a user accessibility to his or her frangible dosage form without the possibility of damaging the dosage form. The blister package of the '423 is also designed to help protect the tablet during storage, shipment and use. The present invention may utilize a similar design.

[0028] In certain embodiments of the present invention,

frangible dosage forms may be disposed in each recess 18 of blister sheet 12 such that the dosage forms engage the walls of each recess 18, and the walls hold the dosage form away from closed bottom 24 of recess 18 and adjacent lidding material 14. Such a configuration is best shown in FIG. 3. This aspect protects the dosage form from damage by preventing shifting of the dosage form during transport. An empty space between each dosage form and closed bottom 24 of the recess 18 in which the dosage form is disposed cushions the dosage form from impact if and when package 10 is dropped or otherwise jarred. Recesses 18 and the corresponding dosage forms disposed in recesses 18 may have essentially any shape. For example, the dosage forms may be disk-shaped tablets, oblong capsules or square-shaped pills. Similarly, shapes for recesses 18 include circular, oblong, polygonal or star shapes in the plane of the blister sheet.

[0029] Furthermore, the walls and closed bottom 24 of recess 18 may define a shape in the form of a surface of revolution, about a vertical axis normal to flange 20 surrounding each of the recesses 18. For example, recesses 18 may have a curved, cup-like shape. Where the dosage forms are disc-shaped, they may each have an edge which contacts the walls of recess 18 in which each dosage form is disposed. The edge and walls define an annular region of contact coaxial with the vertical axis of recess 18. The edge of such a disc-shaped dosage form may comprise a bevel which contacts the walls of recess 18. The annular region of contact prevents shifting of the dosage form within the blister and the damage to the dosage form associated with such shifting.

[0030] The tablet packaging according to the present invention is designed to be child resistant. The packaging can be rated as a highly child resistant package or better. Indeed, tablet package 10 is designed to prevent a relatively high amount of children from accessing the drug in a given

time. Certain embodiments according to the present invention may be rated as high as the well known industry standard known as F1 packaging, as discussed above. Other embodiments may achieve an F2 or F3 rating. Different embodiments are therefore envisioned for housing different types of dosage forms. While the present invention has been discussed with respect to frangible or friable dosage forms, it is also contemplated that other types of dosage forms may also be housed. Of course, it is noted that a user should select proper packaging for the particular active. For example, highly dangerous or poisonous dosage forms should be packaged in a highly child resistant package, while less dangerous dosage forms may be packaged in less child resistant packages.

[0031] Finally, one preferred formation method of the aforementioned blister packages 10, 110 and the packaging process of dosages forms 1 therein will be described. It is to be understood that many different suitable processes may be utilized in accordance with the present invention, and the following is but one preferred method. In such a method/process, sheets of material for forming blister sheet 12 and lidding material 14 are preferably received in roll form and fed or loaded onto a blister machine. It is noted that such machines are well-known in the art. The material forming blister sheet 12 is then preferably moved to a forming station where recesses 18 are formed into the material by tools such as forming plugs. Tablets 1 are then preferably placed into each open recess 18 of blister sheet 12.

[0032] With recesses 18 each containing one or more tablets 1, blister sheet 12 is then preferably moved to a sealing station where upper and lower sealing plates may be utilized to seal lidding material 14 to blister sheet 12. The aforementioned sealing plates preferably utilize heat and pressure over the course of a certain dwell time (cycles/speed) to heat a suitable adhesive (like those described above) to

seal lidding material 14 to blister sheet 12. Subsequent to this sealing step, desired perforations may be formed in the package, and individual blister cards 10 (with multiple recesses 18) may be punched out. It is noted that the formed perforations may be useful in this punch out procedure, but may also remain in the final blister package 10 as discussed above. Ultimately, the individual packages 10 are preferably delivered to final packaging stations via conveyors or the like.

[0033] The dosage forms, usually tablets, which can be packaged using the present invention are not at all limited by the type of tablet or the type of active pharmaceutical ingredient ("API") used therein. These API's include, without limitation, analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, anxiolytics, laxatives, anorexics, antihistamines, antidepressants, antiasthmatics, antidiuretics, antiflatuents, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, beta blockers, peptides, proteins, oligonucleotides and other substances of biological origin, and combinations thereof. Also contemplated are the drugs and pharmaceutically active ingredients described in Mantelle, U.S. Pat. No. 5,234,957, in columns 18 through 21. That text of Mantelle is hereby incorporated by reference. Any of the forgoing API's can be used in the form of any salt, hydrate, solvate, polymorph, or individual optical isomer, and any mixture thereof.

[0034] In particular, opiates, drugs used to treat pain, drugs used in psychiatry or in the treatment of schizophrenia, such as clozapine and cytotoxic substances are particularly preferred. Also preferred is any API which is intended to treat the elderly or any API which requires the use of a child-proof package, and more particularly an "F1" package.

[0035] Legal opiates which may be packaged according to the invention include prescription drugs such as, without

limitation, alfentanil, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, codeine phosphate, desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine, dihydrocodeinone enol acetate, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levorphanol, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, morphine hydrochloride, morphine sulfate, myrophine, nalbuphine, narceien, nicomorphine, norlevorphanol, normethadone, normorphine, norpipanone, opium, oxycodone, oxymorphone, papveretum, pentazocine, phenadoxone, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, propirm, propoxyphene, remifentanil, sufentanil and tilidine. The class of compounds generally known as opiates also includes illicit drugs such as heroin and cocaine. Opiates in accordance with the present invention include those identified above as well as any listed as controlled substances pursuant to 21 C.F.R. § 1308.12. Opiates are given to patients for a variety of reasons, most frequently for pain mitigation of one type or another.

[0036] A cytotoxic substance includes any agent that kills cells. These substances are generally used in the treatment of malignant and other diseases. They are designed to destroy rapidly growing cancer cells. They have been shown to be mutagenic, carcinogenic and/or teratogenic, either in treatment doses or animal and bacterial assays. Cytotoxic drugs that interfere with critical cellular processes including DNA, RNA, and protein synthesis, have been conjugated to antibodies and subsequently used for in vivo therapy. Such drugs, include, but are not limited to:

[0037] i) intercalating agents, in particular doxorubicin

(Adriamycin), daunorubicin, epirubicin, idarubicin, zorubicin, aclarubicin, pirarubicin, acridine, mitoxanthrone, actinomycin D, eptilinium acetate;

[0038] ii) alkylating agents chosen from platinum derivatives (cisplatin, carboplatin, oxaliplatin);

[0039] iii) a compound chosen from the other groups of alkylating agents: cyclophosphamide, ifosfamide, chlormetrine, melphalan, chlorambucil, estramustine, busulfan, mitomycin C, nitrosoureas: BCNU (carmustine), CCNU (lomustine), fotemustine, streptozotocin, triazines or derivatives: procarbazine, dacarbazine, pipobroman, ethyleneimines: altretamine, triethylene-thio-phosphoramide,

[0040] iv) a compound chosen from the other groups of anti-metabolic agents: antifolic agents: methotrexate, raltitrexed, antipyrimidine agents: 5-fluorouracil (5-FU), cytarabine (Ara-C), hydroxyurea antipurine agents: purinethol, thioguanine, pentostatin, cladribine, cytotoxic nucleoside synthesis inducers: gemcitabine,

[0041] v) a compound chosen from the other groups of tubulin-affinity agents, vinca alkaloids which disrupt the mitotic spindle: vincristine, vinblastine, vindesine, navelbine, agents which block the depolymerization of the mitotic spindle: paclitaxel, docetaxel, agents which induce DNA cleavage by inhibition of topoisomerase II: etoposide, teniposide, topoisomerase I inhibitors which induce DNA cleavage: topotecan, irinotecan,

[0042] vi) a DNA splitting or fragmenting agent, such as bleomycin,

[0043] vii) one of the following compounds: plicamycin, L-asparaginase, mitoguazone, dacarbazine,

[0044] viii) an anticancer progestative steroid; medroxy-progesterone, megestrol,

[0045] ix) an anticancer estrogen steroid:

diethylstilbestrol; tetrasodium fosfestrol,

[0046] x) an antiestrogen agent: tamoxifen, droloxifen, raloxifen, aminoglutethimide,

[0047] xi) a steroidal antiandrogenic agent (eg cyproterone) or a non-steroidal antiandrogenic agent (flutamide, nilutamide).

[0048] In addition to the API's mentioned herein, the dosage forms of the invention can, in addition or instead, include vitamins, minerals and dietary supplements. As used in this disclosure, the term "vitamin" refers to trace organic substances that are required in the diet. For the purposes of the present invention, the term "vitamin(s)" includes, without limitation, thiamine, riboflavin, nicotinic acid, pantothenic acid, pyridoxine, biotin, folic acid, vitamin B.sub.12, lipoic acid, ascorbic acid, vitamin A, vitamin D, vitamin E and vitamin K. Also included within the term "vitamin" are the coenzymes thereof. Coenzymes are specific chemical forms of vitamins. Coenzymes include thiamine pyrophosphates (TPP), flavin mononucleotide (FMM), flavin adenine dinucleotide (FAD), Nicotinamide adenine dinucleotide (NAD), Nicotinamide adenine dinucleotide phosphate (NADP), Coenzyme A (CoA), pyridoxal phosphate, biocytin, tetrahydrofolic acid, coenzyme B.sub.12, lipoyllysine, 11-cis-retinal, and 1,25-dihydroxycholecalciferol. The term "vitamin(s)" also includes choline, carnitine, and alpha, beta, and gamma carotenes.

[0049] The term "mineral" refers to inorganic substances, metals, and the like required in the human diet. Thus, the term "mineral" as used herein includes, without limitation, calcium, (calcium carbonate), iron, zinc, selenium, copper, iodine, magnesium, phosphorus, chromium and the like, and mixtures thereof. The term "dietary supplement" as used herein means a substance which has an appreciable nutritional effect when administered in small amounts. Dietary supplements include, without limitation, such ingredients as bee pollen, bran, wheat

germ, kelp, cod liver oil, ginseng, and fish oils, amino-acids, proteins and mixtures thereof. As will be appreciated, dietary supplements may incorporate vitamins and minerals.

[0050] In general, the amount of active ingredient incorporated in each tablet or dosage form (API, vitamin, mineral, dietary supplement and the like), may be selected according to known principles of pharmacy. An effective amount of API is specifically contemplated. By the term "effective amount," it is understood that, with respect, to for example, a "pharmaceutically effective amount" is contemplated. A "pharmaceutically effective amount" is the amount or quantity of a drug or API which is sufficient to elicit the required or desired therapeutic response, or in other words, the amount which is sufficient to elicit an appreciable biological response when administered to a patient. As used with reference to a vitamin or mineral, the term "effective amount" means an amount at least about 10% of the United States Recommended Daily Allowance ("RDA") of that particular ingredient for a patient. For example, if an intended ingredient is vitamin C, then an effective amount of vitamin C would include an amount of vitamin C sufficient to provide 10% or more of the RDA. Typically, where the tablet includes a mineral or vitamin, it will incorporate higher amounts, preferably about 100% or more of the applicable RDA.

[0051] The amount of active ingredient used can vary greatly. Of course, the size of the dosage form, the requirements of other ingredients, and the number of, for example, tablets which constitute a single dose will all impact the upper limit on the amount of pharmacologically active ingredient which can be used. However, generally, the active ingredient is provided in an amount of between greater than zero and about 80% by weight of the finished tablet and, more preferably, in a range of between greater than zero and about 60% by weight thereof. Put in other terms, the active

ingredient can be included in an amount of between about 1 microgram to about 2 grams, and more preferably between about 0.01 and about 1000 milligrams per dosage form, i.e., per tablet.

[0052] Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as defined by the appended claims.

INDUSTRIAL APPLICABILITY

[0053] The present invention enjoys wide industrial applicability including, but not limited to, providing packaging for medications, especially those in tablet form and frangible tablet form.

CLAIMS

1. A non-tearable blister package comprising:

a unitary blister sheet defining a plurality of unit package regions, each unit package region including a recess having an open top and a flange surrounding the recess; and

a unitary sheet of lidding material peelably sealed to said flanges, said blister sheet and said sheet of lidding material defining unsealed areas for facilitating peeling of said lidding material from said blister sheet, wherein said unsealed areas are only accessible by cutting at least a portion of said blister package.

2. The blister package according to claim 1, further including indicia for directing the cutting of said blister package.

3. The blister package according to claim 1, wherein said blister sheet includes six unit package regions.

4. The blister package according to claim 3, wherein at least two cuts must be made to access all of said unsealed areas.

5. The blister package according to claim 1, wherein said recess includes walls and a closed bottom.

6. The blister package according to claim 5, wherein a dosage form may be disposed in said recess and engages said walls of said recess so that said walls hold said dosage form away from said closed bottom and adjacent said lidding material so that there is an empty space between each said dosage form and said closed bottom of said recess.

7. A packaged dosage form including a package as claimed in claim 1 and a plurality of pharmaceutical dosage forms disposed in said recesses.

8. The packaged dosage form claimed in claim 7, wherein the pharmaceutical dosage forms are fentanyl.

9. A method of removing a frangible dosage form from a blister package comprising:

providing a blister package having a blister sheet defining a plurality of unit package regions, each unit package region including a recess having an open top and a flange surrounding the recess and a unitary sheet of lidding material peelably sealed to said flanges, said blister sheet and said sheet of lidding material defining unsealed areas for facilitating peeling of said lidding material from said blister sheet, wherein said unsealed areas are only accessible by cutting at least a portion of said blister package;

cutting at least a portion of said blister package to reveal at least one of said unsealed areas;

peeling away at least a portion of said lidding material to reveal at least one dosage form disposed in said recess; and

removing said at least one dosage form from said recess.

10. The method according to claim 9, wherein said cutting step includes making multiple cuts.

11. The method according to claim 10, wherein said cutting step includes separating at least one unit package region from the other unit package regions.

12. The method according to claim 9, wherein said cutting step reveals multiple unsealed areas.

13. The method according to claim 9, wherein said pealing step includes pealing away a section of lidding material corresponding to said unit package region.

14. A method of removing a dosage form from a blister package comprising:

providing a blister sheet including unit package regions and a lidding sheet for sealing the unit package regions, the lidding sheet including peelable and non-peelable areas, the non-peelable areas surrounding the package periphery;

accessing the peelable areas with a cutting instrument.

15. The method according to claim 14, further including the step of peeling away the lidding sheet.

16. The method according to claim 15, further including the step of removing the dosage form.

17. The method according to claim 14, wherein the cutting instrument is a scissor.

FIG. 1

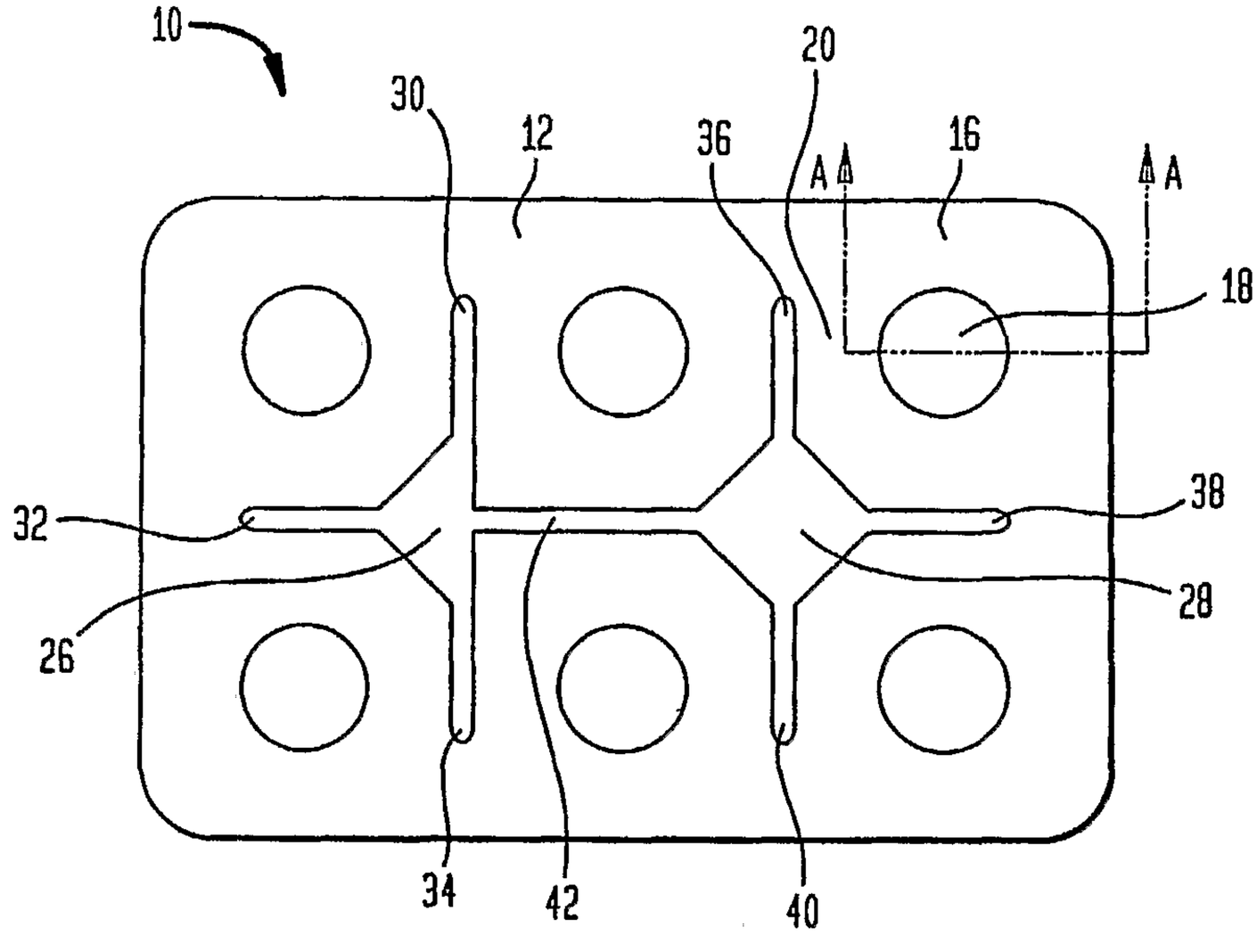


FIG. 2

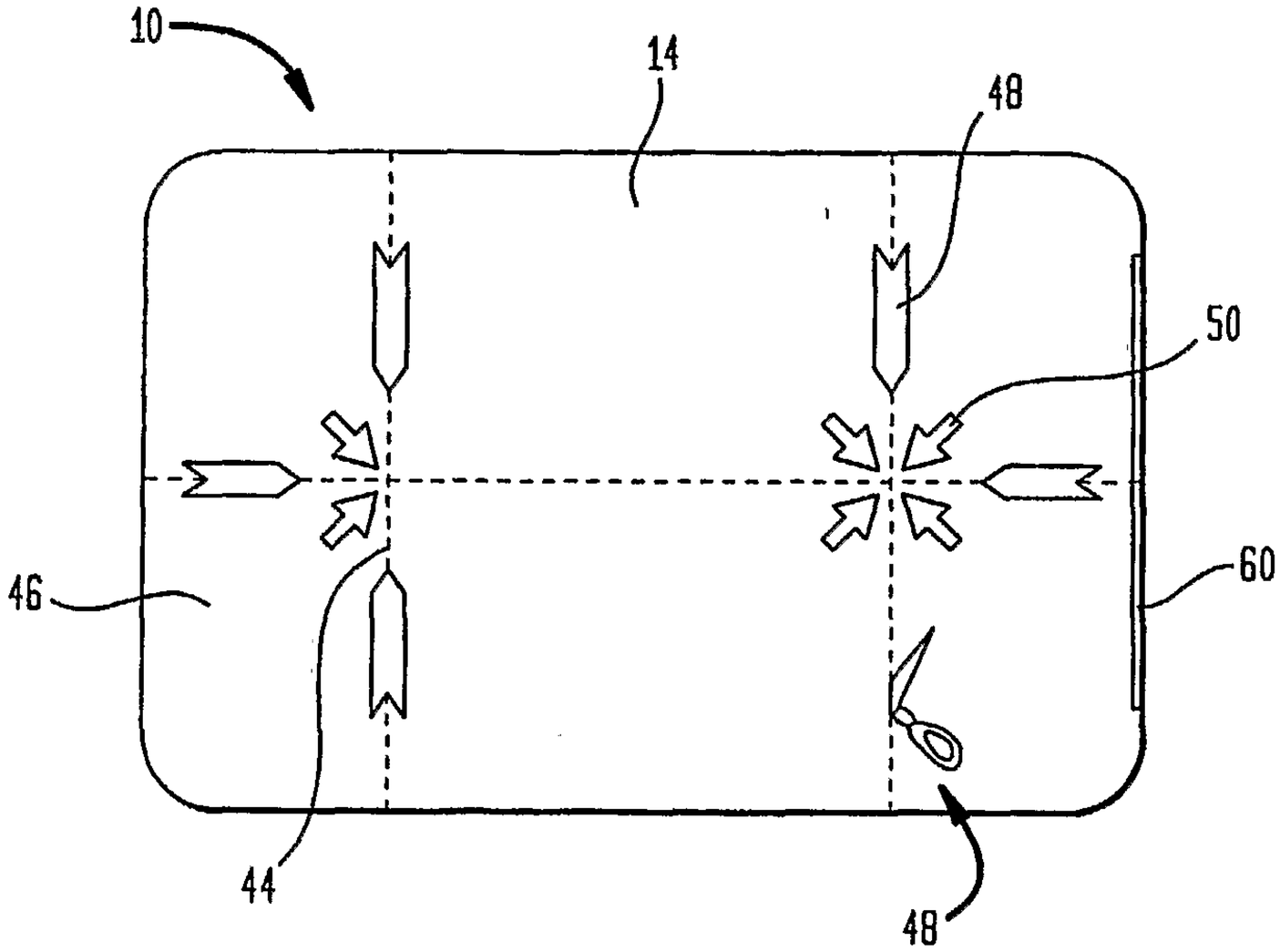


FIG. 3

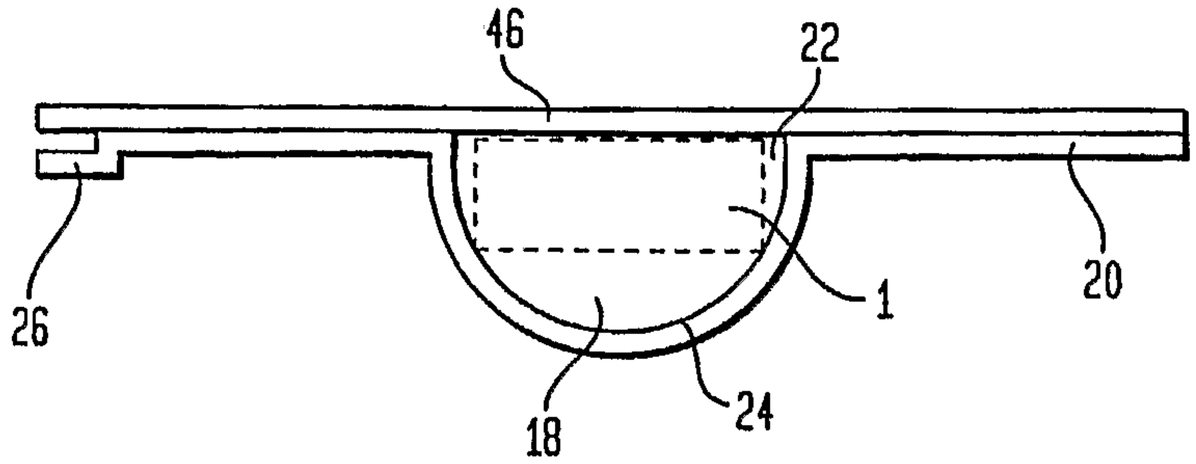


FIG. 4

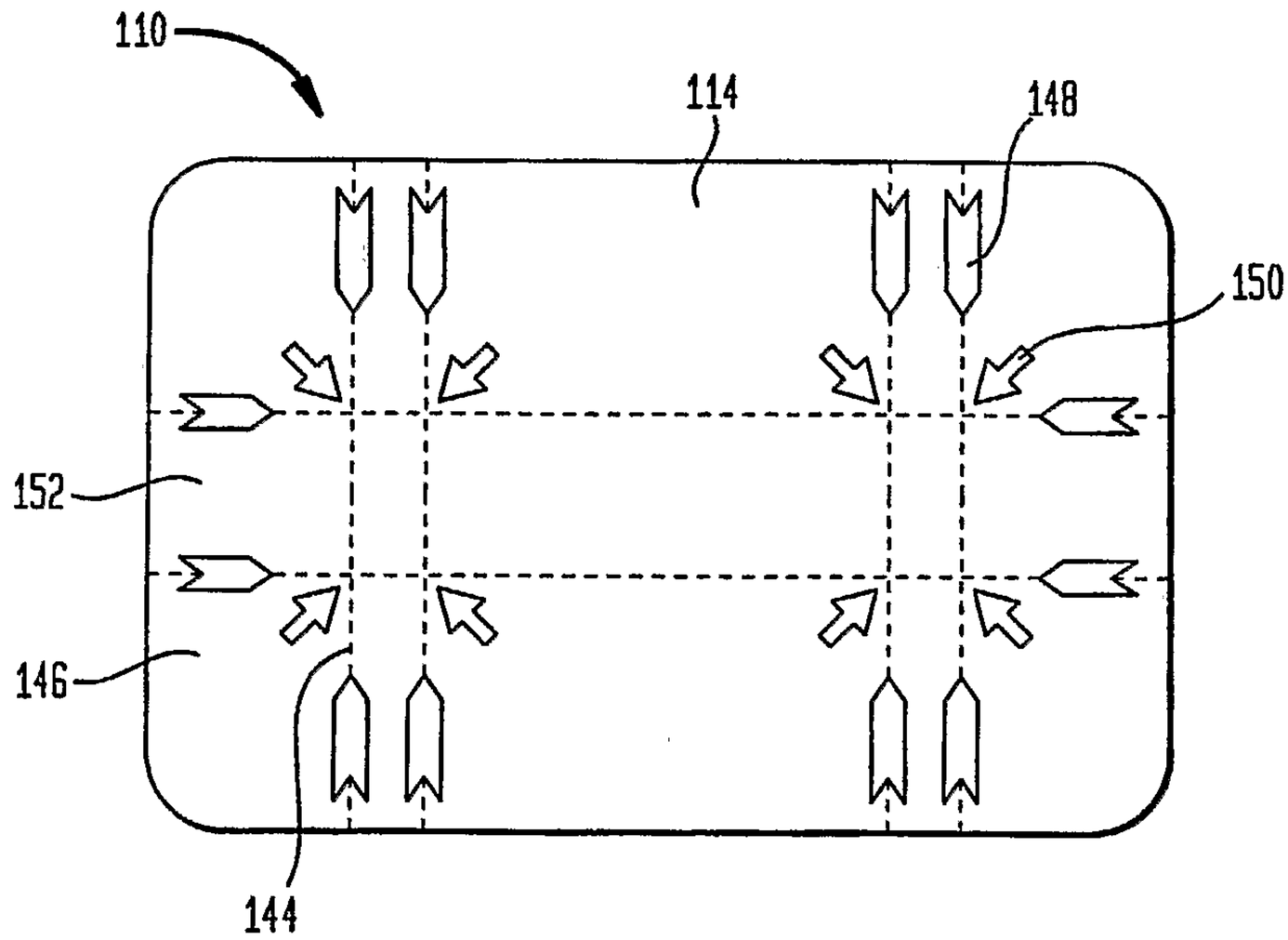
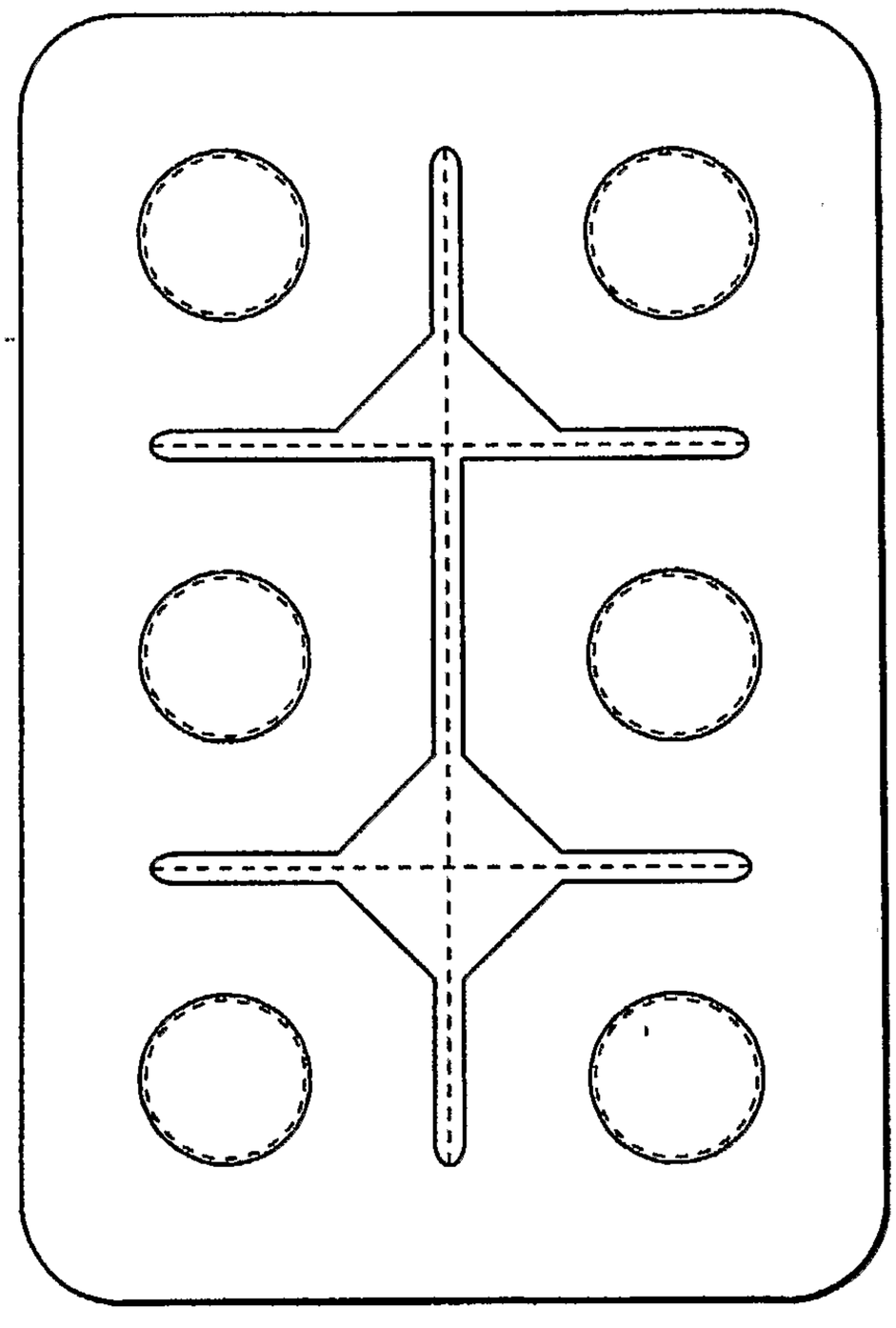
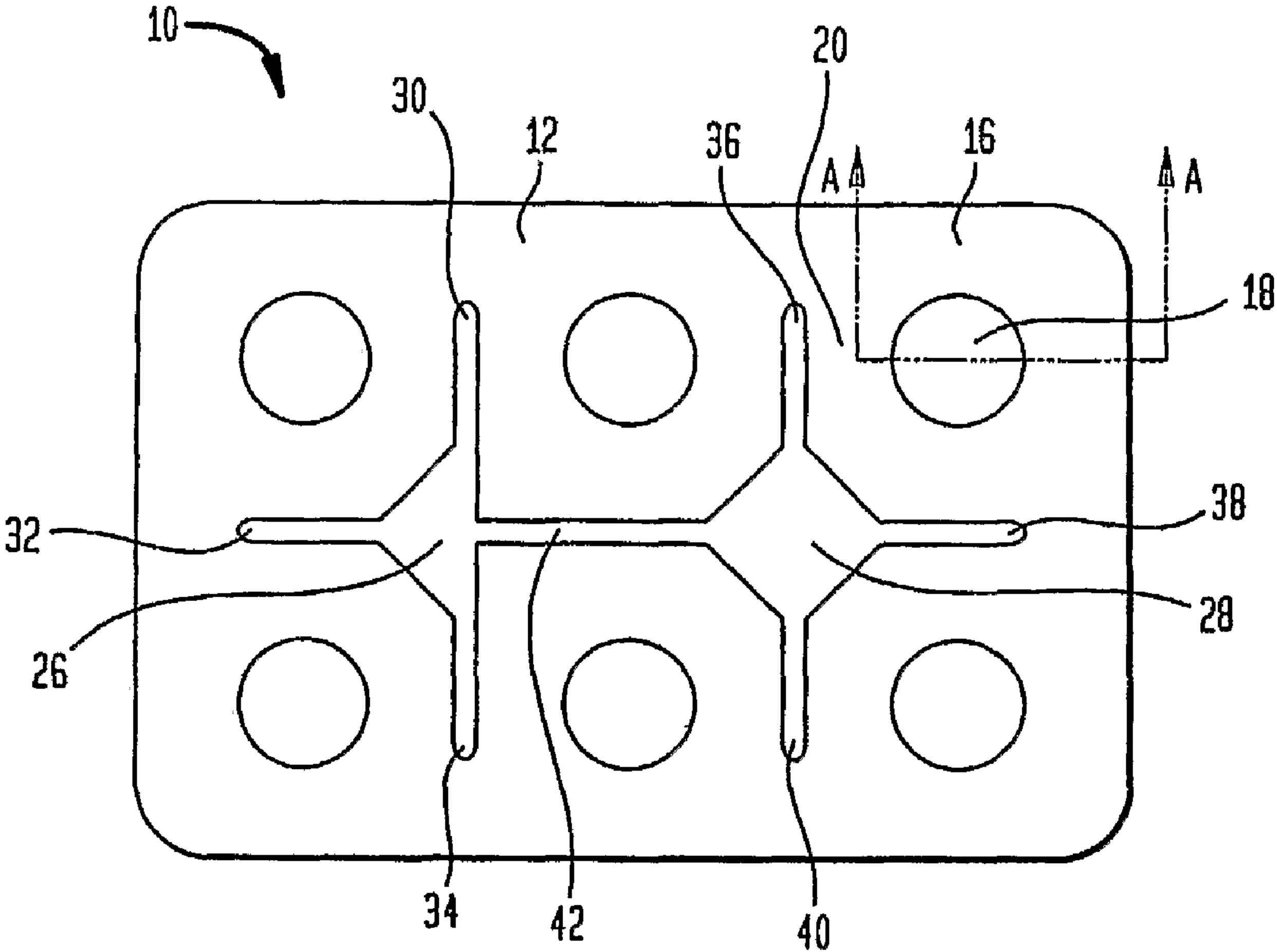


FIG. 5

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