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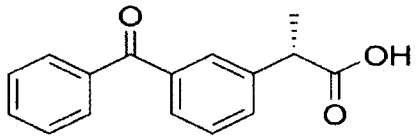
(54) Title: DEXKETOPROFEN FORMULATIONS

(57) Abstract: The present invention relates to pharmaceutical formulations comprising dexketoprofen that shall be used as antipyretic, analgesic, anti-inflammatory in treatment of mild and moderate pain such as toothache, dysmenorrhea, post-surgical pain, musculoskeletal pain.

DEXKETOPROFEN FORMULATIONS

The present invention relates to pharmaceutical formulations comprising dexketoprofen that shall be used as antipyretic, analgesic, anti-inflammatory in treatment of mild and moderate pain such as toothache, dysmenorrhea, post-surgical pain, musculoskeletal pain.

Dexketoprofen was first disclosed in the application numbered EP0668851. In said document, it has been disclosed that dexketoprofen is effective when used as antipyretic, analgesic, anti-inflammatory in treatment of moderate and severe pain such as toothache, dysmenorrhea, post-surgical pain, musculoskeletal pain.



Dexketoprofen is available in the forms of 50 mg/2ml solution for injection, 25 mg film tablet and 25 mg effervescent tablet on the market.

During preparation of the formulations comprising dexketoprofen, it is observed that the formulation adheres to machine parts such as inner walls of the die and the punch. This causes some part of the medicament to remain on the punches and in the dies, which brings some problems to manufacturers during preparation phase of the medicament. In addition, since some part of the medicament remains on the punches and in the dies, the dosage form obtained does not have the desired shape and desired smoothness and this brings some problems at quality control phases. Furthermore, in the case that the formulations are compressed into tablet form, it is seen that the machine parts wear and corrode over time due to friction between the tablet surface and the punch or inner wall of the die during ejection of the tablets. Therefore, these problems seen during preparation of the formulations comprising dexketoprofen pose problems for manufacturers at production and quality control phases and impede to obtain the final product effectively.

As it is seen, there is a need for development of new approaches in order to obtain the medicaments comprising dexketoprofen which are produced in the manner that no problem is observed at production and quality control phases so as to prevent the problems such as adhesion of the formulation to machine parts like the die and punch during preparation and so as to prevent possible corrosions that can arise from friction between tablet surface and inner wall of the die during tablet production.

As a result of the studies they conducted in line with this requirement, the inventors have found that the problems encountered during preparation of the medicaments at production and quality control phases can be solved by the formulations they have developed for preparation of the dosage forms comprising dexketoprofen.

Description of the Invention

The present invention relates to the pharmaceutical formulations comprising dexketoprofen and methods for preparation of these formulations. Surprisingly, the inventors have seen that in the case that the formulations comprising dexketoprofen comprise talc, magnesium stearate, PEG 6000, silicone dioxide, sodium benzoate, potassium benzoate, stearic acid, sodium stearyl fumarate and/or a combination thereof as the lubricant, the formulation does not adhere to the punch and inner walls of the die; wear and corrosion resulting from the possible friction in said machine parts are decreased.

In this respect, the present invention relates to dexketoprofen formulations comprising talc, magnesium stearate, PEG 6000, silicone dioxide, sodium benzoate, potassium benzoate, stearic acid, sodium stearyl fumarate and/or a combination thereof as the lubricant.

In one preferred embodiment of the present invention, the lubricant used is magnesium stearate. **Dioo** value of magnesium stearate used according to the present invention is in the range of 30-250 μιη, preferably in the range of 50- 200 μm, more preferably in the range of 75 -150 μπι.

According to this, a characteristic of the present invention is that magnesium stearate is used as the lubricant and **dioo** value of magnesium stearate used is in the range of 30-250 μⁿι, preferably in the range of 50-200 μιη, more preferably in the range of 75- 150 μm.

On the other hand, the amount of the lubricant used in preparation of the formulations comprising dexketoprofen is an important parameter among the characteristics of the formulation to be obtained. In the case that the lubricant is used less than the desired amount, this results in adhesion of the formulation prepared to the machine parts and its binding to the hollow punches. Using the lubricant more than the desired amount, on the other hand, causes increase in dissolution times of the dosage forms obtained. The inventors have seen that in the case that the amount of the lubricant in the formulations comprising dexketoprofen is in the range of 1-20%, preferably in the range of 1-10%, and more preferably in the range of 1-5% in proportion to total weight of the formulation, the formulations do not adhere to the machine

parts during preparation and furthermore the dosage forms obtained do not have long dissolution times. By this means, said problems encountered during both production and use of the formulations comprising dexketoprofen have been solved.

In another aspect, the present invention relates to the formulations comprising lubricant in the range of 1 -20%, preferably in the range of 1- 10% and more preferably in the range of 1-5% in proportion to total weight of the formulation.

In a preferred embodiment of the present invention, the formulations comprising dexketoprofen are characterized in that said formulations comprise dexketoprofen in the range of 1-20%, preferably in the range of 1-10 %, and more preferably in the range of 1-5%.

In the studies they conducted in order to solve the problem of adhesion of the formulations comprising dexketoprofen to the machine parts, the inventors have unexpectedly found that particle sizes of dexkteprofen and the lubricant have a role in solving this problem effectively.

Another characteristic of the present invention is that the ratio of dioo value of dexketoprofen to dioo value of the lubricant is in the range of 12:1 to 1:1, preferably in the range of 10:1 to 2:1, and more preferably in the range of 8:1 to 3:1.

- According to a preferred embodiment of the present invention, the pharmaceutical composition comprising dexketoprofen is characterized in that the lubricant is used in the range of 1-20%, preferably in the range of 1- 10%, more preferably in the range of 1- 5% in said composition and
- The ratio of $d_{]00}$ value of dexketoprofen to $d_{1_{00}}$ value of the lubricant is in the range of 12:1 to 1:1, preferably in the range of 10:1 to 2:1 and more preferably in the range of 8:1 to 3:1 in said composition.

According to another preferred embodiment of the present invention, the pharmaceutical composition comprising dexketoprofen is characterized in that

- Magnesium stearate is used in the range of 1-20%, preferably in the range of 1-10% and more preferably in the range of 1-5% and
- The ratio of d_{10}o value of dexketoprofen to di_{00} value of the lubricant is in the range of 12:1 to 1:1, preferably in the range of 10:1 to 2:1 and more preferably in the range of 8:1 to 3:1.

Percentage values of amounts given in the present invention have been calculated in proportion to unit dosage weight.

Dexketoprofen comprised in the pharmaceutical formulations of the present invention is in the form of its pharmaceutically acceptable salts, hydrates, solvates, esters, enantiomers, diastereomers or combinations thereof in terms of chemical structure; in crystalline form or amorphous form or combinations thereof in terms polymorphic structure. Preferably, dexketoprofen is in salt form, more preferably in dexketoprofen trometamol form.

The pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be prepared in any of the dosage forms such as tablet, effervescent tablet, effervescent granule, effervescent dry powder, film coated tablet, enterically coated tablet, dry powder, granule, capsule, prolonged release tablet, modified release tablet, delayed release tablet.

The pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant are preferably in the form of powder, tablet and granule, more preferably in the form of tablet, film tablet or effervescent tablet.

In another aspect, the present invention relates to the pharmaceutical formulations comprising dexketoprofen and lubricant in tablet, film tablet or effervescent tablet form.

In another aspect, the present invention relates to the pharmaceutical formulations comprising dexketoprofen and lubricant is in film tablet form.

The pharmaceutical formulation obtained can be formed into any abovementioned dosage forms. In the case that the formulation is in tablet form, the tablets obtained can be treated with film coating agents, for instance, with sugar based coating agents, water soluble film coating agents, enteric coating agents, delayed release coating agents or coating compositions comprising any combination thereof.

Saccharose can be used singly or optionally with any of the agents such as talc, calcium carbonate, calcium phosphate, calcium sulphate, gelatine, gum arabic, polyvinylpyrrolidone and pullulan or any combination thereof as the sugar based coating agent.

The water soluble film coating agent can be selected from cellulose derivatives such as hydroxypropyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, methyl hydroxyethyl cellulose and sodium carboxymethyl cellulose; synthetic polymers such as

polyvinyl acetal diethyl aminoacetate, aminoalkyl methacrylate copolymers and polyvinylpyrrolidone and polysaccharides such as pullulan or combinations thereof.

The enteric coating agents can be selected from cellulose derivatives such as hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, carboxymethyl ethyl cellulose, cellulose acetate phthalate; acrylic acid derivatives such as methacrylic acid copolymer L, methacrylic acid copolymer LD and methacrylic acid copolymer S and natural substances such as shellac or combinations thereof.

The delayed release coating agents can be selected from cellulose derivatives such as ethyl cellulose; acrylic acid derivatives such as aminoalkyl methacrylate copolymer RS, ethyl acrylate-methyl methacrylate copolymer emulsion or combinations thereof.

In a preferred embodiment, the present invention relates to the pharmaceutical formulations wherein said formulation is in film tablet form and film coating agent is selected from a group of titanium dioxide, polyvinyl alcohol, polyethylene glycol, talc, lecithin or their combinations thereof. The pharmaceutical formulations of the present invention comprising dexketoprofen and the lubricant can comprise various excipients in addition to the active agent dexketoprofen and the lubricant.

The pharmaceutical formulations of the present invention comprising dexketoprofen and the lubricant comprise at least one excipient selected from a group comprising disintegrant, diluent, lubricant, glidant, binder, filler, optionally effervescent couple comprising at least one acidic agent and at least one basic agent, colouring agent, pH regulating agent, surfactant, stabilizant, sweetener and/or taste regulating agent, flavouring agent in addition to the active agent dexketoprofen and the lubricant.

The disintegrant that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from a group comprising carboxymethyl cellulose, carboxymethyl cellulose calcium, carboxymethyl cellulose sodium, croscarmellose sodium, crospovidone, hydroxypropyl cellulose, microcrystalline cellulose, methyl cellulose, chitosan, starch, sodium starch glycolate.

As a result of the studies for developing the dissolution rate of the dexketoprofen formulation, the inventors have seen that the weight ratio of the active agent to the disintegrant has an influence on the dissolution of the formulation. They have observed that when the ratio of dexketoprofen active agent to disintegrant is in the range of 10:1 to 1:5, preferably 8:1 to 1:3,

more preferably 6:1 to 1:1, the dissolution rate is increased and thus a high absorption and bioavailability of the formulation is provided.

In another aspect, the present invention relates to the pharmaceutical formulations wherein the ratio of dexketoprofen active agent to disintegrant is in the range of 10:1 to 1:5, preferably 8:1 to 1:3, more preferably 6:1 to 1:1.

The diluent that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from a group comprising calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulphate, microcrystalline cellulose, dextrose, fructose, lactitol, lactose, magnesium carbonate, magnesium oxide, maltitol, maltodextrin, maltose, mannitol, simethicone, sorbitol, starch, sodium chloride, sucrose, talc, xylitol.

The glidant that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and the lubricant can be selected from a group comprising tribasic calcium phosphate, colloidal silicon dioxide, magnesium silicate, magnesium trisilicate, talc.

The binder that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from a group comprising carboxymethyl cellulose sodium, ethyl cellulose, gelatine, hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl cellulose, hypromellose, magnesium aluminium silicate, maltodextrin, methyl cellulose, povidone, starch.

The filler that can be used in the pharmaceutical formulations of the present invention can be selected from a group comprising dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, mannitol, sodium chloride, dry starch and powdered sugar, mannitol, sorbitol, sucrose and inositol.

It is known that the amount of the filler used in preparation of the pharmaceutical formulations comprising dexketoprofen is also an important parameter among the characteristics of the formulation to be obtained. In the case that the amount of the filler used is in an amount of more than 50%, preferably 55-99%, more preferably 60-95% in proportion to the total weight of the tablet formulation, the proper flow of the formulation is obtained during the preparation and thus weight uniformity of the tablet is provided.

In another aspect, the present invention relates to the pharmaceutical formulations wherein the amount of the filler used is in an amount of more than 50%, preferably 55-99%, more preferably 60-95% in proportion to the total weight of the tablet formulation.

The acidic agent composing the effervescent couple comprising at least one acidic agent and at least one basic agent that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from a group comprising organic acids such as malic acid, citric acid, tartaric acid, fumaric acid; and the basic agent can be selected from a group comprising agents such as sodium carbonate, potassium carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate.

The pH regulating agent that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from citrate, phosphate, carbonate, tartarate, fumarate, acetate and amino acid salts.

The surfactant that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from sodium lauryl sulphate, polysorbate, polyoxyethylene, polyoxypropylene glycol and similar agents.

The stabilizing agent that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and the lubricant can be selected from a group comprising tocopherol, tetrasodium edetate, nicotinamide, cyclodextrin.

The sweetener and/or taste regulating agent that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from a group comprising acesulfame, aspartame, dextrose, fructose, maltitol, maltose, mannitol, saccharine, saccharine sodium, sodium cyclamate, sorbitol, sucralose, sucrose, xylitol, sodium chloride.

The flavouring agent that can be used in the pharmaceutical formulations of the present invention comprising dexketoprofen and lubricant can be selected from menthol, lemon, orange, vanilla, berry, raspberry, caramel and similar flavours.

According to a preferred embodiment of the present invention, the pharmaceutical composition comprising dexketoprofen is characterized in that

- the lubricant is used in the range of 1-20%, preferably in the range of 1-10%, more preferably in the range of 1-5% and

- the ratio of **dioo** value of dexketoprofen to di_{00} value of the lubricant is in the range of 12:1 to 1:1, preferably in the range of 10:1 to 2:1 and more preferably in the range of 8:1 to 3:1
- said pharmaceutical formulations comprise at least one excipient selected from a group comprising disintegrant, diluent, lubricant, glidant, binder, effervescent couple comprising at least one acidic agent and at least one basic agent, colouring agent, pH regulating agent, surfactant, stabilizing agent, sweetener and/or taste regulating agents, flavouring agent in addition to dexketoprofen and the lubricant.

According to another preferred embodiment of the present invention, the pharmaceutical composition comprising dexketoprofen is characterized in that

- Magnesium stearate is used in the range of 1-20%, preferably in the range of 1-10%, more preferably in the range of 1-5% and
- The ratio of $\mathbf{d_{10}o}$ value of dexketoprofen to d_{100} value of magnesium stearate is in the range of 12:1 to 1:1, preferably in the range of 10:1 to 2:1 and more preferably in the range of 8:1 to 3:1.

The pharmaceutical formulations of the present invention comprise at least one excipient selected from a group comprising disintegrant, diluent, glidant, binder, effervescent couple comprising at least one acidic agent and at least one basic agent, colouring agent, pH regulating agent, surfactant, stabilizing agent, sweetener and/or taste regulating agent, flavouring agent in addition to dexketeprofen and magnesium stearate.

The pharmaceutical formulations of the present invention comprising dexketoprofen and the lubricant can comprise dexketoprofen in the range of 0.1 to 99% by weight, preferably in the range of 1 to 97% by weight, more preferably in the range of 5 to 95% by weight.

The pharmaceutical formulations of the present invention can comprise dexketoprofen in the range of 5 to 95%, lubricant in the range of 1-5% disintegrant in the range of 0.5-10%, filler in the range of 55-99% in proportion to total weight of the formulation. The pharmaceutical formulations of the present invention comprising dexketoprofen and the lubricant can optionally comprise a second active agent in addition to dexketoprofen. The second active agent can be selected from antacid, anticholinergic, antispasmodic, antiemetic, antidiabetic, antipropulsive, antiallergic, antidiarrheal, antiobesity, antithrombotic, antifibrinolytic, antianemic, antihypertensive, antifungal, antipruritic, antipsoriatic, antibiotic, antiseptic,

antiacneantibacterial, antimycotic, antiviral, antineoplastic, antiarrhythmic, antiadrenergic, antiepileptic, anti-parkinson, antiprotozoal, anthelmintic, anti-inflammatory, diuretic, laxative, sulphonamide, imidazole, corticosteroid, thiazolidinedione, biguanide, immunostimulant, immunosuppressant, myorelaxant, analgesic, psycholeptic, psychoanaleptic peripheral vasodilator, beta blocker, calcium channel blocker and lipid modifying agents; alpha-glucosidase inhibitors, aldose reductase inhibitors, ACE inhibitors; multivitamin and minerals, vitamin A, vitamin D and its analogues, vitamin B_1, vitamin C, vitamin E, vitamin B_6, vitamin B_2, vitamin K, calcium, potassium, sodium, zinc, magnesium, fluoride, selenium.

The pharmaceutical formulation of the present invention can be obtained by a method composed of

- mixing the active agent dexketoprofen and, if available, the second active agent homogeneously and, if required, adding at least one of the abovementioned excipients and the lubricant or
- mixing the active agent dexketoprofen and, if available, the second active agent homogeneously after granulated with at least one the excipients and adding the lubricant or
- mixing the active agent dexketoprofen and, if available, the second active agent with at least one of the excipients and at least one of the abovementioned excipients and optionally granulating them with the granulation solution comprising excipient and mixing the granules obtained with the lubricant and optionally at least one excipient or
- using any of the abovementioned methods separately for the active agent compositions and combining the formulations obtained in the case that two active agents are used.

The pharmaceutical formulation of the present invention can be used as antipyretic, analgesic, anti-inflammatory in treatment of mild and moderate pain such as toothache, dysmenorrhea, post-surgical pain, musculoskeletal pain.

EXAMPLE: Effervescent tablets comprising dexketoprofen and preparation method thereof

Component name	% of amount in unit dose
Dexketoprofen trometamol	20 %
Taste regulating agent	3 %
Effervescent acid	38.7 %
Effervescent base	31.6 %
Binder	3.5 %
Flavouring agent	1.2 %
Magnesium stearate	1 %
Sweetener	1 %

In obtainment of the formulation that shall be used in said invention; a granulation solution is prepared by mixing ethyl alcohol, the binder and the purified water. The effervescent acid, the effervescent base and the taste regulating agent are mixed and granulated with the granulation solution obtained. The granules obtained are dried and then sieved. The mixture of the sweetener and dexketeprofen is added into the granules dried and sieved and the mixture is stirred. The flavouring agent and the lubricant are added into the mixture obtained and mixed again and the final mixture obtained is compressed in tablet form.

CLAIMS

1. A pharmaceutical formulation comprising dexketoprofen, characterized in that said formulation comprises talc, magnesium stearate, PEG 6000, silicon dioxide, sodium benzoate, potassium benzoate, stearic acid, sodium stearyl fumarate and/or a combination thereof as the lubricant.
2. The pharmaceutical formulation comprising dexketoprofen according to claim 1, characterized in that the amount of the lubricant is in the range of 1-20% in proportion to total formulation amount.
3. The pharmaceutical formulation comprising dexketoprofen according to claim 2, characterized in that the amount of the lubricant is in the range of 1-10% in proportion to total formulation amount.
4. The pharmaceutical formulation comprising dexketoprofen according to claim 3, characterized in that the amount of the lubricant is in the range of 1-5% in proportion to total formulation amount.
5. The pharmaceutical formulation comprising dexketorprofen according to any preceding claims, wherein magnesium stearate is used as the lubricant.
6. The pharmaceutical formulation comprising dekxetoprofen according to any preceding claims, wherein the ratio of d_{i00} value of dexketoprofen to d_{100} value of the lubricant is in the range of 12:1 to 1:1.
7. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein the ratio of d_{i00} value of dexketoprofen to dtoo value of the lubricant is in the range of 10:1 to 2:1.
8. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein the ratio of d_{i00} value of dexketoprofen to d_{10}ovalue of the lubricant is in the range of 8:1 to 3:1.
9. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein said formulation is prepared in any dosage forms of tablet, effervescent tablet, effervescent granule, effervescent dry powder, film coated tablet, enteric coated tablet, dry powder, granule, capsule, prolonged release tablet, modified release tablet, delayed release tablet.
10. The pharmaceutical formulation comprising dexketoprofen according to claim 9, wherein said formulation is in the form of tablet, film coated tablet or effervescent tablet.

11. The pharmaceutical formulation comprising dexketoprofen according to claim 10 wherein said formulation is in the form of film coated tablet.

12. The pharmaceutical formulation comprising dexketoprofen according to claims 10-1 1 wherein said formulation is in film tablet form and film coating agent is selected from a group of titanium dioxide, polyvinyl alcohol, polyethylene glycol, talc, lecithin or their combinations thereof.

13. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein said formulation is in the form of its pharmaceutically acceptable salts, hydrates, solvates, esters, enantiomers, diastereomers or combinations thereof in term of chemical structure.

14. The pharmaceutical formulation comprising dexketoprofen according to claim 1 1, wherein dexketoprofen is in pharmaceutically acceptable dexketoprofen trometamol form.

15. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein dexketroprofen is in amorphous or crystalline form or a combination thereof in terms of polymorphic sturucture.

16. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein said formulation comprises pharmaceutically acceptable excipients along with dexketoprofen and the lubricant.

17. The pharmaceutical formulation comprising dexketoprofen according to claims 1- 16, wherein said formulation comprises at least one excipient selected from a group comprising disintegrant, diluent, lubricant, glidant, binder, filler, optionally effervescent couple comprising at least one acidic agent and at least one basic agent, colouring agent, pH regulating agent, surfactant, stabilizing agent, sweetener and/or taste regulating agent, flavouring agent in addition to dexketoprofen and the lubricant.

18. The pharmaceutical formulation comprising dexketoprofen according to claim 17, wherein filler is selected from a group comprising dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, mannitol, sodium chloride, dry starch and powdered sugar, mannitol, sorbitol, sucrose and inositol.

19. The pharmaceutical formulation comprising dexketoprofen according to claims 17-18, wherein the amount of the filler used is in an amount of more than 50%, in proportion to the total weight of the tablet formulation.

20. The pharmaceutical formulation comprising dexketoprofen according to claims 17-19, wherein the amount of the filler used is in an amount in the range of 55-99% in proportion to the total weight of the tablet formulation.
21. The pharmaceutical formulation comprising dexketoprofen according to claims 17-20, wherein the amount of the filler used is in an amount in the range of 60-95% in proportion to the total weight of the tablet formulation.
22. The pharmaceutical formulation comprising dexketoprofen according to claim 17, wherein disintegrant is selected from a group comprising carboxymethyl cellulose, carboxymethyl cellulose calcium, carboxymethyl cellulose sodium, croscarmellose sodium, crospovidone, hydroxypropyl cellulose, microcrystalline cellulose, methyl cellulose, chitosan, starch, sodium starch glycolate.
23. The pharmaceutical formulation comprising dexketoprofen according to claims 17-22, wherein the ratio of dexketoprofen active agent to disintegrant is in the range of 10:1 to 1:5.
24. The pharmaceutical formulation comprising dexketoprofen according to claims 17-23, wherein the ratio of dexketoprofen active agent to disintegrant is in the range of 8:1 to 1:3.
25. The pharmaceutical formulation comprising dexketoprofen according to claims 17-24, wherein the ratio of dexketoprofen active agent to disintegrant is in the range of 6:1 to 1:1.
26. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein said formulation comprises the active agent dexketoprofen in the range of 0.1 to 99% by weight.
27. The pharmaceutical formulation comprising dexketoprofen according to claim 26, wherein said formulation comprises the active agent dexketoprofen in the range of 1 to 97% by weight.
28. The pharmaceutical formulation comprising dexketoprofen according to claims 16 and 27, wherein said formulation comprises the active agent dexketoprofen in the range of 5 to 95% by weight.
29. The pharmaceutical formulation of the present invention according to claims 1-28 wherein said formulation comprises dexketoprofen in the range of 5 to 95%, lubricant in the range of 1-5% disintegrant in the range of 0.5-10%, filler in the range of 55-99% in proportion to total weight of the formulation.

30. The pharmaceutical formulation comprising dexketoprofen according to any preceding claims, wherein said formulation comprises at least one second active agent selected from antacid, anticholinergic, antispasmodic, antiemetic, antidiabetic, antipropulsive, antiallergic, antidiarrheal, antiobesity, antithrombotic, antifibrinolytic, antianemic, antihypertensive, antifungal, antipruritic, antipsoriatic, antibiotic, antiseptic, antiacne, antibacterial, antimycotic, antiviral, antineoplastic, antiarrhythmic, antiadrenergic, antiepileptic, anti-parkinson, antiprotozoal, anthelmintic, anti-inflammatory, diuretic, laxative, sulphonamide, imidazole, corticosteroid, thiazolidinedione, biguanide, immunostimulant, immunosuppressant, myorelaxant, analgesic, psycholeptic, psychoanaleptic peripheral vasodilator, beta blocker, calcium channel blocker and lipid modifying agents; alpha-glucosidase inhibitors, aldose reductase inhibitors, ACE inhibitors; multivitamin and minerals, vitamin A, vitamin D and its analogs, vitamin B_1, vitamin C, vitamin E, vitamin B_6, vitamin B_2, vitamin K, calcium, potassium, sodium, zinc, magnesium, fluoride, selenium in addition to dexketoprofen.

INTERNATIONAL SEARCH REPORT

International application No
PCT/TR2012/0OQ233

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/20 A61K31/19
ADD.

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)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal , WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 739 072 Al (MENARINI LAB [ES]) 3 January 2007 (2007-01-03) exampl e 5	1-30
X	Wo 94/28890 Al (GEISSLINGER GERD [DE] ; BRUNE KAY [DE]) 22 December 1994 (1994-12-22) page 15 - page 16 page 8, l ast paragraph - page 9, paragraph 2	1-20, 22-30
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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

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Information on patent family members

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