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SCIENTIFIC-RESEARCH INSTITUTE OF INTELLECTUAL PROPERTY NATIONAL ACADEMY OF LAW SCIENCES OF UKRAINE

REPORT

Evergreening patents in Ukraine

2020

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One of the problematic areas in the health care system of Ukraine is a high price for drugs. In many cases the reason for this is that Ukrainian legislation allows pharmaceutical companies to obtain so-called «evergreening patents», which provide them with the monopoly on the import (production) of drugs. «Evergreening patents» is a term used to refer to patents for pharmaceutical products to indicate the artificial continuation of the exclusive rights guaranteed by a patent for an active substance of a pharmaceutical by filing a new application and obtaining a new patent for various additional forms and new properties of the active substance, as well as diagnostic, therapeutic and surgical methods of treatment for humans and animals with the use of the specified active substance. Thus, pharmaceutical companies artificially extend the monopoly on a drug in Ukraine due to patents that formally meet the requirements of the law, but in practice do not have significant advantages over existing counterparts.

International organizations, in particular the World Health Organization (WHO) and the United Nations Development Program (UNDP), pay their attention to the dangerous influence of «evergreening patents», International organizations have developed two important documents with recommendations for improving intellectual property law:

Guidelines for the examination of pharmaceutical patents (January 2007), developed with the support of WHO, UNCTAD and ICTSD;

Guidelines for the examination of patent applications relating to drugs (June 2016), developed with the support of UNDP.

These documents of international organizations became the basis for this study. To determine whether an application for a patent of Ukraine for an invention or a patent of Ukraine belongs to the category of «evergreening patents», it is necessary to first classify the object (objects) of patenting. The object of the patent may be a substance presented as an individual chemical compound or composition or a new application of a known substance, or the object may be a method of application of the substance or its preparation or production of intermediates, etc.

To characterize individual chemical compounds, in particular, the following is used:

- for low-molecular compounds: qualitative composition (atoms of certain elements), quantitative composition (number of atoms of each element); bond between atoms, their mutual arrangement in a molecule, expressed by a chemical structural formula, or in a crystal lattice;
- for high-molecular compounds: chemical composition and structure of one link of a macromolecule, structure of a macromolecule as a whole (linear, branched), periodicity of links, molecular mass, molecular mass distribution, geometry and stereometry of a macromolecule, its end and side groups;
- for individual compounds with indeterminate structure: physicochemical and other characteristics, including the characteristics of the method of production, which allow to identify them;
- for individual compounds belonging to genetic engineering objects: nucleotide sequence (for nucleic acid fragments) or physical map (for recombinant nucleic acids and vectors), as well as amino acid sequence, physicochemical and other characteristics that allow to identify them.

To characterize the compositions, in particular, the following criteria are used:

- quality (ingredients) composition;
- quantitative (content of ingredients) composition;
- the structure of the composition;
- the structure of ingredients.

To characterize a new use of a known substance, the identifying signs of a known substance and signs of its new use and purpose are used.

Patents and patent applications with characteristics of «evergreening» belong to the category of «secondary» patents/patent applications, because they are essentially based on the primary patent, which protects or protected a particular innovative chemical compound. At the same time, it should be borne in mind that not every «secondary» patent is automatically «evergreening». In order to determine the «evergreening patent» for an individual chemical compound or composition based on it, it is recommended to test the claimed chemical according to the following criteria, taking into account the presence / absence of differences in technical results:

1. Does the chemical compound fall under the general Markush claim of the previously submitted application?

2. Has it previously been described as specially obtained?

3. Is the technical result different?

4. Is the new chemical compound different from those known for Markush claim of the same type of substituents within one groups (classes)? Is there a pharmaceutical composition under a new application or patent?

5. Is the active substance under the new application and / or patent a result of recrystallization of a previously known substance (into a less stable and stable polymorph, pseudopolymorph or amorphous, or its ester, isomer, including its hydrates and solvates)?

6. Is the chemical compound of the pharmaceutical composition under a new application or patent enantiomer or optical isomer of the active substance of the previously known composition with the same molecular formula and the same therapeutic effect?

7. Is the pharmaceutical composition according to the new application or patent different from the previously known composition only in dosage, i.e. is a new dosage form of a previously known substance, or has a new form of application (e.g., injection along with an existing oral tablet form)?

8. Is the pharmaceutical composition according to the new application or patent different from the previously known composition only in the composition of new salts of known ingredients, esters and ethers, isomers of known molecules, including hydrates and solvates?

9. Is the pharmaceutical composition according to the new application or patent a new combination of previously known active substances?

10. Is the pharmaceutical composition according to the new application or patent a metabolite of the active substance of the previously known composition (except when the active metabolites have excellent safety and efficacy characteristics in the original molecule, causing a different improved therapeutic effect) or its prodrug?

As the number of biotechnological drugs entering the Ukrainian market grows every year, this study could not escape their attention. The approach to the analysis of patents for inventions for biotechnology objects is generally similar to the approach in the Guidelines applicable to other inventions for chemical compounds, substances, compositions, etc. There is no separate methodology that would apply to biotechnological objects yet.

The following methodological approaches have been used in the study for this category of drugs:

1. When analyzing a composition, one of the active elements of which is a biotechnology object, the main criteria for classifying the invention as «evergreening» is the technical result and the prior art of the object. If the technical result is new qualities of the composition that do not affect its therapeutic efficacy (biological activity), and for example, affect stability, it can be concluded that the invention is «evergreening» (unless the problem of stability was known as the main barrier to the use of the object of biotechnology). The data of the description, which should confirm the specified technical result, are also taken into account.

2. A similar approach to the above is carried out for the invention, which relates to a method of manufacturing or purifying or introducing a biotechnology object into the human body. That is, a method aimed at increasing biological activity can be considered not to be «evergreening», and a method aimed at solving another problem can be considered «evergreening».

3. If the object is characterized only by the parameters of heavy and light chains (list of sequences), it is concluded that the invention is not «evergreening». If the object (substance or method) is characterized by additional features (a molecule size, process parameters, etc.), it can be concluded that the invention is «evergreening», but in each separate case.

4. If the object is a new application of a previously known object of biotechnology, in most cases it is concluded that such an invention is not «evergreening».

5. If the owner of the patent for analysis is a company, a manufacturer of generic versions, not the originator, and the object of the invention is a significant improvement, even without affecting biological activity, it is concluded that the patent is not «evergreening» because the purpose of patenting in this case is the protection of the new development, rather than the need to extend the patent protection of a long-known compound.

It is also important what problems accompanied a particular drug during its use and how they were solved or not solved, which can be found in scientific publications in open and accessible sources. This information is used in the analysis of «evergreening», including for biotechnology objects.

Based on these criteria, the Charity Organization «100 Percent Life» with the expert support of the Research Institute of Intellectual Property of the National Academy of Legal Sciences of Ukraine and the law firm «Borovyk and Partners» analyzed 132 patents. The study was based on the patented single-source drugs, the share of which exceeded 100,000 US dollars in centralized procurement in 2017, as well as drugs whose share in hospital and pharmacy procurements exceeded 50 million UAH in 2017.

Additionally, the study included some drugs where the presence of a patent is or has been an obstacle to access to treatment. These can be drugs that have been purchased from one manufacturer for a long time due to a patent monopoly, drugs that are either not purchased (have not purchased for a long time), or their procurement in the future is questionable due to the existence of patent monopolies, and so on.

The study was based on patented drugs if:

132
patents were analyzed

> 100 000 US dollars
a share in centralized procurement of patented single-source drugs

> 50 mil UAH
a share in hospital and pharmacy procurements

drugs - where the presence of a patent is or has been an obstacle to access to treatment

/DRUGS FOR THE TREATMENT OF HIV / AIDS

LOPINAVIR / RITONAVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
1	UA 85564 SOLID PHARMACEUTICAL DOSAGE FORM FOR INHIBITORS OF HIV PROTEASE AND METHOD FOR MANUFACTURE THEREOF / 23.08.2004	Yes	Previously known combination of known active compounds (lopinavir and ritonavir) with specific physicochemical parameters of pharmaceutically acceptable substances, namely the glass transition temperature Tg and the mass fraction of water-soluble polymer and hydrophilic-lipophilic balance (HLB) and the mass fraction of surface-active materials (SAM). The invention is directed to improved oral solid dosage forms for HIV protease inhibitors that have adequate oral bioavailability and stability and that do not feel the need for high volumes of excipient. Document WO 2004/032903 discloses a composition with lopinavir and the above pharmaceutically acceptable substances, document WO 01/34119 discloses a composition with ritonavir and pharmaceutically acceptable substances. There is a supplement of the features of the known compositions with specific parameters of their components.
2	UA 89220 METHOD FOR TREATMENT OF HIV/AIDS BY ADMINISTRATION OF SOLID PHARMACEUTICAL DOSAGE FORMULATION COMPRISING A HIV PROTEASE INHIBITOR IN FASTED STATE 21.02.2006	Yes	A method of using known compounds. A method of treating HIV / AIDS, comprising administering a solid pharmaceutical dosage form comprising lopinavir and ritonavir as a solid solution or solid dispersion with specific parameters of pharmaceutically acceptable substances (glass transition temperature Tg of a water-soluble polymer and hydrophilic-lipophilic SAM balance). The use of a combination of lopinavir and ritonavir as an HIV protease inhibitor is known in the art. The specific parameters of the components of the dosage form are obvious, and their benefits have not been proven. All features of the invention are obvious to those skilled in the art, and their choice is standard.

DARUNAVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
3	UA 100835 PROCESS FOR THE SYNTHESIS OF (3R,3aS,6aR) HEXAHYDRO-FURO [2,3-b] FURAN-3-OL, INTERMEDIATE AND PROCESS FOR THE PREPARATION THEREOF / 31.03.2005	No	A method for the synthesis of an intermediate of formula (6) (3R, 3aS, 6aR)-hexahydrofuro (2,3-b] furan-3-yl), which is used, in particular, in the synthesis of darunavir ethanol ([(3aS, 4R, 6aR)-2,3,3a, 4,5,6a-hexahydrofuro [2,3-b] furan-4-yl] N - [(2S, 3R) -4 - [(4-aminophenyl) sulfonyl-(2-methylpropyl)) amino]-3-hydroxy-1-phenylbutan-2-yl] carbamate) and an intermediate of formula α-(4) for the synthesis of compound (1). Known synthesis of darunavir ethanol without the use of an intermediate compound of formula (6) or a compound of formula α-(4), which, alternately, can be used for the synthesis of substances other than darunavir ethanol. The invention does not relate only to darunavir and therefore is not «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
4	UA 85567 PROCESS FOR THE PREPARATION OF (3R,3AS,6AR)-HEXA-HYDROFURO [2,3-B] FURAN-3-YL (1S,2R)-3-[[(4-AMINOPHENYL) SULFONYL] (ISOBUTYL) AMINO]-1-BEN-ZYL-2-HYDROXYPROPYL-CARBAMATE / 31.03.2005	Yes	A process for the synthesis of a known compound (darunavir ethanol) and intermediates for such synthesis, aimed at increasing the yield of the compound and the degree of purity, simplification and cost efficiency. Darunavir ethanol and certain intermediates are disclosed in US6248775B1. The method does not improve the pharmacological or biological activity of darunavir ethanol.

TENOFOVIR / EMTRICITABINE / EFAVIRENZ

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
5	UA 108594 SINGLE DOSAGE PHARMACEUTICAL FORM / 13.06.2006	Yes	Triple combined dosage form of known antiviral compounds (tenofovir, emtricitabine and efavirenz), which allows to ensure their biocompatibility and the size of the combined product. The invention does not improve the pharmacological or biological activity of the known compounds, but only the consumer quality of the product, which can be achieved in other ways.

TENOFOVIR ALAPHENAMIDE FUMARATE (TAF)

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
6	UA 75889 PHOSPHONATNUCLEOTIDE ANALOGS PRODRUGS, A METHOD FOR SELECTION AND PREPARATION THEREOF / 20.07.2001	Yes	TAF (GS-7340) is one of the prodrugs of the known compound tenofovir (TFV), formed on the basis of another ester compared to the known form of tenofovir disoproxil (TD). TAF contains fumarate, similar to that used in TD. The use of fumarate is obvious in the manufacture of anti-retroviral drugs. As a result of the breakdown of prodrugs in the body, active substances are formed, similar to the breakdown of TDF. Therefore, TAF is not a new compound, despite certain advantages over TDF.
7	UA 115311 TENOFOVIR ALAFENAMIDE HEMIFUMARATE / 15.08.2012	Yes	The patent application protects the hemifumarate of a known compound, which has advantages over monofumarate in the reduction of side effects. The compound does not have sufficient efficacy to indicate its non-obviousness or unexpected efficacy. The lack of side effects can be explained by a reduction in the dose of hemifumarate compared to the known monofumarate. The invention has the characteristics of «evergreening».

ABACAVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
8	UA 29382 6-SUBSTITUTED PURINE CARBOCYCLIC NUCLEOSIDES / 21.12.1990	No	The patent protects a low molecular weight therapeutic compound of a general structure and its enantiomers. The invention first discloses the antiviral activity of the obtained compound through the mechanism of its cleavage in vivo into the previously known active part of carbon triphosphate. However, the compound has not previously been described as specifically prepared. Therefore, the present invention meets the conditions of patentability and is the original patent for abacavir.
9	UA 56231 CARBOCYCLIC NUCLEOSIDES HEMISULFATE AND USE THEREOF IN VIRAL INFECTIONS TREATMENT / 14.05.1998	Yes	The patent protects the hemisulphate salt of abacavir, which has a therapeutic activity similar to abacavir, but has greater optical purity, which gives an advantage in its use in the manufacture of drugs (simplification of the stages of preparation and purification). The invention is obvious and does not have a sufficient inventive step compared to previously disclosed, in particular a patent for an abacavir compound or an application for an abacavir salt in the form of succinates.
10	UA 60293 METHOD FOR TREATING OR PREVENTING SYMPTOMS OF HIV INFECTION EMPLOYING COMBINATION OF SUBSTANCES (VARIANTS), PHARMACEUTICAL COMPOSITION AND PRODUCT (VARIANTS) / 28.03.1996	No	Combination of known compounds: abacavir, lamivudine (3TC) and emtricitabine (or azidothymidine (zidovudine)). Even taking into account the information of each of the components of the combination and its action, the invention declares a new unexpected synergistic effect (prolonged inhibitory effect, toxicity control and mutation control), which is demonstrated in the application and which does not follow directly from the known action of each compound. The patent does not protect each of the compounds separately, but only their combination or a combination of their functional derivatives. The patent is not «evergreening».

RILPIVIRINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
11	UA 78221 PYRIMIDINE DERIVATIVES INHIBITING HIV / 09.08.2002	No	The objects of the invention are: - new pyrimidine derivatives having inhibitory properties against HIV (human immunodeficiency virus) replication, which differ in structure, pharmacological activity and / or pharmacological efficacy from the known analogues described in the description of the invention; - new pharmaceutical compositions based on them; - methods of obtaining and using new pyrimidine derivatives that have inhibitory properties for HIV replication and compositions based on them. Rilpivirine is one of the objects of the invention according to p. 20, which is confirmed by Example B1, B6a (see also table 3) of the description of the invention, which was not previously described as specially obtained.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
12	UA 92469 FUMARATE OF 4-[[4-[[4-(2-CYANO-ETHENYL)-2,6-DIMETHYL-PHENYL]AMINO]-2-PYRIM-IDINYL AMINO BENZONITRILE / 02.09.2005	Yes	The object of the invention is, in particular: - rilpivirine salt; its N-oxide or stereochemically isomeric form represented as «E»-, or «Z» -isomer, or a mixture of isomers; - pharmaceutical compositions based on them; - methods of obtaining and using compounds and compositions based on them. The free base of the claimed salt of rilpivirine falls under the Markush claim invention according to the patent of Ukraine No. 78221. From the standpoint of pharmacological (pharmaceutical) properties, the technical result is the same as that of the object of the invention (compound) according to the patent of Ukraine No. 78221. At the same time, the salt of rilpivirine differs from the free base only in chemical and physical stability in different conditions of humidity and temperature and has better bioavailability, which is explained by the presence of a form in the form of a specific salt.
13	UA 92467 HYDROCHLORIDE OF 4-[[4-[[4-(2-CYANO-ETHENYL)-2,6-DIMETH-YLPHENYL]AMINO]-2-PY-RIMIDINYL] AMINO] BENZONITRILE / 02.09.2005	Yes	The object of the invention is, in particular: - pharmaceutical composition based on rilpivirine salt, polymorphic form of rilpivirine salt or polymorphic form of rilpivirine, its N-oxide or stereochemically isomeric form, presented in the form of «E» -, or «Z» -isomer, or a mixture of isomers; - methods of obtaining and using active active compounds that are part of the compositions. At the same time, the free base of the rilpivirine salt of the claimed composition falls under the general Markush claim of the invention according to the patent of Ukraine No. 78221. From the standpoint of pharmacological (pharmaceutical) properties, the technical result is the same as in the object of the invention (compound, composition) according to the patent of Ukraine No. 78221. At the same time, the salt of rilpivirine differs from the free base only in chemical and physical stability in different conditions of humidity and temperature and has better bioavailability, which is explained by the presence of a form in the form of a specific salt.

ATAZANOVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
14	UA 59432 MONOSULPHATE AZAPEPTIDE DERIVATIVE AND PHARMACEUTICAL COMPOSITION THEREOF / 22.12.1998	Yes	The object of the invention is atazanovir monosulfate, the free base of which is referenced in the description of the invention, and a pharmaceutical composition based on it. From the point of view of pharmacological (pharmaceutical) properties, atazanovir monosulfate has the same technical result as its free base. At the same time, the salt of atazanovir differs from the free base only in physical stability, improved solubility in water compared to other salts and significantly improved bioavailability when administered orally.

VALGANCICLOVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
15	UA 93599 POWDER VALGANCICLOVIR PREPARATION / 03.12.2007	Yes	The objects of the invention are a solid pharmaceutical dosage form intended for oral administration after reconstitution in water, based on a therapeutically effective amount of valganciclovir hydrochloride and its use for the preparation of a medicament for the treatment of herpes simplex and cytomegalovirus-mediated diseases. Valganciclovir hydrochloride is described in detail in US patent No. 6083953, i.e. is a known compound with certain pharmaceutical properties. The technical result of the invention UA 93599 is to obtain a preparation of valganciclovir hydrochloride, intended for use in pediatrics and for patients who need to change the dosage of the drug. This is achieved by means of solid pharmaceutical dosage forms of valganciclovir hydrochloride intended for oral administration after reconstitution in water. At the same time, it is known that in the solid state when stored in environmental conditions, valganciclovir hydrochloride has acceptable physical and chemical stability and light fastness. Thus, the object of patenting is a composition different from the previously known composition by the new form of application.

RALTEGRAVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
16	UA 77454 N-SUBSTITUTED HYDROXYPYRIMIDINONE CARBOXAMIDE INHIBITORS OF HIV INTEGRASE / 21.10.2002	No	The objects of the invention are: - new hydroxy-pyrimidinone carboxamides, which differ in structure, pharmacological activity and / or pharmacological efficacy from the known analogues specified in the description of the invention, their pharmaceutically acceptable salts; - compositions based on the above compounds; - their use as inhibitors of the enzyme HIV integrase. Raltegravir as a free base is described as specially obtained in Example 19 (see also paragraph 24 of table 2) of the description of the invention according to the patent of Ukraine No. 77454. The description of the invention states that «the practical implementation of the invention encompasses all conventional variants, devices and / or modifications», i.e. the pharmaceutically acceptable salt of raltegravir.
17	UA 87884 POTASSIUM SALT OF AN HIV INTEGRASE INHIBITOR / 02.12.2005	Yes	The object of the invention is: - anhydrous crystalline potassium salt of raltegravir; - pharmaceutical composition based on an effective amount of anhydrous crystalline potassium salt of raltegravir; - the use of anhydrous crystalline potassium salt of raltegravir for the preparation of a drug for the treatment / prevention of HIV / AIDS. Raltegravir as the free base of the anhydrous crystalline potassium salt of raltegravir falls under the General Markush claim of the patent of Ukraine No. 77454 was described in the description of the present invention as specially obtained. From the standpoint of pharmacological properties, the technical result is the same as that of the object of the invention according to the patent of Ukraine No. 77454. Herewith, there is an additional technical result, which is explained solely by the crystalline form of the potassium salt, namely: 1) improved solubility in water; 2) improved pharmacokinetics. The pharmaceutical composition based on the anhydrous crystalline potassium salt of raltegravir from the standpoint of pharmacological (pharmaceutical) properties has the same technical result as the pharmaceutical composition based on raltegravir according to the patent of Ukraine for the invention No. 77454.

DORAVIRINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
18	UA 108495 REVERSE TRANSCRIPTASE NUCLEOSIDE INHIBITORS / 28.03.2011	No	The objects of the invention are some 3-(optionally substituted phenoxy) -1 - [(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl) methyl]) pyridine-2 (1H)- compounds and pharmaceuticals compositions based on them. The technical result of the invention UA 108495 are new 3-(optionally substituted phenoxy)-1-[(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl) methyl]) pyridine-2 (1H)- compounds and their use for HIV reverse transcriptase inhibition, HIV prevention, HIV treatment and prevention, treatment and to prevent the occurrence or development of AIDS and / or ARC. Therefore, the subject of the patent are new chemical compounds and pharmaceutical compositions based on them, designed to inhibit HIV reverse transcriptase, HIV prevention, HIV treatment and prevention, treatment and to prevent the occurrence or development of AIDS and / or ARC.

COBICISTAT

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
19	UA 97112 MODULATORS OF PHARMACOKINETIC PROPERTIES OF THERAPEUTICS / 06.07.2007	No	The objects of the invention are: - new compounds that modify the pharmacokinetics of the drug; - pharmaceutical compositions based on the above compounds; - a way to improve the pharmacokinetics of the drug.
20	UA 101193 THE USE OF SOLID CARRIER PARTICLES TO IMPROVE THE PROCESSABILITY OF A PHARMACEUTICAL AGENT / 01.05.2009	Yes	The objects of the invention are: - pharmaceutical compositions based on cobicistat; - methods of obtaining the above pharmaceutical compositions. The technical problem solved by the invention is to create a new pharmaceutical form of a pharmaceutical composition based on a known compound – cobicistat. The new pharmaceutical form of the composition based on cobicistat does not change its pharmaceutical properties. Therefore, the invention according to the patent UA 101193 actually protects a new pharmaceutical form of application of compositions based on the known compound cobicistat.
21	UA 101312 MODULATORS OF PHARMACOKINETIC PROPERTIES OF THERAPEUTICS / 22.02.2008	No	The objects of the invention are: - new compounds that modify the pharmacokinetics of the drug; - pharmaceutical compositions based on the above compounds. The patent application UA 101312 is filed for a period not exceeding 12 months from the priority date of the patent application UA 97112. Therefore, one of the objects of patenting UA 74797 are new compounds that modify the pharmacokinetics of the drug.
22	UA 103224 TABLETS FOR COMBINATION THERAPY / 04.02.2010	Yes	The objects of the invention are pharmaceutical compositions in the form of tablets and a method for producing such tablets. The technical problem solved by the invention is to improve solid dosage forms (e.g., tablets) for the delivery of compositions containing several known agents, in particular cobicistat. The new solid dosage form of the pharmaceutical composition differs from those known in fact in that the APIs are arranged in layers. At the same time, no synergistic effect has been reported in the pharmaceutical properties of such compositions compared to the cumulative pharmaceutical effect from the separate administration of the same APIs. Therefore, the invention according to the patent UA 103224 actually protects a new solid dosage form of pharmaceutical compositions based on known compounds.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
23	UA 108738 METHOD FOR CYTOCHROME P450 MONOOXYGENASE INHIBITOR PRODUCTION AND INTERMEDIATES THAT CAN BE USEFUL / 01.04.2010	No	The objects of the invention are new methods for producing cobicistat and intermediates used in these methods.

ETRAVIRINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
24	UA 70966 PIRIMIDINES INHIBITING HIV REPLICATION / 24.09.1999	No	The objects of the invention are: - pyrimidine compounds; - a method of obtaining the above compounds; - pharmaceutical compositions based on the above compounds. Etravirine falls under the general Markush claim of the invention according to the patent UA 70966. It is a compound that is specially obtained and tested (compound 46, example B14 description of the invention). EP-0834507 discloses substituted diamino 1,3,5-triazine derivatives having the ability to inhibit HIV replication. However, Etravirine and other pyrimidines according to the patent UA 70966 do not fall under the general Markush claim according to the patent EP 0834507. Thus, one of the objects of patenting the invention UA 70966 are new chemical compounds that inhibit HIV replication.
25	UA 74797 ANTIVIRAL COMPOSITION / 31.08.2000	No	The objects of the invention are: - compounds with antiviral properties; - pharmaceutical antiviral compositions based on the above compounds; - methods of obtaining pharmaceutical antiviral compositions. Etravirine falls under the general Markush claim of the invention according to patent UA 74797. It is a compound that is specially obtained and tested (compound 26, example 2B14 description of the invention). However, as noted above, Etravirine is disclosed in patent UA 70966. However, the application for the invention under the patent UA 74797 is filed for a period not exceeding 12 months from the date of priority of the application for the invention under the patent UA 70966. Thus, one of the objects of patenting the invention UA 74797 are new chemical compounds that inhibit the replication of HIV.

ROVAFOVIR ETALAFENAMIDE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
26	UA 88313 PHOSPHONATE ANALOGS OF HIV INHIBITOR COMPOUNDS / 26.07.2005	No	The objects of the invention are: - new compounds with the properties of HIV inhibitors; - pharmaceutical compositions based on the above compounds; - a method of treating HIV-related disorders using the above compounds. The claims cover rovafovir etalafenamide.
27	UA 103329 SALTS OF HIV INHIBITOR COMPOUNDS / 07.07.2009	Yes	The objects of the invention are: - new salts of a known compound having antiviral activity, in particular, having activity against HIV; - pharmaceutical compositions based on the above salts of the compounds. Therefore, one of the objects of the invention is a salt of a known compound, the other is a pharmaceutical composition according to the new application, which differs from the previously known composition only in the composition of the new salts of the known ingredients.

/DRUGS FOR THE TREATMENT OF TUBERCULOSIS

MOXIFLOXACIN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
28	UA 35554 QUINOLNE- AND NAPHTYRIDONE-CARBOXYLIC ACID DERIVATIVES IN THE FORM OF MIXTURE OF ISOMERS, PHARMACEUTICAL COMPOSITION HAVING ANTIBACTERIAL ACTIVITY INTERMEDIATE COMPOUNDS / 16.04.1993	Yes	The object of the invention is: - derivatives of quinolne- and naphthyridone-carboxylic acids, which fall under the known general structural Markush claim, but differ from the known compounds by a new set of radicals of a mixture of isomers or individual isomers; - pharmaceutical compositions based on them. At the same time, the new quinolone- and naphthyridone-carboxylic acid derivatives have better pharmacological activity and / or pharmacological efficacy compared to the known analogues, but have not been previously described as specially prepared. In some cases (for example, for moxifloxacin), new quinolone- and naphtyridone-carboxylic acid derivatives are optical isomers, enantiomers of active substances of previously known compositions with the same molecular formula and the same therapeutic effect.
29	UA 52952 SET FOR ADMINISTERING ANTIBACTERIAL AGENT / 22.06.2010	Yes	The object of the utility model is a kit of an antibacterial drug based on moxifloxacin. The technical result is a set of antibacterial drug that would have high antibacterial properties (due to moxifloxacin) and improve acid-base balance of blood (due to isotonic Ringer's solution). Thus, the object of patenting is a composition that is essentially a new combination of previously known active substances.
30	UA 56286 A METHOD FOR PRODUCING 8-MEHOXY-QUINOLINE CARBOXYLIC ACIDS / 12.11.1998	No	The object of the invention is a method for producing derivatives of 8-methoxy-C-quinolone carboxylic acid of General formula (I). The technical result of the invention is a method for producing derivatives of 8-methoxy-quinolone carboxylic acids, which allows to reduce the reaction time, to carry out work at atmospheric pressure, which provides a complete conversion, as well as simple preparation of the reaction mixture. Thus, the patent does not preclude obtaining moxifloxacin in a manner other than the patent and using it.
31	UA 66812 DRUG FORMULATION WITH CONTROLLED RELEASE OF ACTIVE INGREDIENT / 15.09.1998	No	The object of the invention is a preparative form of a drug based on moxifloxacin. The technical result of the invention is a preparative form of a drug with controlled release of moxifloxacin within specified limits. At the same time, moxifloxacin, its pharmaceutically acceptable salts, its manufacture, tablet forms are described in EP-A-0305733, EP-A-0550903, JP-A-0780390. Thus, the object of patenting is a preparative form of a known drug, but with new, previously unknown, properties for the release of the active substance.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
32	UA 72268 AQUEOUS COMPOSITION CONTAINING MOXIFLOXACIN HYDROCHLORIDE AND SODIUM CHLORIDE / 25.07.2000	No	The object of the invention is an aqueous composition of moxifloxacin hydrochloride and sodium chloride. The technical result is an aqueous composition containing moxifloxacin hydrochloride and sodium chloride for use as a drug for the prevention or treatment of bacterial infections in humans or animals. Moxifloxacin as a highly effective anti-infective agent is first described in the application for European patent EP-A-0350733. However, this application does not describe pharmaceutical preparations suitable for parenteral administration. The drug composition of moxifloxacin chloride, which is isotonized with sodium chloride, on the one hand, is not sensitive to iron ions, on the other hand, the solubility of the active substance moxifloxacin in the form of its hydrochloride in the presence of sodium chloride is really extremely poor. However, it has been found by chance that acceptable moxifloxacin chloride compositions for isotonization with sodium chloride can be obtained by adhering to certain narrow concentration ranges for the active substance and the isotonizing agent. Thus, the object of patenting is an aqueous composition of moxifloxacin hydrochloride and sodium chloride in a narrow range of their concentrations.
33	UA 72483 MOXIFLOXACIN-CONTAINING PHARMACEUTICAL PREPARATION AND METHOD FOR ITS MANUFACTURE / 29.10.1999	No	The objects of the invention are: - a pharmaceutical composition based on moxifloxacin, which additionally contains lactose in an amount of 2.5-25 wt.%; - a method of obtaining such a composition. The technical result is a pharmaceutical form for the production of tablets with sufficient hardness and, accordingly, mechanical strength, which at the same time have excellent release properties of moxifloxacin. Moxifloxacin as a highly effective anti-infective agent is first described in the application for European patent EP-A-0350733. The same application mentions a pharmaceutical preparation based on moxifloxacin with additional substances, among which there is no lactose.

BEDAQUILINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
34	UA 82198 QUINOLINE DERIVATIVES AND USING OF THEM AS MICOBACTERIAL INHIBITORS, PROCESS FOR PREPARATION THEREOF, PHARMACEUTICAL COMPOSITION BASED ON CLAIMED COMPOUNDS, AND TRANSIENT COMPOUND / 18.07.2003	No	The object of the invention is: - new substituted quinoline derivatives suitable for the treatment of mycobacterial diseases, especially diseases caused by pathogenic mycobacteria such as Musobacterium tuberculosis, M.bovis, M.avium and M.marinum, which differ in structure, pharmacological activity and / or known pharmacological efficacy from analogues specified in the description of the invention, their pharmaceutically acceptable acid additive or base additive salts, stereochemically isomeric forms or N-oxide form; - pharmaceutical compositions based on the above compounds; - methods of obtaining and using these compounds and compositions based on them. Bedaquiline is one of the objects of the invention according to claim 26, which is confirmed by Example B7, B6a (see also table 3) of the description of the invention, which was not previously described as specially obtained.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
35	UA 97813 FUMARATE SALT OF (ALPHA S, BETA R)-6-BROMO-ALPHA-[2-(DIMETHYLAMINO) ETHYL]-2-METHOXY-ALPHA-1-NAPHTHALENYL-BETA-PHENYL-3-QUINOLINEETHANOL / 03.12.2007	Yes	The object of the invention is, in particular: - fumarate salt, the free base of which according to p. 1,2,3 of the claims falls under the general Markush claim invention of the patent of Ukraine No. 82198; - pharmaceutical compositions based on them; - methods of obtaining and using compounds and compositions based on them. From the standpoint of pharmacological (pharmaceutical) properties, the technical result is the same as that of the object of the invention (compounds, compositions) according to the patent of Ukraine No. 82198. At the same time, compared to the description of the pharmaceutical composition contained in the description of the invention according to the patent of Ukraine No. 82198, the composition has different dosage forms and different forms of application due to the specification of qualitative and quantitative composition of active substance and excipients.
36	UA 90267 USE OF SUBSTITUTED QUINOLINE DERIVATIVES FOR THE TREATMENT OF DRUG RESISTANT MYCOBACTERIAL DISEASES / 24.05.2005	No	The objects of the invention are: - a composition, product based on substituted quinoline derivatives for the treatment of diseases caused by drug-resistant mycobacteria, their pharmaceutically acceptable acid additive or base additive salts, stereochemically isomeric forms, tautomeric forms or N-oxide forms; - the use of the above compositions, products for inhibiting the reproduction of strains of Mycobacterium resistant to the drug, in particular, a strain of Mycobacterium tuberculosis. Substituted quinoline derivatives, including bedaquiline, are described in International Publication WO 2004/011436 as having antimycobacterial properties against sensitive, susceptible strains of mycobacteria, but these compounds have not been described as being effective against strains of mycobacteria resistant to means, in particular, strains of mycobacteria resistant to several drugs. The description of the invention UA 90267 contains confirmation of the receipt, study of bedaquiline, as well as its properties for inhibiting strains of mycobacteria resistant to the drug. Thus, the object of patenting are chemical compounds that fall under the general Markush claim of the previously filed application and have been described as specially obtained. However, it was not known to use these compounds to achieve a new technical result.
37	UA 92484 PROCESS FOR PREPARING (ALPHA S, BETA R)-6-BROMO-ALPHA-[2-(DIMETHYLAMINO) ETHYL]-2-METHOXY-ALPHA-1-NAPHTHALENYL-BETA-PHENYL-3-QUINOLINEETHANOL / 22.05.2006	No	The objects of the invention are: - a method of isolating bedaquiline from a mixture of stereoisomeric forms of 6-bromo- [2-(dimethylamino) ethyl]-2-methoxy-1-naphthalenyl-phenyl-3-quinolineethanol; - a salt having the following formula: (αS, βR) - 6-bromo-α-[2- (dimethylamino) ethyl] -2-methoxy-α-1-naphthalenyl-β-phenyl-3-quinolineethanol * (11bR) -4-hydroxydinaphtho [2,1-d: 1', 2'-f] [1,3,2] dioxaphosphepin-4-oxide. 6-bromo- [2- (dimethylamino) ethyl] -2-methoxy-1-naphthalenyl-phenyl-3-quinolineethanol and its stereoisomeric forms are disclosed in WO2004 / 011436 as antimicrobial agents used for the treatment of mycobacterial diseases, in particular diseases caused by pathogenic mycobacteria such as Mycobacterium (M.) tuberculosis, M. bovis, M. avium and M. marinum. The enantiomer of (S, R) -6-bromo- [2- (dimethylamino) ethyl] -2-methoxy-1-naphthalenyl-phenyl-3-quinolinethanol corresponds to compound 12 (enantiomer A1) in WO2004 / 011436 and is the desired compound for the treatment of mycobacterial diseases, in particular tuberculosis. Thus, the object of the patent is a new method of isolating bedaquiline from a mixture of stereoisomeric forms of 6-bromo- [2- (dimethylamino) ethyl] -2-methoxy-1-naphthalenyl-phenyl-3-quinolinethanol, which can be used on an industrial scale and give a high yield. The salt mentioned in p. 46 of the claims is an intermediate in the process of isolating bedaquiline from a mixture of stereoisomeric forms of 6-bromo - [2- (dimethylamino) ethyl] -2-methoxy-1-naphthalenyl-phenyl-3-quinolinethanol.

DELAMANID

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
38	UA 83200 2,3-DIHYDRO-6-NITROIMIDAZO[2,1-b] OXAZOLES / 10.10.2003	No	The patented compounds do not fall under the general structure of the Markush claim of analogues and prototypes. Specific compounds according to the patent of Ukraine for the invention No. 83200 are not known as those that were previously specially obtained and studied. The object of patenting is: - the above compounds, their optical active forms (isomers); - pharmaceutical compositions based on them; - methods for producing said compounds. Pharmaceutical compositions according to the patent are based on new, previously not specifically obtained and not studied substances, their optically active forms (isomers) and their pharmaceutically acceptable salts.
39	UA 95251 PHARMACEUTICAL COMPOSITION COMPRISING 2,3-DIHYDRO-6-NITROIMIDAZO [2 ,1-B] OXAZOLE DERIVATIVES / 19.07.2006	No	The objects of the invention are a pharmaceutical composition containing derivatives of 2,3-dihydro-6-nitroimidazo [2,1-b] oxazole. It is known that 2,3-dihydro-6-nitro [2,1-b] oxazole compounds represented by the following General formula (1), their optically active isomers and their pharmaceutically acceptable salts exhibit excellent bactericidal action against tuberculosis microbacteria, multidrug-resistant tuberculosis microbacteria and atypical acid-fast bacteria (see the publication of not past examination of the Japanese patent application №2004-149527 and WO 2005-042542). The technical result of the invention UA 95251 is to provide a pharmaceutical composition with improved solubility in water presented in the claims of an oxazole compound. At the same time, the pharmaceutical properties of the composition compared to analogues remain unchanged. Thus, the object of patenting is a composition different from the previously known composition in the composition of auxiliary ingredients which leads to new properties in terms of solubility in water.

/DRUGS FOR TREATMENT OF VIRAL HEPATITIS

SOFOSBUVIR / LEDIPASVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
40	UA 108610 ANTIVIRAL COMPOUNDS, AND PHARMACEUTICAL COMPOSITION WHICH CONTAINS THESE ANTIVIRAL COMPOUNDS / 12.05.2010	No	Compounds according to the patent of Ukraine for the invention No. 108610 are not known as those that were specially obtained and investigated before the date of filing the application and the date of priority. They also do not fall under the general Markush claim, which would have been known before the date of application and the date of priority. Pharmaceutical compositions based on them were also not known.

SOFOSBUVIR / VELPATASVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
41	UA 110354 ANTI-VIRAL COMPOUNDS / 16.11.2012	Yes	The objects of the invention are previously not obtained and unexplored compounds, their salts, pharmaceutical compositions based on them and methods of treatment. The compounds according to the present invention fall within the general Markush claim of the patent of Ukraine No. 108610, which was known before the filing date and the priority date, but was not known as having been specially obtained and investigated before the filing date. Pharmaceutical compositions based on them were also not known. The main technical result from the standpoint of pharmacological properties is the same as in the invention according to the patent of Ukraine 108610: obtaining new compounds for use in the prophylactic or therapeutic treatment of hepatitis C or disorders associated with hepatitis C. At the same time, in some cases new compounds differ from previously known by Markush claim by the same type of substituents within one group (class).

GLECAPREVIR / PIBRENTASVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
42	UA 113048 ANTI-VIRAL COMPOUNDS / 12.10.2011	No	The objects of the invention are a previously unprocessed and unexplored compound, its salts, and pharmaceutical compositions based on them. The compounds of the present invention do not fall under the general Markush claim known before the filing date and priority date, and are not known to have been specifically prepared and tested prior to the filing date and priority date. Pharmaceutical compositions according to the patent are based on new, previously not specifically obtained and not studied substances, their pharmaceutically acceptable salts.

PARITAPREVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
43	UA 103054 MACROCYCLIC HEPATITIS C SERINE PROTEASE INHIBITORS / 10.09.2009	No	The object of the invention according to the patent is: - low molecular weight compounds or their pharmaceutically acceptable salts, which are characterized by a qualitative and quantitative composition, bonds between atoms and their mutual arrangement in the molecule in accordance with the generic chemical structural formula (I) or (I '), a special case of which is paritaprevir and based on the use of compounds (I) or (I '): - pharmaceutical compositions characterized by a qualitative composition of ingredients; - a method of treating a viral infection caused by hepatitis C in an individual, and - methods of obtaining a compound of formula I or its pharmaceutically acceptable salt. Compounds (I) or (I ') are not specifically described previously, their therapeutic activity is not known, and methods for their preparation are not known as evidenced by the international search report on the application PCT / US2009 / 005082, even with given that compounds similar in structure and therapeutic effect have been previously described in WO 2004/093798 A2 of 04.11.2004 (ENANTA PHARMACEUTICALS, INC.). Conclusion: there are no grounds to classify the patent as «evergreening».
44	UA 109532 MACROCYCLIC INHIBITORS OF THE HEPATITIS C SERINE PROTEASE / 10.09.2009	No	The patent is obtained according to the application selected from the patent application, and protects the compounds or their pharmaceutically acceptable salt for the treatment of HCV infection in a patient, characterized by specific structural formulas corresponding to the compounds listed in the application PCT / US2009 / 005082, namely: - claim 1 of the patent ⟶ compound (25) of the application PCT / US2009 / 005082, - claim 2 of the patent ⟶ compound (28); - claim 3 of the patent ⟶ compound (29); - claim 4 of the patent ⟶ compound (30); - claim 5 of the patent ⟶ compound (32); - claim 6 of the patent ⟶ compound (36); - claim 7 of the patent ⟶ compound (19). Considering the conclusion of the patent, these compounds have not been previously described and their therapeutic activity was not known at the date of application. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
45	UA 104517 SOLID COMPOSITION USEFUL FOR TREATING HEPATITIS C INFECTION AND METHOD FOR ITS MANUFACTURING / 08.03.2011	Yes	The object of the invention according to the patent is: - a composition in solid form, which contains the compound paritaprevir or its pharmaceutically acceptable salt in amorphous form (solid dispersion), hydrophilic polymer and superficially active substance (SAS) to reduce the surface tension of water, ie characterized only by qualitative composition and structure; - the specified composition + ritonavir, and - a method of obtaining the specified composition which consists in drying the solvent in a liquid solution or solidification of the melt, which contains these compounds paritaprevir, polymer and SAS. The paritaprevir compound mentioned in the patent was described, in particular, in solid form, in the application PCT / US2009 / 005082 dated 10.09.2009 (compound (29) in the description and claims), on the basis of which the above patents were obtained. The technical result when using the compounds according to the patents is the same - the treatment of hepatitis C virus infection. The patent protects the pharmaceutical composition, which is a specific dosage form of the previously described composition, so it can be classified as «evergreening patents», even given that the methods of obtaining such a composition have not previously been described. Conclusion: there are grounds to classify the patent as «evergreening».

OMBITASVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
46	UA 103052 ANTI-VIRAL COMPOUNDS / 10.06.2010	No	According to the claims of the invention (hereinafter - the «formula»), the patent protects three high-molecular antiviral compounds of the general structure: - a compound according to claim 1 of the formula (corresponds to the compound according to example 1 from the publication of international application WO2010 / 144646 A2); - a compound according to claim 3 of the formula (corresponds to the 1st compound according to example 34 from the publication of international application WO2010 / 144646 A2); - a compound according to claim 5 of the formula (corresponds to the 2nd compound according to example 34 from the publication of international application WO2010 / 144646 A2) and - pharmaceutical compounds based on them or on the basis of their pharmaceutically acceptable salts (claims 2, 4, 6 of the formula). These compounds are novel and not previously described as specially prepared, i.e. are not known from the prior art. From the prior art known compounds, for example, the compound known from JP2007 / 320925, these compounds differ in the presence of pyrrolidines and esters on both sides of the benzene nucleus, peptide bonds and amino acids (proline, valine). The prior art does not contain information that may indicate the obviousness of such differences. The invention contains information on the presence of antiviral activity of these compounds, obtained by determining the EC50 (semi-maximum effective concentration) by testing using HCV analysis with replicon 1b-con1 in the presence of 5% FBS (fetal bovine serum). Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
47	UA 108904 ANTI-VIRAL COMPOUNDS / 10.06.2010	No	The patent is obtained according to the application selected from the application for a previous patent, and protects the compounds of the general formula IB described in the description of the invention. These compounds are novel and not previously described as specially prepared, in particular, are not known from the documents WO2008021936 and WO2010017401 which are the closest from the prior art. Conclusion: there are no grounds to classify the patent as «evergreening».
48	UA 105434 SOLID COMPOSITION AND METHOD FOR TREATMENT OF HEPATITIS C / 09.06.2011	Yes	The patent protects the drug against HCV in the form of a solid composition containing one of four pyrrolidine derivatives in an amorphous form (OMBITASVIR substitutes), as well as a pharmaceutically acceptable hydrophilic polymer and an optional pharmaceutically acceptable superficially active substance and method for preparing said composition. The composition is characterized by the qualitative composition and structure of the composition, as well as the structure of the ingredients: compounds of formula IA, IV, IC or ID or their pharmaceutically acceptable salts having antiviral activity. These compounds are described in international application WO2010 / 144646 A2 on the basis of which the two above-mentioned patents were obtained. The antiviral activity of the compound of formulas IA, IP, IC or ID is similar to that described in international application WO2010 / 144646 A2. International application WO2010 / 144646 A2 was published after the filing date of application WO2011156578A2 on the basis of which the patent was obtained, and therefore is not included in the prior art for the invention according to the patent. That is, the patent protects a specific form of application of the compounds previously described in the application WO2010 / 144646 A2. Conclusion: there are grounds to classify the patent as «evergreening».
49	UA 118080 ANTI-VIRAL COMPOUNDS / 10.06.2010	No	The object of the patent is an individual chemical compound characterized by the general structural Markush claim which identifies the basic compound of ombitasvir (compound of formula IB) or its pharmaceutically acceptable salt. The compound is an NS5A inhibitor of hepatitis C virus replication. No information has been found that said chemical compound of formula IB falls under the general Markush claim of the foregoing application, and that it has previously been described as specially prepared. The description of the patent confirms the improvement of the antiviral action of the compound of formula IB. Conclusion: there are no grounds to classify the patent as «evergreening».

DASABUVIR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
50	UA 117800 URACIL OR THYMIN DERIVATIVES FOR THE TREATMENT OF HEPATITIS C	No	The object of the invention according to the patent is an individual chemical complex compound or its salt characterized by a qualitative and quantitative composition in the form of a molecular formula which identifies a particular compound of dasabuvir according to one of its variants. The compound is intended to inhibit the replication of hepatitis C virus. Other objects of the patent UA 117800 are a pharmaceutical composition based on the specified compound, as well as a specific crystalline form of dasabuvir. No information was found that this chemical compound falls under the general Markush claim of the previously submitted application, and that it was previously described as specially obtained (Publication WO2009039127 of the international application «URACIL OR THYMINE DERIVATIVE FOR TREATING HEPATITIS C», International Preliminary Report on Patentability, page 3, https://bit.ly/2YVNQMa). The patent is selected from the previously issued patent UA104995 and repeats it to a lesser extent for additional protection of DASABUVIR in the form in which it should be used in therapeutic combinations.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
51	UA 115025 PROCESS FOR PREPARING ANTIVIRAL COMPOUNDS / 15.07.2011	Yes	The object of the invention according to the patent is a method of obtaining a compound according to the patent or its salt, ie a patent for a known compound (described, for example, in the publication WO2009039127) characterized by the method of obtaining it (product by process). The process of obtaining the compound of the patent differs from the process described in WO2009039127. The technical result in the patent is to obtain a composition with no side effects, but compared with interferon or ribavirin, and not compared with the method described in WO2009039127, i.e. the technical result does not differ from that specified in WO2009039127. Conclusion: there are grounds to classify the patent as «evergreening».
52	UA 113498 PHOSPHINE LIGANDS FOR CATALYTIC REACTIONS / 15.07.2011	No	The object of the invention according to the patent are compounds (phosphine ligands) or their salts used in catalytic reactions in the composition of catalytic complexes, in particular, for dasabuvir. The compounds are characterized by the general structural formula (I), which was previously described as specially prepared, as well as its known use in organic reactions for the formation of bonds C-C, C-O, C-N. The inventive step and the new technical result are not confirmed in the description to the patent. Therefore, the patent protects dasabuvir through the process of obtaining it described in known sources (Publication WO2012009698 of the international application «PHOSPHINE LIGANDS FOR CATALYTIC REACTIONS», International Preliminary Report on Patentability, p. 9, https://bit.ly/2UljYnj). Conclusion: there are grounds to classify the patent as «evergreening».

PEGINTERFERON

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
53	UA 56989 PHYSIOLOGICALLY ACTIVE PEG-CONJUGATE OF a-INTERFERON, A METHOD FOR PREPARING THE SAME, A PHARMACEUTICAL COMPOSITION BASED THEREON AND A METHOD FOR TREATMENT OR PROPHYLAXIS OF IMMUNOMODULAR DISEASES / 30.05.1997	Да	The object of the invention is a specific branched structure of the conjugate of peginterferon, a physiologically active pegylated conjugate of α-interferon with polyethylene glycol (PEG) with certain limits of the average molecular weight of the PEG molecule in the specified conjugate. The advantages of the invention are the increase of circulation and half-life time and plasma stay, reduction of immunogenicity, decrease of clearance and increase of antiproliferative activity compared to unmodified α-interferon and increase of antiproliferative activity and virtually disappearance of immunogenicity compared to other pegylated conjugates of α-interferon. The invention uses conventional methods of pegylation of interferon which is a previous version of the compound, and predictable results are obtained which makes it obvious to a person skilled in the art and does not promise to increase the efficiency of the compound compared to the unpegylated version (Roche's Indian patent on Pegasys® revoked, 10.4155 / PPA .12.89 © 2013 Future Science Ltd. Pharm. Pat. Analyst (2013) 2 (1), 13–16, https://www.future-science.com/doi/pdf/10.4155/ppa.12.89). The invention describes a formally modified form of a previously known compound which has certain advantages in reducing renal and significantly increasing the half-life, but has no increase in efficacy in the treatment of hepatitis. Conclusion: there are grounds to classify the patent as «evergreening».

/DRUGS FOR THE TREATMENT OF ONCOLOGICAL DISEASES

TRASTUZUMAB

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
54	UA 92913 EXPRESSION VECTOR AND METHODS FOR PRODUCTION OF HIGH LEVELS OF PROTEINS / 19.06.2006	No	The patent protects individual compounds belonging to genetic engineering objects characterized by a DNA sequence and their use to obtain high expression of proteins and monoclonal antibodies, in particular, which is trastuzumab to the HER2 receptor used in recombinant biological products. The objective of the invention is to provide a vector of gene expression of eukaryotes which increases the expression of protein in transfected with such a vector host cells and thus makes biological products based on monoclonal antibodies more available. The increase in erythropoietin gene (EPO) and fusion protein (TNFR-IgGFc) expression while using the vector of the invention is confirmed by the description. The use of the CMV promoter is not known and is not obvious in terms of the prior art. The invention is aimed at obtaining an expression vector of a list of biological products, an alternative to known analogues, and has advantages over them. Conclusion: there are no grounds to classify the patent as «evergreening».
55	UA 102166 SUBCUTANEOUS ANTI-HER2 ANTIBODY FORMULATION / 28.07.2010	Yes	The patent protects a pharmaceutical composition of a monoclonal antibody to the HER2 receptor (trastuzumab), the use of such a composition for the treatment of gastric cancer, metastatic breast cancer or early breast cancer, an injection device of said composition and a kit containing vials with the composition and device. The composition is characterized by the structure and qualitative and quantitative composition of ingredients: antibodies to HER2 (trastuzumab), buffering agent, stabilizer, SAS and enzyme gualuronidase, known as a regulator of diffusion transport of substances between blood, lymph and tissue cells. The antibody to HER2 (trastuzumab) is already known and disclosed, in particular, in the application W08906692, published 07/27/1989 (JENENTEC, INC. as a division of F. HOFFMANN-LA ROCH AG) which also mentioned compositions based on this antibody for inhibiting the growth of tumor cells, such as carcinoma, in particular carcinoma of the human breast, kidney, stomach and salivary glands of a human or other types of tumor cells expressing the HER2 receptor. That is, the invention protects a pharmaceutical composition other than a previously known composition only by the dosage and qualitative composition of the auxiliary standard ingredients. Conclusion: there are grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
56	UA 104254 COMPOSITION FOR SUBCUTANEOUS ADMINISTRATION CONTAINING ANTI-HER2 ANTIBODY / 28.07.2010	Yes	The patent was obtained on the application selected from the application for another patent for this drug. Like the previous patent, this patent protects a composition characterized by the structure and qualitative and quantitative composition of the ingredients: anti-HER2 antibodies, buffering agent, stabilizer and SAS. The composition according to the claims differs from the composition according to the previous patent only in the absence of the enzyme gualuronidase and a clear definition of trastuzumab, pertuzumab or T-DM1 (trastuzumab entansine) as an anti-HER2 antibody. That is, the invention according to this patent, similarly to the previous patent, protects a pharmaceutical composition other than the previously described composition only by dosage and qualitative composition of the auxiliary standard ingredients. Conclusion: there are grounds to classify the patent as «evergreening».
57	UA 108832 COMBINATION OF CONJUGATE ANTI-HER2 ANTIBODY-DRUG AND CHEMOTHERAPEUTIC AGENTS AND METHODS OF USE / 10.03.2009	Yes	The patent protects a method of treating a hyperproliferative disorder which is, in particular, a malignant tumor expressing ErbB2 by administering a therapeutic combination of trastuzumab-MCC-DM1 and a chemotherapeutic agent selected from GDC-0941 (pictilisib) and GNE-390 (apitolisob). Dependent claims relate to certain forms of the invention and sequences of administration of said therapeutic combination and a pharmaceutical composition comprising said combination and standard excipients (pharmaceutically acceptable carriers, flow regulators, diluents or excipients). The description of the invention declares a synergistic effect from the use of a combination of these monoclonal antibodies and chemotherapeutic agents which is to inhibit the growth of tumor cells in vitro and in vivo illustrated by the quantitative analysis based on the median effect of Chou & Talalay and isobolograms which are used to determine the value of the combination index (CI) to establish synergism, antagonism or additive effect. Mentioned primary application W08906692 (GENENTEC, INC. as a division of F. HOFFMANN-LA ROCHE AG) for trastuzumab also contains information about the possibility of a synergistic effect in combination with chemotherapeutic agents. However, the patent does not disclose for the first time any of the substances, and they are known before. That is, the pharmaceutical composition according to the patent is a new combination of previously known active substances. Conclusion: there are grounds to classify the patent as «evergreening».

RITUXIMAB

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
58	UA 27946 A METHOD FOR THE TREATMENT OF LYMPHOMA OF V-CELLS, IMMUNOLOGICALLY ACTIVE CHIMERIC ANTIBODY ANTI-CD20 / 12.11.1993	No	The object of the invention according to the patent is an immunologically active chimeric antibody anti-CD20, produced by transfectoma which includes anti-CD20 in the vector TCAE8 with the deposit number 69119 ATCC, and a method of treating V-cell lymphoma using the specified antibody. The antibody is expressed through a hybridoma - an artificial hybrid cell line created to produce monoclonal antibodies in large quantities by merging human V-lymphocytes and melanoma cells. The invention is not limited to the protection of rituximab and extends to other substances whose molecules have anti-CD20 antibodies, such as ibritumomab tiuxetan. Patent UA 27946 relates to the «first-generation patent family» (Ulrich Storz, Rituximab How approval history is reflected by a corresponding patent filing strategy, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4171018/) regarding rituximab, so it cannot be classified as an «evergreening» patent. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
59	UA 91961 THERAPY OF AUTOIMMUNE DISEASE IN A PATIENT WITH AN INADEQUATE RESPONSE TO A TNF-ALPHA INHIBITOR / 06.04.2004	Yes	The object of the invention according to the patent is a method of treating rheumatoid arthritis using rituximab at a certain dosage. The subject is characterized by the use of a previously known substance (a molecule from an antibody that binds to CD20 and which kills or reduces V-cells in a mammal when bound to CD20), different from the known only in the dosage. Corresponding patent EP1613350 is revoked by appeal. Patent UA 91961 belongs to the «secondary patent» and is a typical representative of the «evergreening» patents which are also questionable at their patentability. Conclusion: there are grounds to classify the patent as «evergreening».
60	UA 92913 EXPRESSION VECTOR AND METHODS FOR PRODUCTION OF HIGH LEVELS OF PROTEINS / 09.06.2011	No	The object of the invention according to the patent are individual compounds belonging to the objects of genetic engineering characterized by a DNA sequence, and their use to obtain high expression of proteins and monoclonal antibodies (in particular, which is rituximab against TNFR-IgGFc) used in recombinant biological drugs. The objective of the invention is to provide a vector of gene expression of eukaryotes which increases the expression of protein in transfected with such a vector host cells, and thus makes biological products based on monoclonal antibodies more available. The increase in erythropoietin gene (EPO) and fusion protein (TNFR-IgGFc) expression using the vector of the invention is confirmed by the description. The use of the CMV promoter is not known and is not obvious from the prior art. The invention is aimed at obtaining an expression vector of a list of biological products which is alternative to the known and has advantages over them, so the invention cannot be attributed to «evergreening» patents. Conclusion: there are no grounds to classify the patent as «evergreening».
61	UA 94726 METHOD FOR TREATING JOINT DAMAGE / 14.11.2006	Yes	The object of the invention is a method of treating joint damage in an individual with rheumatoid arthritis (RA) using rituximab which differs from the known in additional course of treatment with rituximab with a certain dosage and frequency. From the point of view of referring to «evergreening» patents, this patent is a complete analogue of the patent UA 92913 and relates to the dosage of a previously known substance during treatment. Corresponding patent EP1951304 is issued, but the EPO is currently considering the opposition to this patent. Patent UA 94726 belongs to the «secondary patent» and is a typical representative of the «evergreening» patents. Conclusion: there are grounds to classify the patent as «evergreening».
62	UA 99933 THERAPY OF AUTOIMMUNE DISEASE IN A PATIENT WITH AN INADEQUATE RESPONSE TO TNF-ALPHA INHIBITOR / 06.04.2004	Yes	The object of the invention according to the patent is the use of rituximab for the preparation of a drug and is characterized by doses and sequence of rituximab administration and additional administration of methotrexate (ametopterin, a synthetic drug, folic acid analogue which belongs to the group of immunosuppressants and cytostatics). That is, the patent relates to the dosage of a previously known substance during treatment and its combination with other known substances with a known effect to obtain a previously disclosed favorable clinical response. Conclusion: there are grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
63	UA 104579 METHOD OF TREATING HEMATOLOGIC CANCER USING PNP INHIBITORS SUCH AS FORODESINE IN COMBINATION WITH ALKYLATING AGENTS OR ANTI-CD20 AGENTS / 10.12.2008	No	The object of the invention according to the patent is a method of treating cancer of the hematopoietic system using rituximab and forodesine (purine nucleoside phosphorylase inhibitor, compound which blocks one of the enzymes responsible for the development of T-cell neoplasms, BCX-1777), as well as a pharmaceutical composition and kit for delivery of rituximab and forodesine to the subject being treated (Alonso R., Forodesine has high antitumor activity in chronic lymphocytic leukemia and activates p53-independent mitochondrial apoptosis by induction of p73 and BIM, https://www.ncbi.nlm.nih.gov/pubmed/ 19541822). The invention provides a synergistic effect from the use of a PNP inhibitor (forodesine) together with an anti-CD20 agent (rituximab) which can be demonstrated through the development of a combination index (CI), evaluation of the coefficient interaction for different proportions of cell death. That is, the object of the invention is a pharmaceutical composition with a new combination of previously known active substances, but their synergistic effect from concomitant use is previously unknown in the treatment of leukemia and is not specifically described. However, the scope of patent rights is limited by the mandatory combination of rituximab and forodesine and the scope of use of such a combination - for the treatment of leukemia. Conclusion: there are no grounds to classify the patent as «evergreening».
64	UA 104909 HIGHLY CONCENTRATED PHARMACEUTICAL FORMULATION COMPRISING ANTI-CD20 ANTIBODY / 10.09.2010	Yes	The object of the invention is a pharmaceutical composition comprising rituximab as an active ingredient with an anti-CD20 antibody and known pharmaceutically acceptable substances (buffer, stabilizer, surfactant, glycosaminoglycanase enzyme to increase interstitial space and, accordingly, the volume and therapeutic dose which is safe and which is conveniently administered subcutaneously), as well as the use of such a composition for the treatment of a disease or disorder that can be treated with anti-CD20 antibodies, preferably cancer or non-malignant disease. Patent UA 104909 protects a known pharmaceutical composition with known ingredients which are used in their direct meaning, and differs from the previously known only by dosage, i.e. concentration of ingredients. The applicant also disclosed the effectiveness of the composition for the treatment of the above diseases. Conclusion: there are grounds to classify the patent as «evergreening».

CAPECITABINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
65	UA 39158 DERIVATIVES OF N4-OXYCARBONYL-5'-DEOXY-5-FLUORCYTIDINE AND PHARMACEUTICAL PREPARATION BASED THEREON / 17.12.1993	Нет	The patent was obtained with priority according to the application EP19920121538 from 18.12.1992, which together with the application EP19870116926 from 17.11.1987 protects the chemical compound capecitabine which has not been previously described or obtained. U.S. patents obtained under these applications are listed by the Food and Drug Administration as primary patents that comply with XELODA (Capecitabine). The compound is a prodrug of the known antitumor agent 5-fluorouracil which enzymatically converts to 5-fluorouracil in a tumor and inhibits its growth. That is, the patent UA 39158 describes a new compound that is not known from another application, so the patent UA 39158 does not belong to the category of «evergreening» patents. Conclusion: there are no grounds to classify the patent as «evergreening».

PEMBROLIZUMAB

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
66	UA 118453 MODULATION OF TUMOR IMMUNITY / 18.08.2014	Yes	The object of the invention according to the patent is: - a method of treating a tumor in a patient; - a pharmaceutical combination for this which is based on the use of a combination of two previously known monoclonal antibodies: PD-1 antagonist (MK-3475, Pembrolizumab) and GITR agonist (TRX518 from Leap Therapeutics®, or TRX518 from Tolerx®). Pembrolizumab is protected by earlier patents, for example, US8,168,757B2 from 01.05.2012 or US8,354,509B2 from 15.01.2013. That is, the pharmaceutical composition on which the invention is based on the patent UA 118453, is a new combination of previously known antibodies. Their therapeutic antitumor effect is also known. Conclusion: there are grounds to classify the patent as «evergreening».

BENDAMUSTINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
67	UA 94036 BENDAMUSTINE PHARMACEUTICAL COMPOSITIONS FOR LYOPHILISATION / 13.01.2006	No	The object of the invention according to the patent is a method for the production of a lyophilized preparation of bendamustine, a pre-lyophilization solution or dispersion of bendamustine, a lyophilized powder, a composition for lyophilization, a pre-lyophilized pharmaceutical composition of bendamustine and a lyophilized preparation of bendamustine. The bendamustine compound as an antitumor agent was developed by a company other than SEFALON, INC. (a patent holder of UA 94036). SEFALON is the company that launched bendamustine in the US market under the trademark Treanda in 2008. It is known that bendamustine is obtained in the form of a finished product by lyophilization which provides better stability and long-term storage. Therefore, the patent UA 94036 protects one of the many processes of lyophilization of bendamustine, components of this process and the results of the process in the form of a finished product. However, this method of lyophilization of bendamustine is not the only one, and the patent UA 94036 protects the process that uses SEFALON. Therefore, UA 94036 does not belong to the category of «evergreening» patents, but protects the product of a particular company along with similar products of other companies. Conclusion: there are no grounds to classify the patent as «evergreening».
68	UA 102120 ORAL DOSAGE FORMS OF BENDAMUSTINE / 03.12.2009	No	The object of the invention according to the patent is bendamustine in a specific pharmaceutical composition which is characterized by the structure and qualitative composition of the ingredients. The pharmaceutical composition differs from the previously known use of a pharmaceutically acceptable excipient which is a pharmaceutically acceptable nonionic surfactant selected from the group: macrogol-glycerol hydroxystearate, polyoxyl-35-castor oil and block copolymer of ethylene oxide / propylene oxide (Pluronic® L44 NF or Poloxamer® 124) which allows to obtain an improved dissolution profile. That is, the pharmaceutical composition according to the patent is a new combination of previously known active substances and protects a specific solution for obtaining an improved dissolution profile of bendamustine which is not used by other manufacturers of bendamustine or drugs based on it. Therefore, UA 102120 does not belong to the category of «evergreening» patents, but protects the product of a particular company along with similar products of other companies. Conclusion: there are no grounds to classify the patent as «evergreening».

NILOTINIB

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
69	UA 94234 CRYSTALLINE FORMS OF 4-METHYL-N-[3-(4-METHYL-IMIDAZOL-1-YL)-5-TRIFLUOROMETHYL-PHENYL]-3-(4-PYRIDIN-3-YL-PYRIMIDIN-2-YLAMINO)-BENZAMIDE / 18.07.2006	Yes	The object of the invention according to the patent is an individual chemical compound of nilotinib, characterized by the mutual arrangement of atoms, expressed as parameters of the crystalline forms of the free base, hydrochloride and sulfate of nilotinib. The primary application for the compound nilotinib is application WO2004005281 with priority from 05.07.2002, for which a patent has not been obtained in Ukraine. The crystalline forms according to patent UA 94234 are not described in the application WO2004005281 as specially obtained, but in the description WO2004005281 provides examples of obtaining the compound nilotinib in a crystalline form and specifies the parameters of its production (temperature, pressure and more). The technical result of the invention according to the patent UA 94234 is to obtain crystalline forms of nilotinib for a more active, more stable or cheaper in the manufacture of the drug, however, the patent UA 94234 does not contain evidence of achievement this result compared to other crystalline forms of nilotinib. This indicates that the patent UA 94234 protects the same forms of nilotinib as in the original application WO2004005281, but is characterized by parameters that are not disclosed in the original application. That is, the object of the patent UA 94234 is a polymorphic form of the previously known compound nilotinib which, in particular, is the result of recrystallization of the previously known compound into a more stable polymorph. Conclusion: there are grounds to classify the patent as «evergreening».

TRIPTORELINUM

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
70	UA 99830 SLOW RELEASE PHARMACEUTICAL COMPOSITION MADE OF MICROPARTICLES / 06.06.2008	No	The object of the invention is a pharmaceutical composition made of microparticles for the sustained release of an LHRH agonist. This composition contains a copolymer of lactic and glycolic acids (PLGA) which includes as active ingredient a water-insoluble peptide salt and is disclosed in Swiss patent CH 679207 A5. The technical result of the invention UA 99830 is to provide a long and effective sustained release of the active substance for a period covering at least 6 months after injection of the composition. Therefore, the object of patenting are pharmaceutical compositions based on a known active substance, but with other physicochemical parameters which are achieved through the distribution of microparticles by size.

MELFALAN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
71	UA 107069 ANTICANCER COMBINATIONS CONTAINING MELPHALAN AND ANTIBODY THAT SPECIFICALLY RECOGNIZES THE CD38 / 17.09.2008	Yes	The object of the invention according to the patent is a pharmaceutical combination containing a humanized antibody that specifically recognizes CD38 and melphalan, as well as the use of said antibody for the treatment of neoplastic diseases such as cancer / tumor (lymphoma, myeloma, carcinoma, etc.) due to the ability of the antibody to kill CD38 + cells. This combination is characterized by the amino acid sequences of the light and heavy chains of the humanized antibody. Characterized by such sequences, an antibody that specifically recognizes CD38, as well as its use for the treatment of cancer / tumors, in particular together with melphalan or vincristine, is known from documents EP1914242 (SANOFI (FR)), WO2006099875, WO9962526. That is, SANOFI obtained patent EP1914242 (similar in Ukraine - UA114879) with an earlier filing date (16.10.2007) which fully describes the pharmaceutical combination according to patent UA 107069. Advantages of using this antibody and melphalan in the form of a pharmaceutical combination, i.e. co-administration instead of use in the form of a composition of antibodies and melphalan, as described in the earlier patent SANOFI, not confirmed by the description of the patent UA 107069. Melphalan (Melphalan, Sarcolysin) is a known synthetic drug since 1964. The pharmaceutical combination according to the patent UA 107069 is a new combination of previously known active substances without specifying a new technical result. Conclusion: there is reason to attribute this patent to the «evergreening».

CASPOFUNGIN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
72	UA 55409 PHARMACEUTICAL COMPOSITION FOR INTRAVENOUS ADMINISTRATION, METHOD FOR ITS MANUFACTURE AND METHOD FOR TREATING OR/ AND PREVENTING MYCOSIS (VARIANTS) / 15.04.1997	No	The objects of the invention are: - a pharmaceutical composition based on caspofungin; - a method of treating and / or preventing fungal infections of mammals using the above composition; - a method of obtaining a pharmaceutical composition based on caspofungin. The technical result of the invention UA 55409 are compositions in the form of safe, stable, lyophilized dosage forms for conversion, which are particularly useful for delivering antifungal agents to patients in need thereof. Such compositions are characterized by greater stability, contain fewer unwanted degradation products with extended expiration date. Caspofungin is described in US patent No. 5 378 804. Alternative methods for its preparation are disclosed in US patents No. 5 378 804 and No. 5 552 521 Therefore, the subject of patenting are pharmaceutical compositions based on a known active substance, but with other physicochemical parameters, methods of application of such compositions and creation.

EVEROLIMUS

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
73	UA 110961 COMBINATION COMPRISING PHOSPHATIDYLINOSITOL-3-KINASE (PI3K) INHIBITOR AND mTOR INHIBITOR / 23.04.2012	No	The object of the invention according to the patent is the use of a pharmaceutical combination of known active compounds of NOVARTIS ©: alpelisib (disclosed in the publication WO 2010/029082) and mTOR inhibitor (everolimus) for the treatment of cancer and a method of treating cancer. The description contains data on the synergistic effect of the use of a combination of these compounds which is to improve the therapeutic effect compared to monotherapy of each of these compounds. The improvement is the interaction of these compounds and better inhibition of cell proliferation which makes it possible to reduce the required dose of each compound and leads to a reduction in side effects and increase the long-term clinical efficacy of the compounds in treatment. The patent does not limit the use of each of these active compounds, including monotherapy with everolimus. Conclusion: there are no grounds to classify the patent as «evergreening».
74	UA 118025 ANDROGEN RECEPTOR MODULATOR AND USES THEREOF / 09.01.2014	No	The object of the invention according to the patent are methods of treating prostate cancer of various types, in particular, resistant to castration (CRPC) by oral administration of a pharmaceutical combination of known active compounds or their salts: anti-androgen agent that exhibits antagonistic activity against polypeptide type Apalutamide (Erleada ©), and a phosphoinositide-3-kinase inhibitor (PI3K), a TORC inhibitor, or a dual PI3K / TORC inhibitor (https://en.wikipedia.org/wiki/Apalutamide). Everolimus is one of many variants of the TORC inhibitor. The description of the invention contains data on the synergistic effect of using a combination of these compounds (tables 4, 5 of the description), which is to improve the pharmacokinetic properties of the compounds which leads to improved treatment outcomes across the spectrum of CRPC (castration-resistant prostate cancer). The patent also does not limit the use of each of these active compounds, including monotherapy with everolimus Conclusion: there are no grounds to classify the patent as «evergreening».

/DRUGS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

ADALIMUMAB

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
75	UA 82823 METHOD OF ACTIVITY INHIBITION OF TNFa OF A HUMAN, USE OF ISOLATED HUMAN ANTIBODY IN THE MANUFACTURE OF DRUGS FOR THE TREATMENT OF THE DISORDER IN WHICH TNFa ACTIVITY IS DETRIMENTAL, ISOLATED ANTIBODY WHICH SPECIFICALLY BINDS TO TNFa, AND A PHARMACEUTICAL COMPOSITION CONTAINING IT / 30.09.2002	No	The object of the invention according to the patent are isolated human monoclonal antibodies D2E7 (immunoglobulin molecules) or their antigen-binding parts (antibody fragments) which bind to human TNFa with an affinity that is higher than known from the prior art (dissociate with human TNFa cytokines with an association rate constant Koff = 1x10-3c-1 or less). Nucleic acid sequences, recombinant expression vectors and host cells have been claimed to identify antibodies and fragments thereof. A method of preparing antibodies or antigen-binding portions thereof by recombinant expression of immunoglobulin light and heavy chain genes in a host cell, as well as methods for selecting recombinant human antibodies (screening), are described. The defined pharmaceutical compositions are also suitable for administration to a subject, considering combinations with other therapeutic agents. The use of antibodies and their parts for the treatment of diseases and disorders, in which the activity of TNFa is detrimental, is described. The results of kinetic analysis of human antibody binding to hTNFa (Tables 1–5), neutralization of cytotoxicity caused by hTNFa (Tables 7, 8), confirmation of inhibition of TNFa activity in animals, including primates (Tables 9–16). The claimed antibodies and parts thereof have not been previously described, the confirmation of the claimed inhibition of TNFα activity is provided: this is a primary patent that protects the adalimumab molecule with the D2E7 antibody. Conclusion: there are no grounds to classify the patent as «evergreening».
76	UA 99716 ANTIBODY THAT SPECIFICALLY BINDS TO HUMAN IL-17 RECEPTOR A (IL-17RA) / 01.10.2007	No	The object of the invention relates to antigen-binding proteins that inhibit the cytokines IL-17RA which can be used in combination with TNF inhibitors. The known synergistic effect of IL-17 and TNF for modulating the expression of cytokines in the suppression of melanogenesis as a potential cause of psoriasis (Claire Q.F. Wang et al, IL-17 and TNF synergistically modulate cytokine expression while suppressing melanogenesis: potential relevance to psoriasis, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3830693/). Patent UA 99716 protects a molecule of a substance with the specified antibody, a method of its use for treatment and pharmaceutical preparations based on it, by means of which the increase of effectiveness of treatment of the patients, for whom TNF-inhibitory therapy was powerless, is achieved. The invention also contains confirmation of an additional positive effect from the combination with TNF inhibitors. Patent UA 99716 does not relate directly to adalimumab, but relates to a molecule of a substance with an antibody that has a similar mechanism of action and can be used with adalimumab. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
77	UA 102503 INTERLEUKIN-13 BINDING PROTEINS / 07.09.2007	No	The object of the invention according to the patent are: recombinantly engineered antibodies (proteins) against the glycoprotein IL-13 with improved affinity and neutralization of IL-13 and their use for the prevention and / or treatment of various diseases, including asthma, allergies, chronic obstructive pulmonary disease, fibrosis and cancer. Preparations based on such proteins provide a combination of therapeutic agents, among which are TNF antagonists, such as chimeric, humanized antibodies or human TNF antibodies, in particular D2E7 (Adalimumab). There is a synergistic effect of IL-13 on increasing the expression of TNFa (adalimumab - TNFa antagonist), which is a key factor in the development of the above diseases. That is, the blockade of IL-13 affects the expression of TNFα (Luttmann W1, Matthiesen T, Matthys H, Virchow JC Jr. Synergistic effects of interleukin-4 or interleukin-13 and tumor necrosis factor-alpha on eosinophil activation in vitro, https: // www.ncbi.nlm.nih.gov/pubmed/10030846). Patent UA 102503 does not relate directly to adalimumab, but relates to a molecule of a substance that can be used with adalimumab to enhance the action. Conclusion: there are no grounds to classify the patent as «evergreening».
78	UA 111340 ANTIBODY THAT BINDS SPECIFICALLY TO HUMAN TNF-ALFA / 24.10.2011	No	The object of the invention according to the patent are soluble antibodies-antagonists of TNFα or their antigen-binding fragments, or their single chain. Antibodies are optimized for stability, solubility, in vitro and in vivo binding to TNFα and low immunogenicity. These antibodies are intended for the diagnosis and / or treatment of TNFα-mediated disorders. Another advantage is that the antibodies contain at least one mutation that reduces their aggregation. Antibodies with similar activity against TNFα and a structure comprising CDRs from rabbit antibodies are known from earlier applications of ESBATEK, in particular, WO 2006/131013, WO 2009/155723. The difference is the substitution of lysine with arginine (R) at position 47 and / or at position 50 according to the AHo numbering system of the light chain variable domain, which leads to a decrease in the tendency to aggregation of the modified antibody compared to that of the original antibody. This is known from the prior art and in some way disclosed in the examples of published application WO 2009155723. That is, patent UA 111340 protects a molecule of a compound that contains a substitution made according to known rules with the achievement of a known effect. This may be the reason for challenging the patentability of the present invention, but does not indicate the possibility of classifying the patent as «evergreening», because it represents an improved structure of antibodies-antagonists of TNFα for the treatment of TNFα-mediated disorders and does not apply to antibodies with a similar effect and the presence of lysine instead of arginine. Conclusion: there are no grounds to classify the patent as «evergreening».

TOCILIZUMAB

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
79	UA 80091 REMEDIES FOR INFANT CHRONIC ARTHRITIS-RELATING DISEASES AND STILL'S DISEASE WHICH CONTAIN AN INTERLEUKIN-6 (IL-6) ANTAGONIST / 02.04.2002	Yes	The object of the invention according to the patent is an object of genetic engineering, namely the use of antibodies against the interleukin-6 receptor (IL-6R) or antibodies against interleukin-6 (IL-6) for the production of a therapeutic agent (tocilizumab) for the treatment of chronic children arthritic diseases. Antibodies to the interleukin-6 receptor (IL-6R) and antibodies to interleukin-6 (IL-6) as a treatment for chronic rheumatoid arthritis are known from application PCT95 / 01144 of 07.06.1995. The efficacy of tocilizumab in juvenile rheumatoid arthritis or Still's disease in children has not been specifically identified in PCT95 / 01144, but such use is obvious to those skilled in the art from this field of medicine due to the fact that these diseases are caused by excessive production of interleukin-6, and for their treatment, the use of interleukin-6 antagonists is required. The description of the patent states that antibodies to the IL-6 receptor can be obtained by the method specified in the application PCT95 / 01144. That is, the invention according to the patent UA 80091 uses a previously known therapeutic agent. Conclusion: there are grounds to classify the patent as «evergreening».
80	UA 86587 TREATMENT OF RHEUMATOID ARTHRITIS USING AN ANTIBODY TO AN INTCRLEUKIN-6 RECEPTOR AND METHOTREXATE / 08.04.2004	Yes	The object of the invention is a pharmaceutical composition for the treatment of rheumatoid arthritis, comprising an antibody against the IL-6 receptor (antibody to IL-6R), i.e. tocilizumab, and Methotrexate (MTX), the use of antibodies to IL-6R and MTX for the production of pharmaceutical compositions for treating rheumatoid arthritis and method of treating rheumatoid arthritis. Methotrexate is known as a basic anti-inflammatory drug (immunosuppressant) in the treatment of rheumatoid arthritis. The synergistic effect of its combination with tocilizumab, which is essentially an achievement of the invention, is indicated as the alleviation or prevention of allergic reactions in the treatment of rheumatoid arthritis with antibodies to IL-6R. However, the description of the invention does not confirm this effect. That is, the invention protects a combination of previously known individual compounds, the therapeutic effect of which is confirmed and the improvement of the therapeutic effect from their combination is not confirmed. Conclusion: there are grounds to attribute the patent to «evergreening»
81	UA 85995 CHIMERIC ANTIBODY THAT SPECIFICALLY BINDS HUMAN IL-6, PHARMACEUTICAL COMPOSITION CONTAINING THEREOF / 26.10.2002	No	The object of the invention according to the patent is a chimeric antibody or its fragment that specifically binds to human IL-6 with high binding affinity, an isolated nucleic acid molecule encoding a chimeric antibody or its fragment, a composition, an expression vector and a host cell containing an isolated nucleic acid molecule according to claim 6, an expression vector containing a nucleic acid molecule, a host cell containing an isolated nucleic acid molecule, a method of producing an antibody or fragment thereof, a pharmaceutical composition comprising the antibody or fragment thereof and its use in the manufacture of a medicament, a medicament and a pharmaceutical composition comprising the antibody or a fragment thereof and a carrier, a product containing one container with the antibody or fragment thereof and a manufacturing product comprising a packaging material and container with antibody. Tocilizumab is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R) which binds to both soluble and membrane-bound IL-6R. The object of the invention according to the patent UA 85995 is a chimeric antibody or a fragment thereof which specifically binds to human IL-6. The patent protects Siltuximab (CNTO 328, Sylvant), which is also an IL-6 inhibitor, but with a different mechanism of action and construction. Therefore, patent 3 protects another drug. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
82	UA 97231 ISOLATED ANTIBODY THAT SPECIFICALLY BINDS TO IL-6, COMPOSITION COMPRISING THEREOF AND USES / 28.04.2006	No	The object of the invention according to the patent is an isolated antibody that specifically binds to IL-6, as well as an isolated nucleic and an acid molecule vector, a host cell comprising an isolated nucleic acid molecule, a method of producing an antibody, a composition comprising an antibody, an anti-idiotypic antibody or a fragment that specifically binds to at least one antibody, a method of diagnosing and treating an IL-6-related condition, a medical device containing the antibody, and an industrial product with a solution or lyophilized IL-6 antibody. The patent is based on isolated, human-made antibodies to IL-6 antagonists. These antibodies are a product of CENTOCOR, INC. called Iinfliximab (REMICADE®) and advanced by APPLIED MOLECULAR EVOLUTION, INC. using AMEsystem technology to reduce the immunogenicity potential to improve human tolerability and increase the activity for reduction of doses compared to antibodies before the improvement. Therefore, the patent protects another drug. Conclusion: there are no grounds to classify the patent as «evergreening».
83	UA 96141 NEUTRALISING ANTIBODY HAVING SPECIFICITY FOR HUMAN IL-6 / 04.12.2006	No	The invention relates to a humanized neutralizing antibody having specificity for human IL-6, a separate DNA sequence encoding the heavy and / or light chains of such an antibody, a host cell, an antibody manufacturing process and a pharmaceutical composition comprising the antibody. The neutralizing antibody is characterized by heavy and / or light chain sequences or functional parameters. The action of the humanized monoclonal antibody according to the invention is aimed at the cytokine interleukin-6 (IL-6), in contrast to tocilizumab which acts on the IL-6 receptor. The drug UCB PHARMA S.A., such as Olokizumab (OKZ, CDP6038), has an effect particularly on the cytokine interleukin-6. Therefore, the patent protects another drug. Conclusion: there are no grounds to classify the patent as «evergreening».
84	UA 97645 ANTIBODY WHICH BINDS HUMAN IL-6 RECEPTOR / 01.06.2007	No	The object of the invention according to the patent is an antibody or its antigen-binding fragment, which specifically binds to the human interleukin-6 receptor (hIL-6R), an isolated nucleic acid molecule encoding an antibody or its antigen-binding fragment, a vector for antibody expression or antigen-binding fragment thereof, a «host-vector» system for producing an antibody or antigen-binding fragment thereof, a method for producing an antibody to hIL-6R or an antigen-binding fragment thereof, the use of an antibody or its antigen-binding fragment antibody fragment in the manufacture of the drug. Antibodies or antigen-binding fragments thereof as the main objects of the invention are characterized by sequences represented by the domains of the heavy chain and light chain. REGENERON (a patent holder) in collaboration with Sanofi is the developer of Sarilumab, which is a fully human monoclonal antibody to IL-6R and is generated with the use of Velocimmune technology (developed by REGENERON). According to the invention according to the patent, the new antibodies are also obtained mainly while using Velocimmune technology which indicates that the patent belongs to the drug Sarilumab which is a competitor of tocilizumab. Sarilumab is thought to be covered by patents for tocilizumab, but REGENERON claims there is a difference. Therefore, the patent protects another drug. Conclusion: there are no grounds to classify the patent as «evergreening».

FLURBIPROFEN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
85	UA 83531 PHARMACEUTICAL ORAL DOSAGE FORM CONTAINING NON-STEROID ANTI-INFLAMMATORY DRUG AND POSSESSING A GOOD TASTE / 16.12.2004	Yes	The patent protects a composition of tromethamine and a non-steroidal anti-inflammatory drug (NSAID), which is flurbiprofen as one of the representatives and a compound selected from glycine, vitamin B6 or a mixture thereof. The advantage of the composition according to the invention is better tolerability of NSAIDs and taste appeal. The invention has no advantages in increasing the therapeutic effect. That is, the invention describes a new combination of previously known active substances without a new biological effect. Conclusion: there are grounds to classify the patent as «evergreening».
86	UA 89656 ORALLY DISPERSIBLE PHARMACEUTICAL COMPOSITION AND PROCESS FOR THE PREPARATION THEREOF / 25.11.2005	Yes	The patent protects: - a method of preparing a solid dosage form dispersible orally; - a solid dosage form in which the active ingredient is included in a matrix containing at least one hydrophilic natural polymer with a high molecular weight. The active ingredient is selected from the group consisting of ibuprofen, naproxen and flurbiprofen. The advantage of the invention is the masking of taste or the release of the above active ingredients with an unpleasant taste. The advantage is achieved by using an additional inactive component, a hydrophilic natural polymer with a high molecular weight. The invention has no advantages in increasing the therapeutic effect. That is, the invention describes a solid dosage form of previously known active substances without a new biological effect and a method for its preparation. Conclusion: there are grounds to classify the patent as «evergreening».
87	UA 104159 CONTROLLED RELEASE ORAL FORMULATION AND PROCESS FOR ITS PREPARATION / 08.01.2010	Yes	The patent protects: - a controlled release pharmaceutical or food composition comprising an active pharmaceutical or food ingredient dispersed in a mixture of glycogen and polysaccharide; - a method of obtaining such a composition; - a slow release system represented by a mixture of glycogen and polysaccharide, - the use of such a system for the manufacture of pharmaceutical or food compositions of slow release. The active ingredient is among many other flurbiprofen. The advantage of the invention is the ability of the composition to release the active ingredient with release kinetics of almost zero order, i.e. is constant over time and does not depend on concentration. This advantage is achieved by using certain known formers. The invention has no advantages in increasing the therapeutic effect. That is, the invention describes a composition of previously known active substances without a new biological effect. Conclusion: there are grounds to classify the patent as «evergreening».
88	UA 117200 ORAL TOPICAL AQUEOUS PHARMACEUTICAL COMPOSITIONS OF FLURBIPROFEN AND DEXPANTHENOL / 24.12.2015	Yes	The patent protects a composition of flurbiprofen and dexpanthenol or in addition with chlorhexidine for topical application in the oral cavity. The advantage of the invention is to ensure optimal delivery of these components through the surface of the oral mucosa by providing the desired level of solubility, improved taste and improved absorption from the surface of the mucous membrane. The advantage is achieved by using sodium hydroxide in the specified composition to bring the pH of the solution to a value of from 6 to 7. The invention has no advantages in increasing the therapeutic effect. That is, the invention describes a composition of previously known active substances without a new biological effect, for example, from a combination of two or more active substances. Conclusion: there are grounds to classify the patent as «evergreening».

ETANERCEPT

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
89	UA 113172 STABLE LIQUID FORMULATION OF ETANERCEPT / 01.06.2012	No	The patent protects a liquid composition of etanercept with a stabilizer (methionine and lysine) which has increased stability. Etanercept is known as a biological modulator of inflammation, in particular with US5447851A (Immunex Corp), as well as its biological analogues, such as Sandoz, are known. That is, the invention describes a pharmaceutical composition that contains a combination of previously known substances, one of which is active. However, the description of the invention contains confirmation that methionine and lysine significantly affect the stabilization of etanercept by reducing the total content of impurities compared to free from the stabilizer drug. The invention does not block the use of other known drugs based on etanercept, for example, Enbrel® which does not contain these stabilizers and the like. Conclusion: there are no grounds to classify the patent as «evergreening».

/DRUGS FOR THE TREATMENT OF OTHER DISEASES

AGOMELATINE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
90	UA 78825 METHOD FOR AGOMELATINE SYNTHESIS, CRYSTALLINE FORM OF AGOMELATINE, AND PHARMACEUTICAL COMPOSITION / 11.02.2005	Yes	The objects of the invention are: - method of industrial synthesis of agomelatine; - crystalline II form of agomelatine; - a pharmaceutical composition containing as active ingredient crystalline form II of agomelatine. Thus, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic use have been disclosed in the Description of European patent application EP 0 447 285 and Yous et al. Journal of Medicinal Chemistry, 1992, 35 (8), 1484-1486], the crystalline form described in Tinant et al. Acta Cryst., 1994, C50, 907-910. The description of the invention states that the new crystalline form exhibits valuable filtering properties and ease of formulation. The description does not confirm this thesis. As well as confirmation of qualitative and quantitative changes in pharmaceutical properties.
91	UA 83719 NEW CRYSTALLINE FORM III OF AGOMELATINE, A PROCESS FOR ITS PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING IT / 02.08.2006	Yes	The objects of the invention are: - a crystalline form of III agomelatine; - a method of industrial synthesis of a crystalline form of III agomelatine; - a pharmaceutical composition containing as active ingredient crystalline form of III agomelatine. Therefore, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic use have been disclosed in the Description of European Patent Application EP 0 447 285. The description of the invention states that the pharmacological study of crystalline form III has shown that it has significant activity against the central nervous system and against the microcirculation. The description does not contain confirmation of this thesis in the context of qualitative and quantitative changes in pharmaceutical properties compared to other known crystalline forms of agomelatine.
92	UA 83718 NEW CRYSTALLINE FORM IV OF AGOMELATINE, A PROCESS FOR ITS PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING IT / 02.08.2006	Yes	The objects of the invention are: - a crystalline form of IV agomelatine; - a method of industrial synthesis of a crystalline form of IV agomelatine; - a pharmaceutical composition containing as an active ingredient a crystalline form of IV agomelatine. Therefore, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic use have been disclosed in the Description of European patent application EP 0 447 285. The description of the invention states that a pharmacological study of crystalline form IV has shown that it has significant activity against the central nervous system and against microcirculation. The description does not contain confirmation of this thesis in the context of qualitative and quantitative changes in pharmaceutical properties compared to other known crystalline forms of agomelatine.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
93	UA 83720 NEW CYRSTALLINE FORM V OF AGOMELATINE, A PROCESS FOR ITS PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING IT / 02.08.2006	Yes	The objects of the invention are: - a crystalline form V of agomelatine; - a method of industrial synthesis of crystalline form V of agomelatine; - a pharmaceutical composition containing as active ingredient crystalline form V of agomelatine. Therefore, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic use have been disclosed in the Description of European patent application EP 0 447 285. In the description of the invention, it is stated that the pharmacological study of crystalline form V showed that it has significant activity against the central nervous system and microcirculation. The description does not contain confirmation of this thesis in the context of qualitative and quantitative changes in the pharmaceutical properties compared to other known crystalline forms of agomelatine.
94	UA 97478 CRYSTALLINE FORM VI OF AGOMELATINE, A PROCESS FOR ITS PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING IT / 04.11.2008	Yes	The objects of the invention are: - a crystalline form VI of agomelatine; - a method of industrial synthesis of crystalline form VI of agomelatine; - a pharmaceutical composition containing as an active ingredient crystalline form VI of agomelatine. Therefore, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic application have been disclosed in the Description of European patent application EP 0 447 285. In the description of the invention it is stated that the pharmacological study of crystalline form VI showed that it has significant activity against the central nervous system and in relation to microcirculation. The description does not contain confirmation of this thesis in the context of qualitative and quantitative changes in the pharmaceutical properties compared to other known crystalline forms of agomelatine.
95	UA 100476 CRYSTALLINE FORM VI OF AGOMELATINE, PREPARATION METHOD AND USE THEREOF / 09.03.2010	Yes	The objects of the invention are: - a crystalline form VI of agomelatine; - a method of obtaining crystalline form VI of agomelatine; - a pharmaceutical composition containing as an active ingredient crystalline form VI of agomelatine. Therefore, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic use have been disclosed in the Description of European patent application EP 0 447 285. Patents PRC CN2005100716116, CN200610108396.7, CN200610108394.8 and CN200610108395.2 respectively disclose crystalline forms II, III, IV, V of agomelatine and methods for their preparation. In the description of the invention, it is stated that the crystalline form VI of agomelatine exhibits valuable characteristics for pharmaceutical compositions. At the same time, the examples given in the description indicate that the purity of crystalline form VI of agomelatine before the experiment is lower compared to other known crystalline forms of this compound, and after - is at the level of a similar indicator for a crystalline form IV of agomelatine. The situation is similar with regard to the results of the study on solubility in water. The pharmacological study of crystalline form VI of agomelatine according to this invention showed that a crystalline form VI of agomelatine can be used in the treatment of diseases of the melatoninergic system, sleep disorders, stress, anxiety, seasonal affective disorder or major depression, cardiovascular disease, digestive diseases fatigue due to circadian arrhythmias, schizophrenia, phobias, depression and the like. The description does not contain confirmation of qualitative and quantitative changes in the pharmaceutical properties compared to other known crystalline forms of agomelatine. Therefore, a crystalline form VI of agomelatine is a less stable and stable polymorph of known forms of agomelatine.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
96	UA 113058 NEW CRYSTAL FORM VII OF AGOMELATINE, PREPARATION METHOD AND USE THEREOF AND PHARMACEUTICAL COMPOSITION CONTAINING SAME / 22.03.2012	Так	The objects of the invention are: - a method of obtaining a new crystalline form VII of agomelatine; - a new crystalline form VII of agomelatine; - a pharmaceutical composition containing as active ingredient a new crystalline form VII of agomelatine. Therefore, the object of patenting is a polymorphic form of agomelatine and a pharmaceutical composition based on it. Agomelatine is a known compound, its preparation and therapeutic use have been disclosed in the Description of European patent application EP 0 447 285. Patents PRC CN200510071611.6, CN200610108396.7, CN200610108394.8 and CN200610108395.2, CN200910047329.2, CN200910245029.5, respectively, disclose various crystalline forms of agomelatine and methods for their preparation. The description of the invention states that the crystalline form VII of agomelatine exhibits valuable properties for pharmaceutical compositions. The examples given in the description indicate that the purity of crystalline form VII of agomelatine before and after the experiment is higher by at least 0.1% compared to other known crystalline forms of this compound. The solubility in water is within the solubility of other known crystalline forms of agomelatine. The pharmacological study of crystalline form VII of agomelatine according to the present invention showed that crystalline form VII of agomelatine can be used to treat diseases of the melatoninergic system, sleep disorders, stress, anxiety, seasonal affective disorder, major depression, cardiovascular disease, digestive diseases, fatigue caused by changing time zones, schizophrenia, phobias and depression. The description does not contain confirmation of qualitative and quantitative changes in the pharmaceutical properties compared to other known crystalline forms of agomelatine.

RIVAROXABAN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
97	UA 73339 SUBSTITUTED OXAZOLIDINONES AND USE THEREOF FOR THE PREVENTION OF BLOOD COAGULATION / 11.12.2000	No	The object of the invention according to the patent are individual chemical compounds (derivatives of 2-oxazolidone which are direct inhibitors of factor Xa (activator of thrombin formation), a method for their preparation, a drug containing these individual chemical compounds, their use for treatment and / or prevention of thromboembolic diseases and a method of preventing blood coagulation in vitro in canned blood or biological samples by means of these individual chemical compounds. Individual chemical compounds are characterized by the general chemical structural formula falling within the general Markush claim of the previously submitted application (WO1999 / 31092, MERCK PATENT GMBH (DE). Individual chemical compounds according to claims 1–7 of the formula differ from the compounds in WO1999 / 31092 by the same type of substituent within one group (group NR8 is replaced by a piperazine ring). However, individual chemical compounds according to claims 1–7 of the formula have not previously been described as specially derived. Also, the technical result - increasing the selectivity of inhibition of blood coagulation factor Xa - is different from WO1999 / 31092. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
98	UA 82986 COMBINATION OF ACTIVE SUBSTANCES, PROCESS FOR THE PREPARATION OF THE COMBINATION, MEDICINAL AGENT AND USE OF THE COMBINATION / 07.06.2002	Yes	The object of the invention according to the patent is a combination of previously known active substances: compounds (A) - oxazolidinones of formula (I) (rivaroxaban described in patent application UA 73339 (1st line of the table), and compounds (B) selected from the group : platelet aggregation inhibitors, anticoagulants, fibrinolytics, lipid-lowering substances, a drug for the treatment of coronary heart disease and / or vasodilators, and a method of preparing such a combination, a drug for the prevention and / or treatment of thromboembolic diseases containing such a combination and the use of a combination for the preparation of a drug. The unexpected effect of the combination compared to the effect of individual compounds is due to the antithrombotic effect of rivaroxaban and the reduction of the risk of thrombus recurrence. That is, the direct administration of rivaroxaban, which is already known in the art, helps other active compounds (B) to act more effectively after opening blood vessels blocked by thrombosis and reducing the dose of compounds (B) to achieve the desired effect. Conclusion: there are grounds to classify the patent as «evergreening».
99	UA 84591 PROCESS FOR THE PREPARATION OF 5-CHLORO-N-({(5S)-2-OXO-3-[4-(3-OXO-4-MORPHOLINYL)-PHENYL]-1,3-OXAZOLIDINE-5-YL}-METHYL)-2-THIOPHENE CARBOXAMIDE / 31.12.2004	No	The object of the invention according to the patent is a method for producing oxazolidinones of formula (I) (rivaroxaban). This method is an improvement of the method described in claim 15 of the patent UA 73339. The improvement is a simplified method of obtaining compound (I) suitable for industrial use, avoiding the use of toxic solvents or reagents, especially in the last stages of the method by eliminating side effects components due to the use of amino-methyl-oxazolidinone (VII) in a form other than in patent UA 73339. Conclusion: there are no grounds to classify the patent as «evergreening».
100	UA 85693 SOLID ORALLY APPLICABLE PHARMACEUTICAL COMPOSITION, ITS MANUFACTURE AND USE / 13.11.2004	No	The object of the invention according to the patent is a method of obtaining oxazolidinones of formula (I) (rivaroxaban) using the active substance (I) in a hydrophilized form for rapid release, a pharmaceutical composition with rivaroxaban in a hydrophilized form, the use of such a pharmaceutical composition for the prevention and / or treatment of thromboembolism diseases. The preparation of the granulate with the active substance (I) in the hydrophilized form by wetting granulation followed by its conversion into a pharmaceutical composition is not specifically described in UA 73339 and UA 84591 on the method of obtaining the active substance. The problem solved by the invention according to the patent, namely to improve the oral bioavailability of the active substance (I) and increase the biological stability of the rate of absorption of the substance, is also not known. Other objects of the invention obtained by this method are not specifically described and are not known. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
101	UA 90545 SOLID ORALLY ADMINISTERABLE PHARMACEUTICAL DOSAGE FORMS WITH RAPID RELEASE OF INHIBITOR OF COAGULATION FACTOR XA / 21.09.2006	Yes	The object of the invention according to the patent is a solid pharmaceutical dosage form for oral administration with rapid release of the active substance – oxazolidinones of the formula (I) (rivaroxaban) - in amorphous form or in thermodynamically metastable crystalline modification, claims 1–14 of the formula. The pharmaceutical composition is a polymorphic form of a previously known composition, the characteristics of which are expressed through a new form of application of the active substance – an amorphous form or a thermodynamically metastable crystalline modification, which leads to the release of 80% of active substance (I) in less than 2 hours according to the method of release according to the US Pharmacopoeia which is faster compared to the use of the active substance (I) in hydrophilized form (patent UA 90545, 4th row of the table). These forms of the previously known composition are generally known from the application for which the patent UA 73339 was obtained. The patent does not contain data on the faster release of the active substance (I) compared to the invention UA 73339. Conclusion: there are grounds to classify the patent as «evergreening».
102	UA 91355 PREVENTION AND TREATMENT OF THROMBOEMBOLIC DISORDERS / 19.01.2006	Yes	The object of the invention according to the patent is a method of treating thromboembolic disorder using rivaroxaban in the form of a rapid-release tablet of various dosages, claims 1–3 of the formula. In addition, a characteristic of the method is the tablet regimen which increases the safety of rivaroxaban by achieving its effective target concentration in the patient's blood plasma by reducing the dose. The scheme of reception is known. The pharmaceutical composition differs from the previously known composition only in dosage. Conclusion: there are grounds to classify the patent as «evergreening».
103	UA 94428 POLYMORPHOUS FORM AND THE AMORPHOUS FORM OF 5-CHLORO-N-({(5S)-2-OXO-3-[4-(3-OXO-4-MORPHOLINYL)-PHENYL]-1,3-OXAZOLIDINE-5-YL}-METHYL)-2-THIOPHENE CARBOXAMIDE / 22.09.2006	Yes	The object of the invention according to the patent is a chemical compound of formula (I) - rivaroxaban - in modification II in crystalline or amorphous form characterized by signals in the near IR region. The advantage of modifying compound II is to increase the solubility and bioavailability of the compound. Modification II in crystalline form is obtained by recrystallization of modification I obtained by the method known from Patent 1. The chemical compound according to the patent is a polymorphic form (crystalline form of modification II) of a previously known compound (modification I) having high purity. Signals in the near IR region, which are the main distinguishing parameter for the object of the invention, are determined by conventional basic methods and do not affect the therapeutic effect of the compound. The modification II has the same therapeutic effect compared to modification I (in the description of the invention there is no information about improving the therapeutic effect). Conclusion: there are grounds to classify the patent as «evergreening».

IMIGLUCERASE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
104	UA 113840 PERSONALIZED PRODUCTION OF BIOLOGICS AND METHOD FOR REPROGRAMMING SOMATIC CELLS / 03.01.2012	No	The object of the invention is a method for producing an isolated therapeutic recombinant biological polypeptide or protein for the treatment of a disease. The technical result of the invention UA 113840 is a method of obtaining polypeptide and protein products having reduced levels of antigenicity in animals to be treated with this biological product. Therefore, the object of the patent is a method for producing a therapeutic recombinant biological polypeptide or protein for the treatment of a disease which does not impose restrictions on such compounds obtained by another method.

DYDROGESTERONE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
105	UA 75371 DELAYED RELEASE PHARMACEUTICAL COMPOSITION AND METHOD FOR ITS PREPARATION / 28.09.2001	No	The objects of the invention are a pharmaceutical composition with delayed release, the active substance of which may be chemical compounds of various pharmaceutical action, including dydrogesterone; a method of obtaining such compositions. The technical result of the invention UA 75371 is to create a composition of slow action, which is in fact independent of the ionic strength of the solvent medium which is usually a gastrointestinal fluid, even in the absence of coating. Therefore, the object of patenting is a composition that differs from the previously known compositions by the presence of a hydrophilic gelling matrix, due to which the claimed technical result is achieved - slow release of the active substance.

ERTAPENEM

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
106	UA 62920 CARBAPENEME ANTIBIOTIC, A COMPOSITION AND A METHOD FOR THE PREPARATION / 23.05.1997	No	The objects of the invention are, in particular: - carbapenem compound; (II) - a composition based on the above compound. Compound (II) specified in the claims can be synthesized according to the method described in US Patent. No. 5478820 and falls within the general structural Markush claim set forth in the claims of this patent. However, compound (II) was not known to be specially prepared and tested. That is, there is a selective invention. The pharmaceutical composition based on compound (II) and the quantitative characteristics of its properties as an antibiotic were not known from the prior art.

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
107	UA 78524 A PROCESS FOR PREPARATION OF CARBAPENEM COMPOUNDS / 20.09.2002	Yes	The objects of the invention are: - a method of purification of carbapenem compounds from organic solvents; - a method of obtaining crystal hydrate forms of carbapenem compounds. The carbapenem compound described in claims UA 78524 as having crystal hydrate forms A, B, C, in the form of a racemic mixture is known from patent UA 62920. In both cases, the compounds have antibiotic properties. Therefore, the object of the patent is the isomeric and crystal hydrate form of the known compound.

LENOGRASTIM

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
108	UA 89364 GRANULOCYTE COLONY STIMULATING FACTOR PEPTIDE CONJUGATE (G-CSF) / 03.12.2004	No	The objects of the invention are new glycopegylated peptides of G-CSF and methods for their highly efficient and industrial synthesis. The present invention was directed to a glycopegylated G-CSF that is therapeutically active and has improved pharmacokinetic parameters and properties compared to identical or closely related analogs of the non-glycopegylated G-CSF peptide.
109	UA 98001 LIQUID FORMULATION OF G-CSF CONJUGATE / 27.08.2008	No	The object of the invention is an aqueous composition containing a polymer-G-CSF conjugate. The problem underlying the present invention is to provide a polymer-GCSF-conjugate composition intended for such conjugates, which would be stable at elevated temperatures, i.e. above the temperature of the refrigerator, which is usually in the range from 2 to 8 ° C. Additionally, the object of the present invention is to provide a pharmaceutical composition which does not require reconstitution at any of the manufacturing stages and which causes as little irritation as possible when administered to a patient. Therefore, the invention according to the patent UA 98001 actually protects a new aqueous composition containing a conjugate of polymer-G-CSF with new properties.
110	UA 99454 METHODS OF TREATMENT USING GLYCOPEGYLATED G-CSF / 01.04.2008	No	The objects of the invention are: - a method of treatment using glycopegylated G-CSF; - a dosage form for oral administration based on covalent conjugate of peptide G-CSF and water-soluble polymer. The present invention provides improved glycopegylated G-CSF which has therapeutic activity, as well as improved pharmacokinetic parameters and properties compared to non-glycopegylated identical peptide G-CSF or its close analogue. Therefore, one of the objects of patenting the invention UA 74797 are dosage forms based on improved glycopegylated G-CSF.

TENECTEPLASE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
111	UA 97486 USE OF TENECTEPLASE FOR TREATING ACUTE ISCHEMIC STROKE / 01.08.2007	Yes	The patent protects: - a method of treating acute ischemic stroke in humans by administering tenecteplase in certain doses in a certain sequence; - a kit for carrying out this method in the form of a container with tenecteplase and instructions for use of the kit; - a described kit in addition to a container with another drug, such as a neuroprotective agent, a thrombolytic agent, a glycoprotein IIb / IIIa antagonist or an antibody to CD18. Tenecteplase is known as a means to obtain increased specificity for fibrin, effective as a thrombolytic agent when administered as a bolus at a relatively low dose (B A Keyt et al., A faster-acting and more potent form of tissue plasminogen activator. Proc. Natl. Acad. Sci USA. 1994 Apr 26 91 (9): 3670–3674. Access mode https://www.ncbi.nlm.nih.gov/pmc/articles/PMC43643/). Therefore, the patent protects the use of a previously known compound, different only in dosage, i.e. is a new dosage form of a previously known substance, and also has a new form of application (container). Conclusion: there are grounds to classify the patent as «evergreening».

NITISINONE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
112	UA 110979 LIQUID PHARMACEUTICAL FORMULATION COMPRISING NITISINONE / 20.06.2012	Yes	The patent protects a liquid pharmaceutical composition, in particular for the treatment of hereditary tyrosinemia type I (HT-I), suitable for oral administration, which includes nitisinone as active substance and citric acid-based buffer to adjust the pH within the desired limits. Nitisinone as a 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor is known from patent US5550165A dated 27.08.1996 (AstraZeneca UK Ltd, Syngenta Ltd). Acid buffer is also known to regulate the acidity of the composition. The advantage of the invention is a more stable composition of nitisinone, also in terms of the formation of secondary degradation products, but the advantages of increasing the therapeutic effect are not specified. That is, the pharmaceutical composition according to the patent UA 110979 is a new combination of previously known substances, one of which is active, and does not have any different technical result. Conclusion: there are grounds to classify the patent as «evergreening».

SILDENAFIL

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
113	UA 112540 SILDENAFIL-FREE BASE-CONTAINING FILM PREPARATION AND METHOD FOR PRODUCING SAME / 13.02.2012	No	The patent protects: - a method of manufacturing a film for oral dosage form with control of the particle size of the free base of sildenafil and the content of ingredients when dispersing the free base of sildenafil as an active ingredient in a polymer solution; - the film itself, prepared in this way. Sildenafil was previously known as the active compound in the form of a citrate for a medicinal product manufactured by Pfizer under the trademark Viagra® and other companies under other trademarks for the treatment of male erectile dysfunction. The technical result of the invention is to increase the content of sildenafil in the film by dispersing the free base of sildenafil which has no taste and differs from the bitter citrate of sildenafil, in the polymer without significant dissolution. The technical result is achieved by controlling a predetermined range of particle size of the free base of sildenafil. That is, the invention is directed to a method for producing a previously known compound, but with technical features based on the use of a free base to overcome the disadvantages of sildenafil citrate or control the particle size of the drug to obtain better physical safety or film properties. These features are confirmed by the experimental results described in tables 6-8 of the description of the invention. According to the Preliminary Opinion of the International Searching Authority, there are other methods of preparing a film containing sildenafil, for example, described in US6552024B1 (the owner - Thallium Holding Company LLC). It is obvious that the invention according to the patent UA 112540 does not limit other methods of manufacturing a film containing sildenafil, which are used by many other manufacturers of drugs based on sildenafil. Conclusion: there are no grounds to classify the patent as «evergreening».
114	UA 113061 DRUG DELIVERY SYSTEM / 14.05.2012	No	The patent protects: - a time-regulated immediate delivery system of the drug with immediate release for oral administration of the active ingredient to a patient in need thereof; - a device for such delivery, including such a time-adjustable system of delivery of the drug with immediate release, in which the first shell of the delivery system of the drug is surrounded by a second shell, including another active ingredient. Sildenafil is a special case of the active ingredient along with many other PDE5 inhibitors, 5HT1a receptor agonists and neutral endopeptidase inhibitors, because the developer has tested the system and device on active substances for the treatment of sexual dysfunction, lack of desire or erectile dysfunction and, preferably, for use in the treatment of decreased libido. That is, the invention does not relate directly to sildenafil, but is one of the means of its introduction into the human body (among many others, for example, the oral form described in the following patent) together with another active substance. That's, the invention itself is the creation of such a dual dosage form (two active substances with immediate release). Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
115	UA 114629 PHARMACEUTICAL COMPOSITION IN SPRAY FOR TREATMENT OF ERECTILE DYSFUNCTION AND PULMONARY ARTERY HYPERTENSION / 10.10.2016	No	The patent protects a pharmaceutical composition in the form of an oral spray containing sildenafil. The task of the utility model is the introduction of sildenafil through the oral cavity to eliminate unwanted side effects that are accompanied by the reception of known solid oral dosage forms of sildenafil. That is, the utility model describes a new form of application of the previously known active ingredient - sildenafil. However, the patent does not limit other known compositions of sildenafil in the form of a spray, specified in the description of the utility model, as well as other mechanisms of administration of sildenafil, in particular in the form of solid oral dosage form. Conclusion: there are no grounds to classify the patent as «evergreening».

HIDAZEPAM (GIDAZEPAM)

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
116	UA 65257 METHOD FOR MANUFACTURING SUBLINGUAL TABLETED FORMULATION POSSESSING SEDATIVE AND SPASMOLYTIC EFFECTS / 16.062011	No	The patent protects a method for producing a pharmaceutical composition containing known active compounds of sedative and antispasmodic action. Hidazepam is one such compound along with phenobarbital or diazepam or their derivatives. The advantage of this method is to obtain a stable composition of these compounds with beta-cyclodextrin for improved bioavailability. The method does not limit other methods of making compositions with hidazepam, for example, in a tablet form. Conclusion: there are no grounds to classify the patent as «evergreening».
117	UA 97777 METHOD FOR THE PREPARATION OF SEDATIVE AND SPASMOLYTIC MEDICINAL AGENT IN THE FORM OF A SUBLINGUAL TABLET / 16.06.2011	No	The patent (for the invention) is similar to the previous patent (for a utility model) and therefore there are no grounds to classify the patent as «evergreening».

FLUTICASONE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
118	UA 77656 S-FLUOROMETHYL ESTER OF 6-ALPHA, 9-ALPHA-DIFLUORO-17-ALPHA-[(2-FURANYLCARBONYL) OXY]-11-BETA-HYDROXY-16-ALPHA-METHYL-3-OXOANDROSTA-1,4-DIEN-17-BETA-CARBOTHIOACID AS ANTI-INFLAMMATORY AGENT / 03.08.2001	No	The patent protects: - a fluticasone furoate (FF) compound; - its solvates and unsolvated forms, polymorphs; - a method of obtaining such a compound. Fluticasone furoate is a synthetically fluoridated corticosteroid, however, unlike fluticasone propionate (FP) known in the 1990s, it was approved by the FDA in 2007 and first marketed in the United States in 2009. FF differs from FP in that it has 17α-furoate ether in contrast to 17α-linear ether in FP, and FF and FP also differ in chemical and pharmacological parameters. That is, the chemical compound according to patent UA 77656 is not previously described as specially obtained (this patent is primary). Conclusion: there are no grounds to classify the patent as «evergreening».

AMBAZONE

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
119	UA 78470 METHOD FOR THE PURIFICATION OF 1,4-BENZOQUINONE GUANYLHYDRAZONE THIOSEMICARBAZONE (AMBAZONE)	No	The patent protects the method for the purification of the antiseptic ambazone which has been known since 1957. The method allows obtaining ambazone of pharmaceutical quality with reduced quantity of serum as an impurity (reaching 99,5% of ambazone purity). The description also contains different methods of ambazone purification, which used to be applied before, however, are ineffective in obtaining the ambazone of required purity. Thus, the method of ambazone purification provided in the patent has not been described before and doesn't block any other possible methods of ambazone purification.

LEVOSIMENDAN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
120	UA 73954 LEVOSIMENDAN-CONTAINING SOLUTION FOR PHARMACEUTICAL USE, PARTICULARLY FOR INTRAVENOUS ADMINISTRATION / 08.09.2000	Yes	The patent protects levosimedan in the form of a solution suitable for intravenous (infusion) administration through the use in the form of ethanol concentrate (levosimedan or its pharmaceutically acceptable salt dissolved in dehydrated ethanol), as well as a pharmaceutical solution based on it. Levosimedan as a compound with a hemodynamic effect for humans and its pharmacokinetics when administered intravenously are disclosed earlier: - the use of levosimendan in the treatment of myocardial ischemia described in WO 93/21921; - the use of levosimendan in the treatment of pulmonary hypertension described in WO 99/66912; - the use of levosimendan in the treatment or prevention of coronary graft spasm described in WO 1/00211. The advantage of the invention according to the patent is the increased stability of the solution. Problems with the stability of chemical and physical factors of levosimendan for its intravenous solutions have also been known, in particular, sensitivity to chemical factors, storage temperature, insolubility in water and tendency to precipitate during storage, which can lead to blockage of blood vessels during intravenous administration. That is, the solution was previously known, the problems of its use, and it is obvious that solutions were known to solve such problems, because the solution in this form (for intravenous administration) was tested. Conclusion: there are grounds to classify the patent as «evergreening».

DAPTOMYCIN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
121	UA 82824 COMPOSITIONS AND METHODS TO IMPROVE THE ORAL ABSORPTION OF ANTIMICROBIAL AGENTS / 18.06.2001	Yes	The patent protects a pharmaceutical composition containing daptomycin as a preferred variant of the lipopeptide antimicrobial agent (antibiotic) included in the composition. Daptomycin as a lipopeptide antibiotic with activity against gram-positive organisms is known previously, for example, from US 4,537,717; US 5,912,226 and some articles. An advantage of the invention is to improve the absorption of the antimicrobial agent from the intestine, for which the composition further comprises a biopolymer, a metal cation combined with the antimicrobial agent and the biopolymer, and a campule known as an absorption enhancer. The pharmaceutical composition according to the patent is a new combination of previously known active substances, one of which is daptomycin. Conclusion: there are grounds to classify the patent as «evergreening».
122	UA 105785 PROCESS FOR PURIFYING LIPOPEPTIDES / 19.02.2010	No	The patent protects the method of purification of daptomycin. The owner of the patent is XELLIA PHARMACEUTICALS APS (DK) as one of the manufacturers of a generic version of daptomycin, the originator of which is CUBIST PHARMACEUTIKALS, INS. (US), owner of a previous patent. There are similar methods of purification of daptomycin, for example, described in US 4,885,243, US 4,874,843, US 6,696,412 and others. The invention according to the patent describes an improved method of purification of daptomycin, which results in greater purity of the product, herewith, this method is simpler and ecological. Patent 4 does not block any other versions of daptomycin, but protects the product created by XELLIA PHARMACEUTICALS APS (DK) in the manufacture of a generic version of daptomycin. Conclusion: there are no grounds to classify the patent as «evergreening».

PEGFILGRASTIM

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
123	UA 93581 AGENT CONTAINING G-CSF FOR PREVENTING AND TREATING DIABETIC PERIPHERAL NEUROPATHY / 29.10.2007	No	The object of the invention is a new use of recombinant pegylated granulocyte colony-stimulating factor (G-CSF) as a means for the treatment of diabetic peripheral neuropathy. G-CSF is known as a drug for the induction of neutrophils in anticancer chemotherapy, megadoses therapy of anticancer drugs, combination therapy with radiotherapy and after bone marrow transplantation due to its specific effect on neutrophil precursor cells, promoting the proliferation and differentiation of neutrophils and enhancing the antibody-dependent cellular cytotoxicity of neutrophils. However, the use of G-CSF for the treatment of diabetic peripheral neuropathy is unknown, i.e. there is a new use of a known substance, characterized by identifying features of the known substance and characteristics of its new use. Conclusion: there are no grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
124	UA 97414 HUMAN GM-CSF ANTIGEN BINDING PROTEINS / 18.09.2008	No	The patent protects an individual compound belonging to the objects of genetic engineering – a human GM-CSF antigen binding antibody, as well as an isolated antigen-binding protein, a nucleic acid molecule, a vector, a host cell, a method for producing antibodies, a pharmaceutical composition and the use of isolated antibody. The isolated human antibody is characterized by CDRH and CDRL chains that have not previously been described as specifically prepared. The international search report does not contain data on patent documents for similar compounds / preparations where the applicant / owner is AMGEN INC. (US). Conclusion: there are no grounds to classify the patent as «evergreenig».

ILOPROST

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
125	UA 113161 COMPOSITION CONTAINING PROSTACYCLINE ANALOGUE AND PDE4 INHIBITOR FOR TREATMENT OF CYCQUISCIDOSIS / 03.02.2012	Yes	The object of the invention according to the patent is the use of a composition characterized by a qualitative composition (ingredients) for the treatment of cystic fibrosis. Iloprost is one of the alternatives to prostacyclin in the composition. The pharmaceutical composition is a new combination of previously known active substances (prostacycline) (iloprost) and PDE4 inhibitor (nuclear phosphodiesterase). A therapeutic effect of prostacycline (iloprost) and PDE4 inhibitor is also known for the treatment of cystic fibrosis (cystic fibrosis) by enhancing the production of cAMP in the epithelial cells of the lungs (Pierre Tissie`res, MD, Laurent Nicod, MD, Constance Barazzone-Argiroffo, MD, Peter C. Rimensberger, MD, and Maurice Beghetti, MD 'Aerosolized iloprost as a bridge to lung transplantation in a patient with cystic fibrosis and pulmonary hypertension', Ann Thorac Surg 2004;78:e48–50) v© 2004 by The Society of Thoracic Surgeons, https://www.annalsthoracicsurgery.org/article/S0003-4975(04)00754-4/pdf та Liu S1, Veilleux A, Zhang L, Young A, Kwok E, Laliberté F, Chung C, Tota MR, Dubé D, Friesen RW, Huang Z. Dynamic activation of cystic fibrosis transmembrane conductance regulator by type 3 and type 4D phosphodiesterase inhibitors, J Pharmacol Exp Ther. 2005 Aug;314(2):846-54. Epub 2005 May 18, https://www.ncbi.nlm.nih.gov/pubmed/15901792)

CARBETOCIN

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
126	UA 73501 b-ARYL-a-OXYSUBSTITUTED ALKYLCARBOXYLIC ACIDS, A METHOD FOR THE PREPARATION THEREOF (VARIANTS), PHARMACEUTICAL COMPOSITION BASED THEREON (VARIANTS), METHODS FOR PREVENTION AND TREATMENT WITH USE THEREOF, INTERMEDIARY COMPOUNDS AND A METHOD FOR THE PREPARATION THEREOF (VARIANTS) / 25.04.2000	No	The object of the invention according to the patent is: - a compound characterized by the general Markush claim (a chemical composition and a branched structure of the macromolecule as a whole); - a method of obtaining it; - a pharmaceutical composition based on this compound for the treatment or prevention of type II diabetes, glucose intolerance, insulin resistance, leptin resistance, dyslipidemia, X-related diseases, some kidney diseases. The chemical compound is not previously described as specially prepared. The chemical compound does not apply to carbetocin. Conclusion: there are no grounds to classify the patent as «evergreening».

TICAGRELOR

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
127	UA 66801 TRIAZOLE [4,5-D] PYRIMIDINE COMPOUNDS, METHOD OF PREPARATION (OPTIONS), PHARMACEUTICAL COMPOSITION BASED ON THEM AND METHOD OF TREATMENT / 15.07.1998	No	The object of the invention according to the patent is: - triazole [4,5-d] pyrimidine compound, characterized by the general Markush claim (a chemical composition and a branched structure of the macromolecule as a whole); - ways of obtaining it. The compound is a P21 receptor antagonist and is used as an antithrombotic agent. The chemical compound is not previously described as specially prepared. Its therapeutic effect is unknown. Conclusion: there are no grounds to classify the patent as «evergreening».
128	UA 73181 CRYSTALLINE AND AMORPHOUS FORMS OF TRIAZOL(4,5-d) PIRIMIDIN, METHOD FOR OBTAINING THEREOF, PHARMACEUTICAL COMPOSITON AND METHOD OF THERAPY OR PROPHILAXIS OF ARTERIAL THROMBOTIC COMPLICATIONS / 31.05.2001	Yes	The object of the invention according to the patent is: - crystalline and amorphous form of triazol [4,5-d] pirimidin compound; - the specified compound in the form of a hydrate; - a method of obtaining these compounds; - a pharmaceutical composition based on them; - a method of treating arterial thrombotic complications using a therapeutically effective amount of the above compounds. The triazol [4,5-d] pirimidin compound has already been disclosed in previous patent applications (for example, in international publications WO 99/05143 or WO 00/34283). Therefore, the patent protects certain forms of the previously known compound, in particular crystalline, amorphous or in the form of hydrate. Such forms of this compound have not previously been described as specially prepared, but are generally obtained by known methods without significant invention. Moreover, polymorphs or individual forms of a previously known compound are not specifically invented, but only established by the conventional research of an existing compound. The patent does not contain data on the presence of a new therapeutic effect in the polymorphic or amorphous form of the known triazol [4,5-d] pirimidin compound or other previously unknown effect. Conclusion: there are grounds to classify the patent as «evergreening».

#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
129	UA 99105 PHARMACEUTICAL COMPOSITION COMPRISING A TRIAZOLO [4, 5-D]PYRIMIDIN DERIVATE / 20.08.2007	Yes	The object of the invention according to the patent is a pharmaceutical composition containing ticagrelor (in various forms, mainly in crystalline) as an active agent and other components that are pharmaceutically acceptable components and are required for oral administration of the agent. That is, the invention protects a combination of previously known substances, all of which are used for their direct previously known purpose. According to the description, the invention is aimed at increasing the bioavailability of the composition with the agent, but does not contain evidence of improved bioavailability compared to previously known forms of application of the agent. Conclusion: there are grounds to classify the patent as «evergreening».

EPOETIN BETA

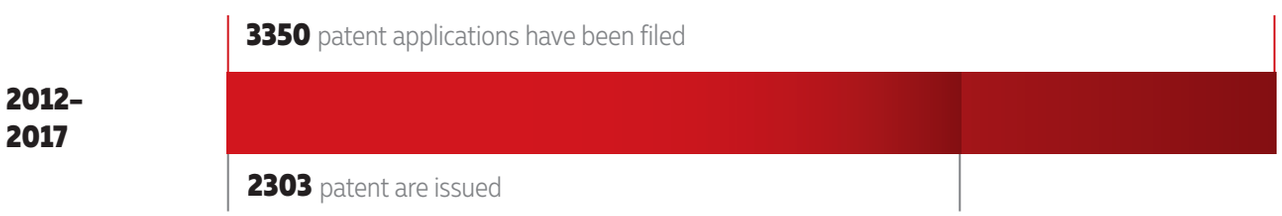
#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
130	UA 73468 CONJUGATE OF ERYTHROPOIETIN, COMPOSITIONS CONTAINING IT, AND METHODS FOR PREVENTION AND/OR TREATMENT OF DISEASES / 30.06.2000	No	The object of the invention according to the patent is: - an individual compound belonging to the objects of genetic engineering, namely a conjugate that includes a glycoprotein of erythropoietin with biological activity in vivo to stimulate the production of erythrocytes; - a method of obtaining compounds; - pharmaceutical composition and - a method of treating or preventing anemia using such a compound
131	UA 73468 STABLE AQUEOUS SOLUTION OF HUMAN ERYTHROPOIETIN NOT CONTAINING SERUM ALBUMINE / 07.06.2004	No	The object of the invention according to the patent is an aqueous composition of human erythropoietin and additional pharmaceutically acceptable substances (stabilizers, isotonic reagents and buffer reagents), aimed at increasing the duration of preservation of the biological activity of human erythropoietin. The invention can be applied to a composition with erythropoietin of any therapeutic activity and origin (not only for epoetin of beta company F. HOFFMANN LA ROCHE AG). The description of the invention contains evidence of the effectiveness of the composition compared to other test compositions of erythropoietin, in particular, increasing the purity and yield of erythropoietin after a long (4 weeks) shelf life. Conclusion: there are no grounds to classify the patent as «evergreening».

IDURSULFASE

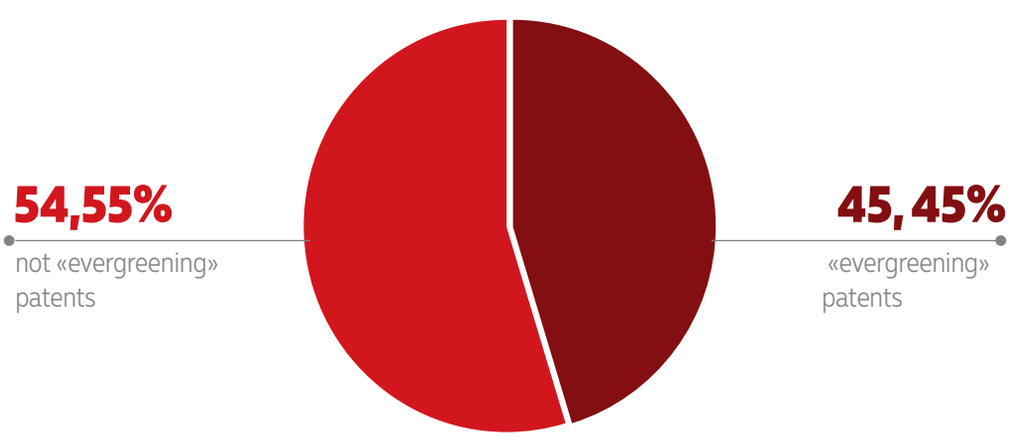
#	Patent number / title invention / date of application	Relation of patent to «evergreening» (Yes / No)	Grounds for classifying the invention as «evergreening»
132	Application a201413826 «PURIFICATION OF IDURONATE-2-SULFATASE» / 28.06.2013	Yes	The patent protects: - the use of specially purified recombinant enzyme (iduronate-2-sulfatase, I2S), a product of genetic engineering as part of the drug (Elaprase) to eliminate the absence or defect of this enzyme in the human body, which leads to symptoms of Hunter syndrome; - method of purification of I2S; - a method of treating Hunter syndrome using I2S purified by the claimed method. The object of the invention is characterized by a nucleotide sequence for a full-length complementary DNA clone to obtain I2S from human endothelial cells. The use of a recombinant enzyme for this purpose was first described in patents US5728381A, US5798239A, US5932211A, US6153188A, US6541254 B1, applications for which were filed in 1994-2000 and the exclusive right to which were obtained by SHIRE HUMAN GENETIC THER. A positive effect of the invention is to increase the degree of purification of the previously known recombinant enzyme from untreated biological materials while simplifying the method and increasing the content of FGly important for I2S activity. That is, the object of the invention is the previously described protein compound with the previously described pharmaceutical action. No new therapeutic activity has been reported. Conclusion: there are grounds to classify the patent as «evergreening».

/RESEARCH SUMMARY

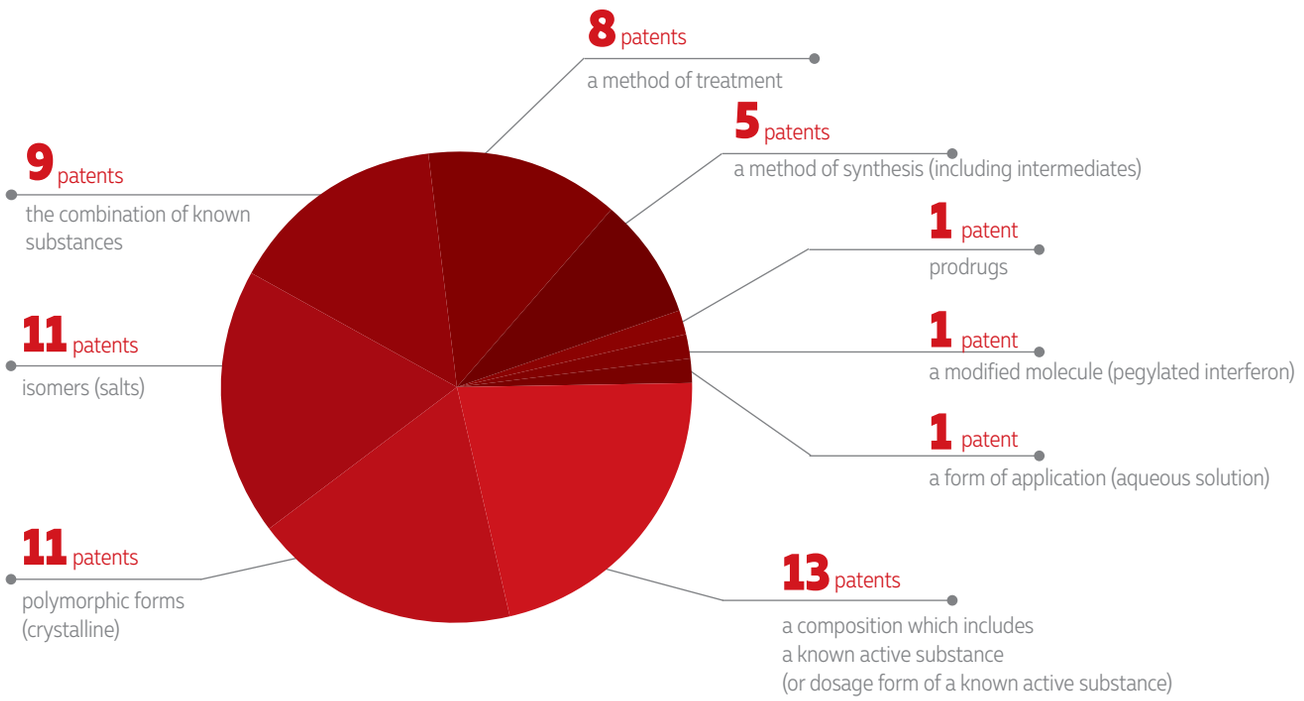
In this study, 132 patents related to drugs were analyzed. It should be noted that the field of medicines is quite attractive for applicants: during the 5 years preceding the start of this study (2012-2017), 3350 patent applications were filed in these areas and 2303 patents were issued. According to the analysis, 60 patents can be attributed to the category of «evergreening», the remaining 72 patents do not belong to the category of «evergreening».



132
patents were analyzed

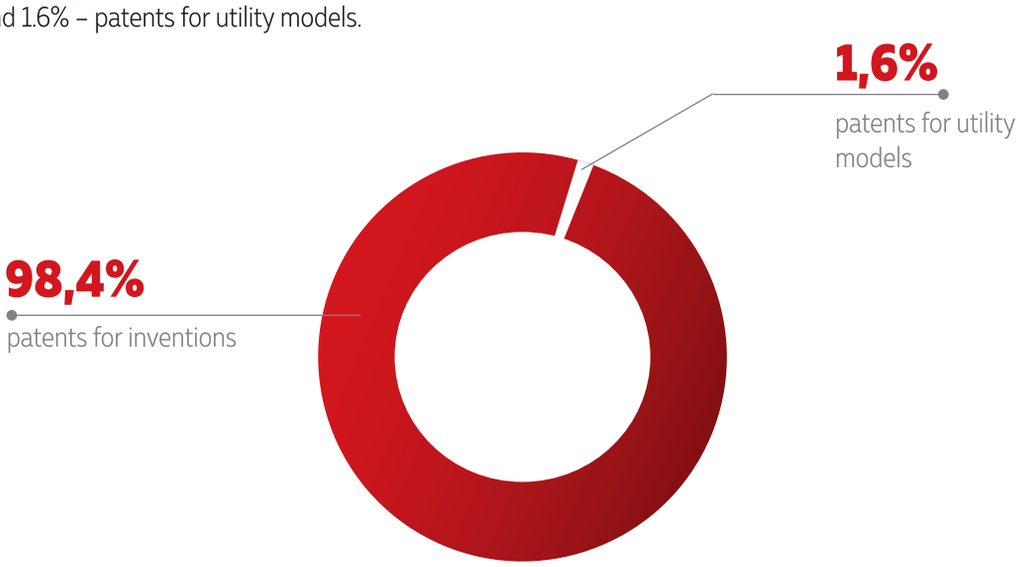


The identified **60 «evergreening»** patents have the following distribution by the objects of patenting:

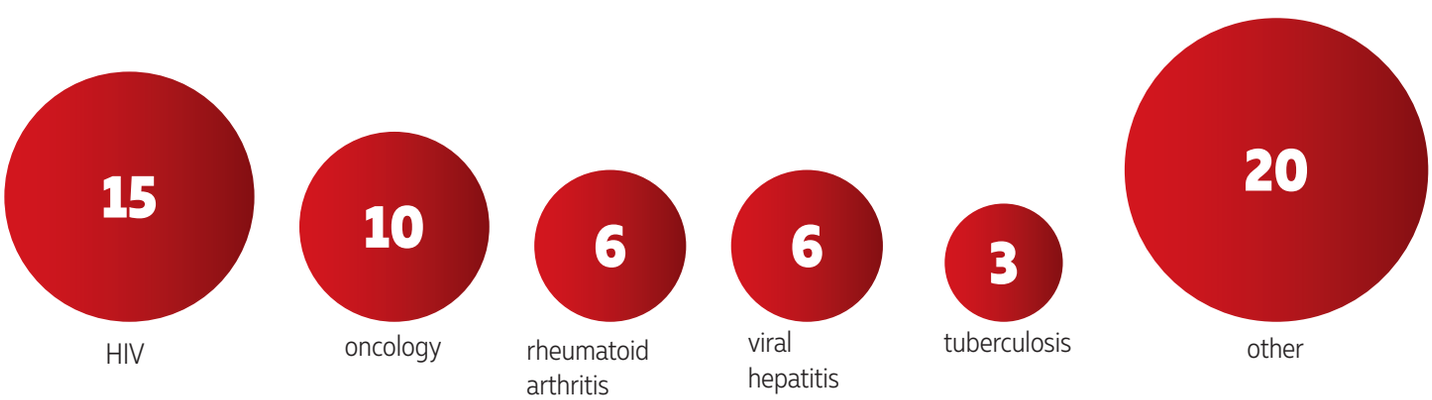


Of the «evergreening» patents, 98.4% were filed by foreign applicants and 1.6% by national ones.

Of the «evergreening» patents, 98.4% are patents for inventions and 1.6% – patents for utility models.



Of the «evergreen» patents: 15 – HIV, 10 – oncology, 6 – rheumatoid arthritis, 6 – viral hepatitis, 3 - tuberculosis, 20 – other.



The fact that almost half of the analyzed patents are «evergreen» and was filed almost exclusively by foreign applicants, negatively affects the availability of medicines and inhibits the development of domestic pharmaceutical production. In this regard, the state should take measures to prevent the issuance of «evergreening» patents.

To do this, it is advisable to follow the qualification standard for chemicals and pharmaceuticals, as well as pay additional attention to the so-called secondary applications, in which protection is provided not for the active substance itself, but for the method of its production, dosage form, composition of drugs and so on.e.

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