EXTRUDATE ENZALUTAMIDE COMPOSITIONS

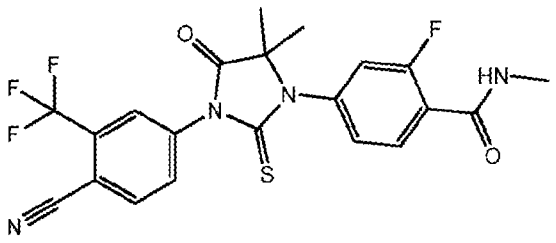
FIELD OF THE INVENTION

The present invention relates to novel oral extrudate pharmaceutical compositions of enzalutamide. Methods of preparing such compositions are also provided.

BACKGROUND OF THE INVENTION

Prostate cancer is the development of cancer in the prostate, a gland in the male reproductive system. Most prostate cancers are slow growing; however, some grow relatively quickly. The cancer cells may spread from the prostate to other parts of the body, particularly the bones and lymph nodes. Prostate cancer is a common cancer in men, especially in the US and in Europe.

Enzalutamide is an androgen receptor signaling inhibitor. The chemical name is 4-{3-[4-cyano-3-(trifluoromethyl)phenyl]-5,5-dimethyl-4-oxo-2-sulfanylide-neimidazolidin-1-yl}-2-fluoro-N-methylbenzamide. The structural formula is:



Enzalutamide is non-hygroscopic, crystalline solid that remain unionized over the physiologic pH range. It is poorly soluble; in particular sparingly soluble in absolute

ethanol and practically insoluble in water between pH 1 and 11, soluble in acetone and N-methyl-2-pyrrolidone (NMP). It is a Class II drug as per the biopharmaceutics classification system. Poor drug solubility however represents a bottleneck for dissolution, which in turn critically affects drug bioavailability.

Enzalutamide is marketed as XTANDI® and used for the treatment of castration-resistant prostate cancer. Enzalutamide also is reported for treating breast cancer, prostate cancer, benign prostate hyperplasia and ovarian cancer.

According to the FDA, XTANDI® is a liquid-filled soft gelatin capsule for oral administration comprising enzalutamide. The recommended dose of XTANDI® is 160 mg, which should be administered orally once daily in the form of four capsules each containing 40 mg of active pharmaceutical ingredient, wherein the active pharmaceutical ingredient is dissolved in the caprylocaproyl polyoxylglycerides solvent (Labrasol®). The administration of XTANDI® is reported to be independent of food uptake. The patient should swallow the whole capsule which should not be chewed, dissolved or opened prior to swallowing.

A disadvantage of the recommended dose is taking four capsules daily (160 mg once daily). Further, these capsules are reported to be very large due to the great amount of Labrasol® necessary to keep the active pharmaceutical ingredient in solution. Due to its large size (capsule size 12) and the high number of capsules that has to be taken, this dosage form is difficult to swallow, in particular for older men, resulting in a poor patient compliance, especially in said important patient group.

Moreover, the above-mentioned composition comprising enzalutamide shows poor dissolution behaviour at acidic conditions, especially under simulated gastric fluid which appears to be incomplete. In particular, the API does not remain dissolved but seems to precipitate.

Thus, there remains a need to develop a stable pharmaceutical composition of enzalutamide with improved patient compliance by providing small dosage forms, in weight and in physical volume, in order to be easily swallowable by patients and come in a small number of units per daily recommended dose, preferably in single dosage unit. Recently, in Europe and Japan, a 40 mg and 80 mg XTANDI® tablets were approved which are although smaller in size than the earlier approved 40 mg XTANDI® Capsules, but it would still require 4 or 2 tablets to be administered to meet the recommended dose. Further, there is no single unit dose 160 mg enzalutamide composition approved in any other market. This single unit dose composition would reduce the pill burden and thereby would improve the patient compliance. Further desirable object includes improved dissolution and bioavailability associated with the current softgel dosage form.

US20140179749 discloses solid dispersion compositions of enzalutamide and polymer. The '749 application discloses various enzalutamide compositions which are made by mechanical processes such as spray-drying, spray coating, milling, solvent modified fusion, solvent processes include non-solvent precipitation and hot-melt extrusion. However the single unit dose 160 mg enzalutamide compositions were prepared via spray-drying technology.

WO2015118015 discloses solid adsorbate or solid dispersion compositions of enzalutamide.

WO2015022349 discloses enzalutamide composition in first and second solvent and optionally an oil component, wherein the enzalutamide is present in a dissolved form.

In an attempt to develop novel oral improved enzalutamide compositions, preferably a single unit dose 160 mg enzalutamide composition, the present inventors have surprisingly found that extrudate pharmaceutical compositions of enzalutamide with

one or more suitable polymers prepared by using twin screw extrusion or hot melt extrusion resulted in chemically stable compositions having improved drug loading, improved patient compliance and minimize the use of solvents.

SUMMARY OF THE INVENTION

The present specification relates to novel oral extrudate pharmaceutical compositions of enzalutamide.

In one aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) 160 mg or 80 mg enzalutamide, and
(ii) one or more polymers.

In another aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) enzalutamide,
(ii) one or more polymers, and
(iii) one or more pharmaceutically acceptable excipients.

In yet another aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) enzalutamide,
(ii) hydroxypropyl cellulose and or hydroxyethyl cellulose, and
(iii) one or more pharmaceutically acceptable excipients.

In yet another aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:

(i) enzalutamide,
(ii) one or more non-cellulosic polymers, and
(iii) one or more pharmaceutically acceptable excipients.

The pharmaceutical compositions of the present specification may be used for the treatment of prostate cancer, breast cancer, benign prostate hyperplasia and ovarian cancer.

BRIEF DESCRIPTION OF FIGURE

Figure 1: Comparative dissolution profile between the present invention (example 3a) and dissolution profile of the spray dried tablet composition (example 24 of US 20140179749).

DESCRIPTION OF THE INVENTION

The present specification relates to novel oral extrudate pharmaceutical compositions of enzalutamide.

In one aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) 160 mg or 80 mg enzalutamide, and
(ii) one or more polymers.

In another aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) enzalutamide,
(ii) one or more polymers, and

(iii) one or more pharmaceutically acceptable excipients.

In yet another aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) enzalutamide,
(ii) hydroxyproplyl cellulose and or hydroxyethyl cellulose, and
(iii) one or more pharmaceutically acceptable excipients.

In yet another aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) enzalutamide,
(ii) one or more non-cellulosic polymers, and
(iii) one or more pharmaceutically acceptable excipients.

As used herein, the term "oral pharmaceutical composition" refers to an oral dosage form comprising tablets, pills, sachets, or capsules. The preferred oral dosage form is in the form of capsule or tablet. The term "extrudate oral pharmaceutical composition" refers to the compositions prepared by twin screw extrusion or hot melt extrusion using a conventional extruder well known in the art.

For example, the composition is obtained by solidifying a poorly water-soluble drug and a polymer through hot-melt extrusion improves bioavailability of the drug because the drug is molecularly dispersed in an amorphous form in the polymer carrier and the apparent solubility of the drug shows a marked increase. Further, the hot-melt extrusion can avoid using a solvent so that it has various advantages over spray-dried composition recently approved. For example, the hot-melt extrusion can be applied to a drug not stable in water, is safe and environmentally friendly because of unnecessity of solvent recovery, can save energy spent for the solvent recovery, and provides a working environment with improved safety. Still further, differing from conventional

batch production, this method permits continuous production so that it has attracted attentions also from the standpoint of hourly productivity and consumption energy.

The term "enzalutamide" refers to enzalutamide and esters, salts, or derivatives thereof. Enzalutamide could be crystalline or amorphous (i.e., in a non-crystalline state) forms as known in the prior art. Amorphous enzalutamide may be prepared by any known means, including spray-drying, hot melt extrusion, and precipitation from solution on addition of a non-solvent. Amorphous enzalutamide dissolves more quickly and to a greater extent than crystalline enzalutamide in an aqueous use environment, such as an aqueous dissolution medium of an in vitro dissolution test (e.g., phosphate buffered saline or model fasted duodenal fluid or simulated gastric fluid) or the in vivo environment of the stomach or small intestine. The amount of enzalutamide present in the extrudate compositions is about 10 to 250 mg, preferably from 20 to 160 mg.

Polymers suitable for use in the extrudate compositions of the present specification are inert, are pharmaceutically acceptable (i.e. are non-toxic), and have at least some solubility in aqueous solution at physiologically relevant pH (e.g. 1-10). The polymers may be cellulosic or non-cellulosic. The polymers may be neutral or ionizable in aqueous solution.

Exemplary neutral non-ionizable cellulosic polymers of the present specification include hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, hydroxyethyl ethyl cellulose and any mixtures thereof.

Exemplary cellulosic polymers that are at least partially ionized at physiologically relevant pH include: hydroxypropyl methyl cellulose acetate succinate (HPMC-AS), hydroxypropyl methyl cellulose succinate, hydroxypropyl cellulose acetate succinate, hydroxyethyl methyl cellulose succinate, hydroxyethyl cellulose acetate succinate,

hydroxypropyl methyl cellulose phthalate, hydroxyethyl methyl cellulose acetate succinate, hydroxyethyl methyl cellulose acetate phthalate and any mixtures thereof. A particularly desirable subset of cellulosic ionizable polymers are those that possess both a carboxylic acid functional aromatic substituent and an alkylate substituent and thus are amphiphilic.

In some embodiments, the polymers used in the present specification comprises neutral non-cellulosic polymers, including, but not limited to, vinyl polymers and copolymers having substituents of hydroxyl, alkylacyloxy and cyclicamido polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers; polyvinyl pyrrolidone; polyvinylpyrrolidone vinyl acetate; and polyethylene polyvinyl alcohol copolymers.

Another class of polymers comprises ionizable non-cellulosic polymers, including, but not limited to, carboxylic acid-functionalized vinyl polymers, such as the carboxylic acid functionalized polymethacrylates and carboxylic acid functionalized polyacrylates such as the EUDRAGIT®.

Non-cellulosic polymers that are amphiphilic are copolymers of a relatively hydrophilic and a relatively hydrophobic monomer. Examples include acrylate and methacrylate copolymers. Commercial grades of such copolymers include the EUDRAGIT®, which are copolymers of methacrylates and acrylates; and graft copolymers of polyethylene glycol, polyvinylcaprolactam, and polyvinylacetate, one commercially available version of a graft copolymer known as SOLUPLUS®.

The amount of polymer used in the extrudate pharmaceutical compositions of the present specification relative to the amount of enzalutamide may vary widely. Preferably, the amount of enzalutamide and polymer are present in a weight ratio from about 1:05 to 1:5, e.g. 1:0.7, 1:1, 1.2.

In one aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) 160 mg enzalutamide, and
(ii) one or more polymers, wherein the amount of enzalutamide and polymer are present in a weight ratio from about 1:05 to 1:3.

In one aspect, the present specification relates to an oral extrudate pharmaceutical composition comprising:
(i) 80 mg enzalutamide, and
(ii) one or more polymers, wherein the amount of enzalutamide and polymer are present in a weight ratio from about 1:05 to 1:3.

In another aspect, the extrudate single dose pharmaceutical composition of 160 mg enzalutamide of the present specification would exhibit therapeutic equivalence to four commercially available 40 mg enzalutamide soft gelatin/tablet composition or two commercially available 80 mg enzalutamide tablet composition.

In another aspect, the extrudate single dose pharmaceutical composition of 160 mg enzalutamide of the present specification would exhibit bioequivalence to four commercially available 40 mg enzalutamide soft gelatin/tablet composition or two commercially available 80 mg enzalutamide tablet composition.

In yet another aspect, the extrudate single dose pharmaceutical composition of 160 mg enzalutamide of the present specification would exhibit pharmacokinetic equivalence to either four commercially available 40 mg enzalutamide soft gelatin/tablet composition or two commercially available 80 mg enzalutamide tablet composition.

The extrudate oral pharmaceutical composition according to the present specification may further comprise one or more pharmaceutically acceptable excipients. Such excipients include fillers, disintegrants, binders, lubricants, glidants, film-forming agents and coating materials, sweeteners, flavoring agents, plasticizers, surfactants and coloring agents such as pigments. Other excipients known in the field of pharmaceutical compositions may also be used.

Fillers or diluents, may be selected from the group consisting of different grades of starches, such as maize starch, potato starch, rice starch, wheat starch, pregelatinised starch, fully pregelatinised starch; cellulose derivatives, such as microcrystalline cellulose or silicified microcrystalline cellulose; sugar alcohols such as Mannitol, erythritol, sorbitol, xylitol; monosaccharides like glucose; oligosaccharides like sucrose and lactose such as lactose monohydrate, lactose anhydrous, spray dried lactose or anhydrous lactose; calcium salts, such as calcium hydrogenphosphate; particularly preferably the fillers are selected from the group consisting of, microcrystalline cellulose, silicified microcrystalline cellulose, lactose monohydrate, spray dried lactose, and anhydrous lactose.

Suitable disintegrants may be selected from the group consisting of carmellose calcium, carboxymethylstarch sodium, croscarmellose sodium (cellulose carboxymethylether sodium salt, crosslinked), starch, modified starch such as pregelatinized starch, starch derivatives such as sodium starch glycolate, crosslinked polyvinylpyrrolidone (crospovidone), and low-substituted hydroxypropylcellulose, and disintegrating aids such as magnesium alumino-metasilicate and ion exchange resins like polacrilin potassium; particularly preferably the disintegrants are selected from the group consisting of sodium starch glycolate, croscarmellose sodium and crospovidone.

Suitable binders may be selected from the group consisting of polyvinyl pyrrolidone (Povidone), polyvinyl alcohol, copolymers of vinylpyrrolidone with other vinyl derivatives (Copovidone), hydroxypropyl methylcellulose, methylcellulose, hydroxypropylcellulose, powdered acacia, gelatin, guar gum, carbomer such as carbopol, polymethacrylates and pregelatinized starch.

Suitable lubricants may be selected from the group consisting of stearic acid, talc, glyceryl behenate, sodium stearyl fumarate and magnesium stearate; particularly preferably the lubricant is magnesium stearate and sodium stearyl fumarate.

Glidants, if used, may be selected from the group consisting of colloidal silica, hydrophobic colloidal silica and magnesium trisilicate, such as talc; particularly preferably the glidants are selected from the group consisting of colloidal silica and hydrophobic colloidal silica.

Suitable film-forming agents and coating materials, if used, e.g. for the preparation of film coatings on API-containing tablets, may include, but are not limited to hydroxypropyl methylcellulose (Hypromellose), hydroxypropyl cellulose, polyvinylalcohol, , methylcellulose, ethylcellulose, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, shellac, liquid glucose, hydroxyethyl cellulose, polyvinylpyrrolidone, copolymers of vinylpyrrolidone and vinylacetate such as Kollidon® VA64 BASF, copolymers of acrylic and/or methacrylic acid esters with trimethylammoniummethylacrylate, copolymers of dimethylaminomethacrylic acid and neutral methacrylic acid esters, polymers of methacrylic acid or methacrylic acid esters, copolymers of acrylic acid ethylester and methacrylic acid methyl ester, and copolymers of acrylic acid and acrylic acid methylester.

Suitable sweeteners may be selected from the group consisting of aspartame, saccharin sodium, dipotassium glycyrrhizinate, aspartame, stevia, thaumatin, and the like.

Plasticizers, if used, may include, but are not limited to polyethylene glycol, diethyl phthalate and glycerol. Preference is given to polyethylene glycol.

Suitable surfactants as component can be selected from the group consisting of anionic surfactants, preferably sodium lauryl sulphate; polyethylene glycols (PEGs), preferably those PEGs having molecular weight in the range of about 2000 to 10000, more preferably PEG 3350, PEG 4000, PEG 6000, PEG 8000; Polysorbates, preferably Tween 20, Tween 80 or Span 80; fatty acid esters, preferably propylene glycol caprylates such as Capmul PG-8, Capryol 90; esters of glycerol and fatty acids, preferably glycerol oleates and caprylates (Capmul MCM); esters of polyethylene glycol and fatty acids, such as Labrasol and Solutol; castor oil ethoxylate (glycerol polyethylene glycol ricinoleate) such as Cremophor EL and Cremophor RH 40. More preferably the surfactant is selected from the group consisting of sodium lauryl sulphate; PEG 3350, PEG 4000, PEG 600 or, PEG 8000 and preferably PEG 6000; Tween 20 or Tween 80; and esters of polyethylene glycol and fatty acids, most preferably sodium lauryl sulphate and PEG 6000 and in particular sodium lauryl sulphate.

The extrudate composition of the present specification may further include an antioxidant. The antioxidant may be selected from one or more of DL-alpha-tocopherol, butylhydroxy toluene (BHT), butylhydroxy anisole (BHA), ascorbyl palmitate, ascorbic acid and propyl gallate.

As suitable dosage forms, the extrudate pharmaceutical composition according to the present invention is in the form of a capsule or a tablet. For example, a capsule such as a gelatine capsule may be filed with extrudate formed through twin screw extrusion or

hot melt extrusion or a tablet is compressed using such extrudate and other pharmaceutically acceptable excipients useful for such technologies and optionally further film-coated.

The extrudate pharmaceutical compositions of the present specification may be prepared by conventional twin screw or hot melt extrusion process for oral solid dosage forms. For example, the extrudates may be prepared by using dry-powder blends of enzalutamide and polymer. Various drug and polymer ratio has been studied. Using a Gravimetric powder feeder, the blends are fed at a controlled rate to a twin screw extruder. The extruder has a temperature controller and is equipped with a cylindrical die. Extrudates are collected at the die end and milled in to different sizes for direct use or further processing accordingly. The milled extrudate can be mixed with suitable excipients and filled into a hard gelatin capsule or compressed in to a tablet and suitably packed in conventional blister pack or stick pack.

In some embodiments, the amount of enzalutamide present in the extrudate pharmaceutical compositions of the present specification is 80 mg or 160 mg. The final extrudate compositions when compressed in to tablets or filled in the capsule has a suitable size and thus reduce the number of administered units such that the patient compliance can be improved.

In some embodiments, enzalutamide present in the final extrudate pharmaceutical compositions is mainly in amorphous state, preferably substantially amorphous state. "Mainly" amorphous denotes "more than 50%", "substantially" amorphous denotes that at least 90 %, preferably 95 % or 97 %, more preferably all of the respective compound is amorphous. In other words, "amorphous" means minor amounts and preferably no substantial amounts, of crystalline portions of the respective compound, as e.g. measurable upon X-ray powder diffraction (XRPD) analysis.

The extrudate pharmaceutical composition according to the present specification is particularly useful in medical treatments, specifically in the treatment of prostate cancer and breast cancer, benign prostate hyperplasia and ovarian cancer and in particular in the treatment of male patients with metastatic castration-resistant prostate cancer.

The extrudate pharmaceutical compositions of the present specification would be subjected to in-vitro dissolution studies and accelerated and long term stability studies.

In one aspect of the present specification, an oral extrudate pharmaceutical composition comprising 160 mg enzalutamide and one or more polymers, wherein the composition would be therapeutically equivalent to four commercially available 40 mg Xtandi® soft gelatin/tablet composition or two commercially available 80 mg Xtandi® tablet composition.

The therapeutically equivalence can be easily established by a comparative pharmacokinetic study or bioequivalence testing as routinely adopted industrially.

The present specification may be further illustrated below by reference to the following examples. However, one skilled in the art will appreciate that the specific methods and results discussed are merely illustrative of the present invention, and not to be construed as limiting the application. Some exemplary extrudate composition according to the present specification is given below.

Example 1: Extrudate enzalutamide compositions

The extrudate composition was prepared by following steps:

1. Required amount of enzalutamide and polymer were taken and blended well.
2. The blends were fed at a controlled rate to a twin screw extruder through a gravimetric powder feeder and extruded at a controlled temperature.

3. Extrudates were collected at the die end of the extruder and milled in to different sizes for direct use or further processing accordingly.

Table 1: represents the extrudate enzalutamide and polymer compositions with different ratio, extrusion temperature, glass transition temperature (Tg) the crystallinity of the dispersion and the physical appearance of the extrudates.

Extrudate composition	**Ratio**	**Temperature (°C)**	**Tg (°C)**	**Crystallinity by PXRD**	**Appearance**
Enzalutamide: HMPC AS	1:3	180-200	95	Amorphous	Transparent Strand
Enzalutamide: HMPC AS	1:2	180-200	93	Amorphous	Transparent Strand
Enzalutamide: HMPC AS	1:0.7	180-220	98	Partially Crystalline	Translucent Strand
Enzalutamide: SOLUPLUS	1:2	180-200	84	Amorphous	Transparent Strand
Enzalutamide: SOLUPLUS	1:1	190-200	79	Partially Crystalline	Translucent Strand

Example 2: Tablet compositions comprising enzalutamide extrudates

Example 2a	**Example 2b**	**Example 2c**	**Example 2d**	**Example 2e**	**Example 2f**
Enzalutamide HPMC-AS Hydroxypropyl cellulose Lactose Magnesium Stearate	Enzalutamide PLA-PVA-PEG graft polymer Hydroxyethyl cellulose Microcrystalline cellulose Croscarmellose sodium Magnesium Stearate	Enzalutamide Eudragit® L (100-55) Microcrystalline cellulose Croscarmellose sodium Magnesium Stearate	Enzalutamide CO-PVP Polyvinyl pyrrilidone lactose Magnesium Stearate	Enzalutamide PVP-VA 64 Eudragit® L (100-55) Lactose Magnesium stearate	Enzalutamide PVP-VA 64 Eudragit® E 100 Lactose Magnesium stearate

The following procedure was used to form tablets compositions comprising enzalutamide extrudates. First the extrudate compositions of enzalutamide and polymer was prepared according to example 1. The extrudates were mixed with the excipients as specified in the examples (2a-2f) and blend it well and granules were prepared by dry granulation method and finally the granules were compressed in to tablets.

Example 3: Stability study

The stability of the extrudate compositions of present specification were evaluated through accelerated stability studies. A tablet composition comprising 160 mg enzalutamide was prepared according to the formula described in Table 2 and the process of example 2. The tablet composition was subjected to stability study at various temperature and humidity conditions. The composition was found to be stable at accelerated conditions. Table 3 represents the study result data.

Table 2: Enzalutamide 160 mg tablet composition

Ingredients	**Example 3a Quantity (mg)**	**Example 3b Quantity (mg)**
Enzalutamide	160	160
HPMC AS	320	106
Microcrystalline cellulose	101.1	94.8
Lactose	101.1	94.8
Croscarmellose Sodium	14.0	40
Magnesium Stearate	1.3	1.3
Colloidal silicon dioxide	2.5	2.5
Total	700	499.4

Table 3: Stability data of Enzalutamide 160 mg tablet composition

Stability Data- Example 3a						
Condition	**Assay**	**Moisture Content**	**Purity**	**RRT**		
				0.9	**0.9**	**1.11**
Initial	97.9	2.84	99.91	0.02	0.05	0.02
25°C/60% RH (1M)	96.6	2.79	99.91	0.02	0.05	0.02
25°C/60% RH (2M)	95.9	2.62	99.91	0.02	0.05	0.02
40°C/75% RH (1M)	96.7	2.91	99.90	0.03	0.05	0.02
40°C/75% RH (2M)	96.6	2.94	99.89	0.04	0.05	0.02

Dissolution Studies:

The drug release pattern of the composition prepared according to the example 3a was evaluated through dissolution studies accomplished by paddle method described in the United States Pharmacopoeia (USP-34-NF 29). The drug release property was evaluated in pH 6.8 dissolution media (USP-II- 50 rpm). The dissolution profile is shown in Figure 1. The composition exhibits improved dissolution characteristics when compared to the dissolution profile of the spray dried tablet composition (refer example 24 of US 20140179749).

Dated this on 8th day of August 2018

For DR. REDDY'S LABORATORIES LIMITED

Signature: _____

Dr. Poonam Raghuvanshi

CLAIMS

1. An oral extrudate pharmaceutical composition comprising:
(i) 160 mg or 80 mg enzalutamide, and
(ii) one or more polymers.

2. The composition as claimed in claim 1, wherein the amount of enzalutamide and polymer are present in a weight ratio from about 1:0.5 to about 1:5.

3. The composition as claimed in claim 1, wherein the amount of enzalutamide and polymer are present in a weight ratio of 1:0.7 to 1:2.

4. The composition as claimed in claim 1, wherein the polymer is selected from one or more of cellulosic polymer or non-cellulosic polymer or mixtures thereof.

5. The composition as claimed in claim 4, wherein the cellulosic polymer is selected from one or more of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, hydroxyethyl ethyl cellulose, hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose succinate, hydroxypropyl cellulose acetate succinate, hydroxyethyl methyl cellulose succinate, hydroxyethyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, hydroxyethyl methyl cellulose acetate succinate, hydroxyethyl methyl cellulose acetate phthalate and any mixtures thereof.

6. The composition as claimed in claim 4, wherein the non-cellulosic polymers is selected from one or more of vinyl polymers and copolymers, polyvinyl alcohol polyvinyl acetate copolymers; polyvinyl pyrrolidone; polyvinylpyrrolidone vinyl acetate, polyethylene polyvinyl alcohol copolymers, carboxylic acid-functionalized

vinyl polymers, copolymers of methacrylates and acrylates, graft copolymers of polyethylene glycol, polyvinylcaprolactam, and polyvinylacetate and any mixtures thereof.

7. The composition as claimed in claim 4, wherein the polymer is graft copolymers of polyethylene glycol, polyvinylcaprolactam, and polyvinylacetate.

8. The composition as claimed in claim 4, wherein the polymer is hydroxypropyl methyl cellulose acetate succinate.

9. The composition as claimed in claim 4, wherein the composition further comprising one or more pharmaceutically acceptable excipients.

10. An oral extrudate pharmaceutical composition comprising:
(i) 160 mg enzalutamide, and
(ii) one or more polymers selected from hydroxypropyl methyl cellulose acetate succinate, graft copolymers of polyethylene glycol, polyvinylcaprolactam and polyvinylacetate,
wherein the amount of enzalutamide and polymer are present in a weight ratio of 1:2 or 1:1.

ABSTRACT

The invention relates to novel oral extrudate pharmaceutical compositions of enzalutamide. The extrudate compositions comprise one or more suitable polymers and are prepared using twin screw extrusion or hot melt extrusion. Methods of preparing such compositions are also provided. The extrudate compositions may be used for the treatment of prostate cancer.

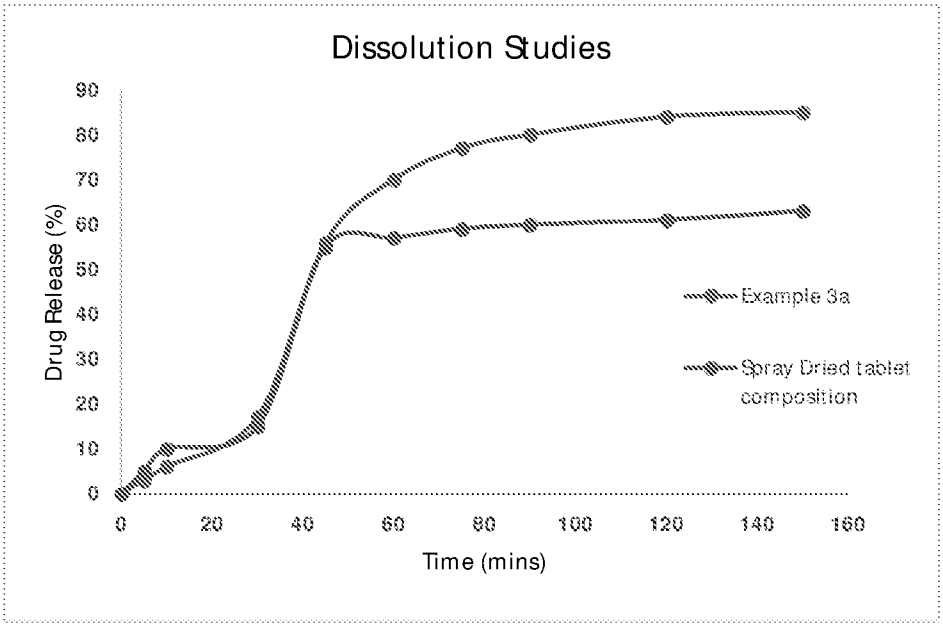


Figure: 1

For DR. REDDY'S LABORATORIES LIMITED

Signature: _____

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