PHYSICOCHEMICAL CHARACTERISTICS OF ABIRATERONE ACETATE USED FOR THE TREATMENT OF PROSTATE CANCER

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Prostate cancer is the most common cancer among men and often has no early symptoms. The major treatment options that include surgical or medical castration cause ablation of the production of testosterone, dihydrotestosterone and related androgens by the testes. These procedures do not affect adrenal, prostate and other tissues androgen production, therefore they are combined with androgen receptor antagonists to block their action. Recent studies have established that in castration-resistant prostate cancer many androgen-regulated genes become re-expressed and tissue androgen levels increase despite low serum levels [1].

Abiraterone acetate inhibits the key enzyme cytochrome P450 17α-hydroxy/17,20-lyase (CYP17) which catalyzes the biosynthesis of androgens and provides the effective treatment of prostate cancer patients.

The aim of this work was abiraterone acetate polymorph diagnostics and physcicochemical characteristics of polymorphs.

Polymorphism is the ability of a compound in the solid state to exist in different crystalline forms. Molecules, having the same chemical composition, exhibit different spatial arrangements and/or exist in different conformations. Substances that exist in a non-crystalline solid state are said to be amorphous. The term pseudopolymorphism is used to describe solvates (including hydrates). Different polymorphs of a solid compound exhibit distinct physical properties such as, e.g.: hygroscopicity, solubility, dissolution rate, melting point and stability. All of which play a very important role in the pharmaceutical industry. The undesirable polymorphic form with lower solubility and consequently with a lower absorption rate decreases the concentration of active substance in the blood. The Biopharmaceutics Classification System classifies drugs taking into account their solubility. Because a change in a polymorphic form may influence on a drug product affectivity and its toxic properties the regulations required by the ICH Q6A guideline according to the decision tree no 4 [2] demand the control of solid state behavior.

Therefore, the polymorphic behavior of abiraterone acetate has to be carefully investigated and all found polymorphs have to be fully characterized. Abiraterone acetate was characterized by following methods: X-ray powder diffraction, infrared and Raman spectroscopy, differential scanning calorimetry. Polymorph screening was performed and single crystals were obtained by a vapour diffusion crystallisation. The structure of abiraterone acetate was solved by the single crystal X-ray diffraction. Additionally the structure was confirmed by the direct sample injection method (DI).

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References

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