Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 8 Issue 11 November 2024

Mini Review

Analytical Methods for the Estimation of Relugolix – A Review

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Received: October 18, 2024

Published: October 28, 2024

Abstract

Relugolix is used to treat advanced prostate cancer in men. Relugolix is used in the treatment of advanced hormone sensitive prostate cancer and also to manage heavy menstrual bleeding and severe pain. In the present study the authors have reviewed and summarised the analytical methods so far developed for the estimation of Relugolix in pharmaceutical formulations as well as biological fluids.

Keywords: Relugolix; Pain

Introduction

Relugolix (CAS: 737789-87-6) is chemically 1- [4- [1-[(2,6-difluoro phenyl) methyl]-5-[(dimethyl amino) methyl]-3-(6-methoxy pyridazin-3-yl)-2,4-dioxothieno[2,3-d] pyrimidin-6-yl] phenyl]-3-methoxy urea with molecular weight 623.6 g/mol. Relugolix is used in the treatment of advanced hormone sensitive prostate cancer [1] and also to manage heavy menstrual bleeding and severe pain [2-4]. Relugolix is soluble in organic solvents such as Ethanol, DMSO and dimethyl formamide and the solubility in these solvents is approximately 1, 20 and 25 mg/ml respectively and the pKa value is 8.63. Relugolix is a competitive antagonist of Gonadotropin-releasing hormone receptors, thereby decreasing the release of Luteinizing hormone and ultimately Testosterone.

Relugolix is available as tablets with label claim 120 mg with brand names Rexigo (Zydus Cadila), R-Golix (Ipca Laboratories Ltd), OrgOnist (Sun Pharmaceuticals), Xelucip (Cipla Ltd) in India.

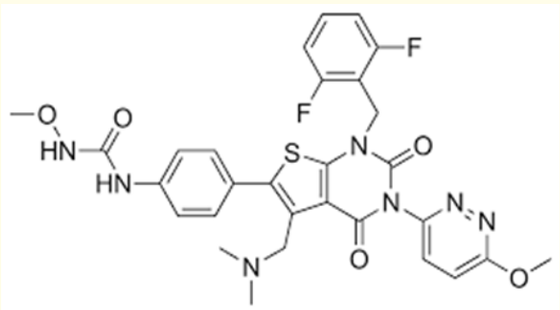

Figure 1: Chemical structure of Relugolix ($C_{29}H_{27}F_2N_7O_5S$).

The analytical methods such as UPLC-MS/MS [5], UPLC-MS [6], LC-MS/MS [7] RP-UPLC [8] RP-HPLC [9,10] were developed for the estimation of Relugolix and its impurities were studied by different authors in pharmaceutical dosage forms as well as biological fluids and some of the parameters were discussed in detail in Table 1.

Method	Mobile phase (v/v)	Column	Linearity (µg/mL)	Reference
UPLC-MS/MS (Rat plasma)	0.1% Formic acid: Acetonitrile	C18	0.0007-1.000	[5]
UPLC-MS (Impurities)	Acetonitrile: 0.1% ortho phosphate (50:50)	C18	1.25-7.5	[6]
LC-MS/MS (Rabbit plasma)	Acetonitrile: 0.1% Formic acid (90: 10)	Inertsil C18	0.0039-1.5	[7]
RP-UPLC (Gradient mode)(Impurities)	1 % ortho phosphoric acid: Acetonitrile	BEH RP-18	0.1-2.0	[8]
RP-HPLC	Acetonitrile: 0.1N Ammonium formate (55:45)	Zorbax	15-90	[9]
RP-HPLC (Gradient mode)LC-MS, HRMS, NMR	0.1% Formic acid: Acetonitrile	BEH C18	-	[10]

Table 1: Review of analytical methods.

Conclusion

The authors have briefly reviewed the analytical methods for the estimation of Relugolix in pharmaceutical dosage forms as well as biological fluids.

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