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A Review on Analytical Method Development and Validation for Lusutrombopag

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Abstract: ***Chemistry is the study of matter and composition, its structure, its physical properties, and its reactivity. Although there are different ways to study chemistry, traditionally we divide it into five areas: organic chemistry, inorganic chemistry, biochemistry, physical chemistry, and analytical chemistry. Patients with chronic liver disease, thrombocytopenia is allegedly produced by reduced thrombopoietin (TPO) production in the impaired liver, accelerated platelet destruction due to an enlarged spleen, and decreased hematopoietic capability of the bone marrow as a result of alcohol use or viral infection. . Here, we report our real-life experience of lusutrombopag for cirrhotic patients with low platelet counts. Lusutrombopag is a synthetic form of a protein that rises production of platelets (blood-clotting cells) in your body. Due to use of Lusutrombopag it lowers the risk of bleeding by increasing platelets in your blood. In adults Lusutrombopag is used to treat thrombocytopenia (a lack of platelets in the blood) with chronic liver who are scheduled to undergo a medical procedure.***

Keywords: Anti-thrombolytic drug, thrombocytopenia, Spectroscopic Methods, Chromatographic Methods, Characterization

1. Introduction[1]

Patients with chronic liver disease and by decreased thrombopoietin (TPO) production in the impaired liver it causes thrombocytopenia, accelerated platelet destruction due to an enlarged spleen, and reduced hematopoietic capability of the bone marrow as a consequence of alcohol use or viral infection. The number of thrombocytopenia keeps to increase with the degree of exacerbated hepatic function. Platelet reduction (platelet count <150, 000/μL) in patients with liver cirrhosis is as high as 76% compared with 6% in patients without cirrhosis. Complications including liver cancer, gastro esophageal avarices, as cites, and hepatic encephalopathy are common and require frequent invasive procedures in patients with chronic liver disease. Thus, thrombocytopenia is an important problem that must be medicated earlier to these procedures.

Lusutrombopag is not option for thrombocytopenia, it will not make your platelet counts normal.

Lusutrombopag may too be employed for desires not listed in this medication guide

1.1 Lusutrombopag side effects[2]

Common side effects may include:

- Weakness
- vision or speech Problems
- Swelling in an arm and leg
- Fever
- Stomach pain, vomiting
- jaundice
- Bloody or tarry stools, coughing up blood or vomit
- Headache

2. Drug Type[3]

2.1 Thrombopoietin-agent

This medication is employed by people with chronic liver disease and a definite blood (low platelet count) that are arranged to have a medical or dental procedure. Low platelet count is gives more the risk of too much bleeding during certain procedures. This medication rises the growth of platelets by your body to help stop too much bleeding from the procedure.

2.2 Mechanism of action[3]

It is the biological actions of endogenous thrombopoietin (TPO) by acting as an agonist for the thrombopoietin receptor (TPOR) termed on megakaryocytic. It stimulates the proliferation and differentiation of bone marrow progenitor cells into megakaryocytic, which undergoes maturation to act as precursor cells for platelets. It essentially binds to the transmembrane domain of the receptor and cause thrombocytopoiesis by targeting the same signal transduction system as that of endogenous TPO, which involves the activation of JAK and STAT pathways. A single megakaryocyte makes and releases thousands of platelets upon maturation and series of remodeling events. Lusutrombopag indicates high specificity regards human TPORs when compared to marine TPORs. It may affect other hematopoietic lineages involving elytroid, granulocytic and lymphoid lineages. One case of rises leukocyte and erythrocyte counts that incessant for over 120 days was reported following administration in a patient with liver cirrhosis (LC) due to hepatitis C virus.

3. Analytical Method Devlopment[4]

- Analytical method development and validation play important part in the determination, development and production of pharmaceutical products.
- Effective method development certified that laboratory

resources are developed, while methods connect the principles
- Methods may also support safety and characterization studies or determinations of drug performance.
- Analytical methods are employed for the qualitative and quantitative estimation of concentration of a compound by using different techniques such as titrations, spectroscopies, chromatography, and gravimetric analysis. Analytical methods Journals use the idea of qualitative and qualitative analysis.

3.1. Significance of Analytical Method Devlopment[4]

- Analytical methods development and validation take important part in the determination.
- Development and manufacture of pharmaceuticals.
- The official test methods that result from analytical method development are used by quality control laboratories to check the identity, purity, potency, and performance of drug products.
- To provide compliance with quality and safety standards.

3.2 Types of Analysis

- Qualitative analysis: The Qualitative analysis describes the nature of substance, and if it is mixture, the nature of the component present.
- Quantitative analysis: The Quantitative analysis describes the elemental composition of the substance and the quantitative distribution of each component.

3.3 Need for analytical method development[5-7]

The reasons for the development of newer methods of drug analysis are: No any official method is available in IP, BP and USP for estimation of drug or combination of drugs.

A actual analytical procedure for the drug may not be available in the literature due to patent regulations; Analytical methods may not be available for the drug in the form of a formulation due to the interference produced by the formulation incipient.

Spectrometric techniques:
- Ultraviolet and VisibleS pectrophotometry
- X-Ray Spectrophotometry
- Atomic Spectrometry
- Infrared Spectrometry
- Raman Spectrometry
- Fluorescence and Phosphorescence Spectrometry
- Nuclear Magnetic Resonance Spectroscopy
- Electron Spin Resonance Spectroscopy

ChromatographicTechniques:
- Gas Chromatography
- High Performance Liquid Chromatography
- Thin Layer Chromatography
- High Performance Thin Layer Chromatography

Selecting an Analytical Method
- Accuracy.
- Precision.
- Sensitivity.
- Specificity and Selectivity.
- Robustness and Ruggedness.
- Scale of Operation.
- Equipment, Time, and Cost.
- Making the Final Choice.

3.4 PK Analysis[8-9]

A first Step in the Drug Development Process. Pharmacokinetics (PK) determines what the human body does to a given pharmaceutical, from the time of administration to absorption, distribution, metabolism, and excretion from the body. To check the safety and efficacy of these molecules and also perform robust bioanalytical pharmacokinetic (PK) assays that can accurately quantify drug concentrations are needed. This data are employed to evaluate drug exposure and safety as well as to identify PK/pharmacodynamics (PD) relationships.

3.5 Drug Profile of Lusutrombopag: [10-14]

Lusutrombopag is employed to treat thrombocytopenia, a condition of abnormally low platelet counts in adult patients with severe liver dysfunction who are arranged to undergo a medical or dental procedure. Low platelet counts can produces to uncontrollable bleeding during surgery.

Figure 1: Structure of Lusutrombopag

Table 1: Drug profile of Lusutrombopag[15-18]

	LUSUTROMBOPAG
Molecular weight	591.54gm/mole
Chemical formula	C29H32Cl2N2O5S
Drug Category	Antihemorrhagics
Chemical Name	(*E*)-3-[2, 6-Dichloro-4-[[4-[3-[(1*S*)-1hexoxyethyl]-2-methoxyphenyl]-1, 3-thiazol-2-yl]carbamoyl]phenyl]-2-methylprop-2-enoic acid
Appearance	White to slightly yellow wise white powder
Solubility	Freely soluble in N, N dimethylformamide, slightly soluble in ethanol and methanol, very slightly soluble in acetonitrile, and insoluble in water
Melting Point	142-145°C
Pka	3.778
LogP	8.08
Uses	It used to treat thrombocytopenia

4. Literature Review

4.1 Official method for Estimation of Lusutrombopag[19-20]

Pharmaco kinetic method: UPLC-MS/MS[21]
Stationary phase – lusutrombopag and poziotinib on a CORTECS UPLC C18 column (2.1.50mm, 1.6um), Mobile

phase – Acetonitrile and water containing 0.1% formic acid and Flow rate – 0.4ml/min.

Lusutrombopag in Rat plasma: liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) [22]
Stationary phase – polar RP column (50.2.0mm, 4mm), Mobile phase – water and acetonitrile (20: 80v/v) containing 0.2% formicacid and Flow rate – 0.4 ml/min

4.2 Rationale of proposed work[21-22]

Lusutrombopag is FDA approved for the Thrombocytopenia in adults with chronic liver disease.

- It is noted that none of the methods are reported for the lusutrombopag.
- Hence there is wide scope of Analytical methods to be developed for Lusutrombopag drug like UV –Visible Spectroscopy, HPLC, HPTLC and many more.
- The result of study can be helpful in welfare to the researchers who are in analytical field in the terms of analytical invention and benefits in future to the investigator at a considerably reliable, accurate speedy and uncomplicated and result can be easily understood.

5. Conclusion

Above review reveals that there is ample scope for Analytical method development and validation for the drug Lusutrombopag. Upon successful development and validation, the developed methods can be used for the routine analysis of lusutrombopag in various formulations. Further in future more analytical methods can be developed and used for pharmaceutical analytical application like HPTLC, HPLC and researcher can go up to LC MS.

Conflicts of interest:
The author reports no conflicts of interest.

Acknowledgment:
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