AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

Formulation Development and Compatibility Study of Parenteral Dosage Form Containing Antiemetic Drug Palonosetron

Srikant Pimple[1]*, Pravin Maurya[1], Akash Joshi[1], Krupal Salunke[1], Ruby Singh[1]
1. Research and Development, Emcure Pharmaceuticals Limited, Pune, Maharashtra, India.

ABSTRACT

The purpose of this study was to formulate a stable parenteral formulation of Palonosetron HCl 0.05 mg/mL which is pharmaceutically equivalent to Reference Drug Product. Preformulation study was performed to evaluate the compatibility of product with materials which come in contact with the product during manufacturing. Compatibility study was carried out with metal, silicon tubes, PVDF filters and stoppers. Thermal cycling and photostabilty study were also performed to ensure the stability of the product. Palonosetron injection was formulated by dissolving the API and excipients in WFI in a S.S vessel under continuous stirring. Stability studies at different conditions were also performed. Compatibility study results indicate that drug product was compatible with the product contact materials. Thermal cycling and photostabilty data indicates that there was no significant degradation in the formulation. As a part of Sterilization cycle development, terminal sterilization was performed at 121^0C for 15, 20 and 30 minutes time intervals and finalized cycle was 20 minutes. A stable Palonosetron Injection was developed and evaluated. Compatibility and accelerated stability studies at different conditions were performed and it can be concluded that the product is compatible with product contact materials, thermal and photostable.

Keywords: Palonosetron Hydrochloride, Compatibility Study, Thermal Cycling, Terminal Sterilization, Stability Study.

**Corresponding Author Email: Srikant.Pimple@emcure.co.in
Received 01 June 2015, Accepted 03 July 2015

Please cite this article as: Pimple S *et al*., Formulation Development and Compatibility Study of Parenteral Dosage Form Containing Antiemetic Drug Palonosetron. American Journal of PharmTech Research 2015.

INTRODUCTION

Chemotherapy is one of the main treatment methods for numerous types of cancer. However, it is capable of inducing the release of 5-HT3 from enter ochromaff in cells, which interacts with its receptors to cause vagal afferent nervous excitation, leading to the vomiting reflex. Nausea and vomiting are the two most common adverse reactions in cancer patients who receive chemotherapy. More than 70% of all patients with cancer who are receiving chemotherapy will experience nausea, vomiting, or both in the absence of any antiemetic. In addition, 10%–44% will experience anticipatory nausea and vomiting. Chemotherapy-induced nausea and vomiting (CINV) is a serious adverse effect of chemotherapy that limits patients' physical, mental, and functional capabilities and may cause a delay or cessation of treatment. Antiemetic therapy can reduce the incidence of CINV. Antiemetic agents are the most common intervention in the management of treatment-related nausea and vomiting (emesis) (N&V). The basis for antiemetic therapy is the neurochemical control of vomiting. It is well appreciated that a number of things (e.g., various insults, chemotherapeutic agents, radiation) may lead to the release of serotonin from the enterochromaffin of the gastrointestinal tract. Released serotonin may then bind to certain 5-HT3 receptors and promote nausea/vomiting. 5-HT3 receptor antagonists may ameliorate nausea/vomiting in a number of circumstances and have been utilized as important antiemetics for multiple conditions such as chemotherapy-induced nausea/vomiting (CINV), radiation-induced emesis (RIS), and postoperative nausea/vomiting (PONV). Palonosetron is a relatively new 5-HT3 receptor antagonist that was approved in 2003 by the US FDA for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderate to highly emetogenic cancer chemotherapy. It has at least 30-fold higher affinity for the 5-HT3 receptor compared with the first-generation 5-HT3 receptor antagonists like ondansetron, granisetron and dolasetron. Parenteral dosage forms and delivery systems include injectables (i.e., solutions, suspensions, emulsions, and dry powders for reconstitution), intramammary infusions, intravaginal delivery systems, and implants. The term parenteral has its derivation from the Greek words para and enteron, meaning beside the intestine, and denotes route other than the oral route. Through parenteral route, drugs are administered by injection under or through one or more layers of skin or mucous membrane into body tissues and many times directly into blood. Parenteral medications are a vital component of the modern therapeutic armamentarium. They offer a number of advantages over other dosage forms. The immediate availability of the drug to the system and successful administration of drugs sensitive to the digestive system are the most significant gains.

It also enhances the bioavailability. Parenteral delivery systems must be syringeable and injectable to allow for the simple and reproducible administration of a drug product. Maintenance of stability is a next major problem while formulating injection. The main objective of the present study was to formulate a stable formulation of Palonosetron Hydrochloride. All related studies such as compatibility study stability study were performed to make the formulation stable.

MATERIALS AND METHOD

Palonosetron Hydrochloride was procured from Emcure Pharmaceuticals Ltd. Pune, Mannitol was received from Roquette, Edetate Disodium Dihydrate, Trisodium Citrate Dihydrate, and Citric Acid Monohydrate were received from Merck and Water for Injection form Emcure Pharmaceuticals Ltd. Pune.

Bulk solution preparation:

Hot water for Injection was stored in a sterilized S.S. 316L jacketed manufacturing tank equipped with stirrer. Cooling of Water for Injection was done up to 20°C to 25°C by circulating chilled water through jacket of the manufacturing tank. Palonosetron Hydrochloride, Mannitol, Edetate disodium dehydrate, Sodium citrate dihydrate and Citric acid monohydrate were dissolved in Water for Injection under continuous stirring. pH of the bulk solution was adjusted with 1N HCl and/or 1N NaOH. Volume was adjusted with Water for Injection, and bulk solution was blanketed with nitrogen gas. pH of bulk solution (at 25°C) was recorded.

Filtration:

Bulk solution was filtered through Sterilized Optiseal Durapore PVDF cartridge filter 0.45micron, followed by sterilized Optiseal Durapore PVDF cartridge filter 0.22 micron.

Table 1: Manufacturing Formula and Manufacturing Steps

Sr. No.	Ingredients	Qty/ vial
1	Palonosetron Hydrochloride	0.056 mg
2	Mannitol	41.500 mg
3	Edetate Disodium dihydrate	0.50 mg
4	Trisodium citrate dihydrate	3.70 mg
5	Citric acid monohydrate	1.56 mg
6	Water for Injection	q.s to 1 mL
Manufacturing steps	**Material/Equipment used**	
Preparation of bulk solution	SS316L vessel	
Filtration	0.45 µm membrane PVDF filters and 0.22 µm membrane PVDF filter	
Filling	5 mL & 2 mL Clear glass vials	
Stoppering and Sealing	13 mm rubber stopper & 13 mm aluminium seal	

Filling & Sealing:

Filtered solution was filled in sterilized 5 mL and 2mL clear glass vials, stopper with 13 mm coated rubber stopper & sealed with aluminium seal.

Preformulation Study:

Preformulation is defined as that phase of research and development process, where physical, chemical and mechanical properties of drug substance are characterized alone and when combined with excipients in order to develop safe, effective and stable formulation. Excipients used in drug product were similar to reference listed drug and well documented in different pharmacopoeia. As a part of pre-formulation studies, the following studies were performed:

- Metal (SS316L) compatibility study
- Platinum cured silicone tubing compatibility study
- Filter compatibility study
- Stopper compatibility
- Thermal cycling (Freeze thaw & Cool thaw cycle)
- Photostabilty study
- Filter validation study

Compatibility study of Palonosetron Hydrochloride Injection with metal (SS 316L)

SS 316L vessel is used as storage tank for prepared solution and as such must not interact with the drug product. The effect of SS 316L vessel on formulation was tested. About 150 mL of the unfiltered bulk solution was stored into SS 316L sterile holding tank and was kept at room temperature for 48 hrs. Samples were periodically collected from the container at 24 and 48 hours and given for analysis of the bulk solution for description, Identification by HPLC, pH, Related Substances (RS) and assay. The analytical results are given in the Table 2.

Platinum cured silicone tube compatibility study with Filtered bulk solution

In pharmaceutical manufacturing, silicone tubing is used in transfer of solution and as such must not interact with the drug product. About 100 mL of the filtered bulk solution was stored into glass containers. Clean (soaked with WFI) and dried Platinum cured silicone tubing of approx.10 cm length was immersed into the glass container and kept at room temperature for 48 hrs. Samples were periodically collected from the container at 24, 48 & 72hours and given for analysis of the bulk solution for description, Identification by HPLC, pH, RS & assay. The analytical results are given in the Table 3

Compatibility study of Palonosetron Injection with PVDF membrane filters (0.45µm and 0.22 µm filter)

The compatibility study of filter is the most important test for sterility of final formulation. About 100 mL of the filtered bulk solution was stored into glass container. Clean and dried 0.45µm and 0.22µm PVDF membrane filter was immersed into the glass container and the container was kept at room temperature for 48 hrs. Samples were periodically collected from the container at 24, 48 hours and given for analysis of the bulk solution for description, Identification by HPLC, pH, RS & assay. The analytical results are given in the Table 4.

Compatibility of Palonosetron Injection with rubber stopper

The container-closure system is an essential part of the final presentation of a pharmaceutical product. It defines the closure, protection, and functionality of a container while it ensures the safety and quality of the drug product over the product shelf life. To establish the compatibility of Palonosetron Injection with rubber stopper, prepared bulk solution of Palonosetron Injection was filtered through 0.45micron and 0.22 micron PVDF membrane filters. Filtered solution was filled in 5 mL and 2 mL USP Type -I clear glass vials, stoppered and sealed with rubber stoppers and aluminum seal. Sealed vials were subjected at different Stability conditions. The analytical results of stopper compatibility study are given in the table 5 and 6.

Thermal Cycling (Freeze thaw & Cool thaw cycle) study

The Freeze thaw & Cool thaw cycle study ensures that the product attributes at the extreme conditions of temperature are not altered. This study was designed to simulate the conditions that the product may experience during shipping.

Cool thaw cycle study:

Cycle-I: Charge the samples in upright orientation in the refrigerator maintained at temperature between 2ºC to 8°C for 2 days. On 3rd day remove all vials from the refrigerator. Place the above samples in the 40 ± 2°C/75 ± 5 % RH chamber s for 2 days.

Cycle-II: On 5th day remove all the vials from the 40 ± 2°C/75 ± 5 %RH stability chamber. Store them in refrigerator maintained at temperature between 2ºC to 8°C for 2 days. On 7th day remove all vials from the refrigerator. Place them in the 40 ± 2°C/75 ± 5 %RH chamber for 2 days.

Cycle-III: On 9th day remove all the vials from the 40 ± 2°C/75 ± 5 %RH stability chamber. Store them in refrigerator maintained at temperature between 2ºC to 8°C for 2 days. On 11th day remove all vials from the refrigerator. Place them in the 40 ± 2°C/75 ± 5 %RH chamber for 2 days. Upon completion of Cycle-III, remove all samples from the 40 ± 2°C/75 ± 5 % RH chambers. Analyze the samples as per test parameters.

Cool thaw cycle study (Study-I)

Samples (Quantity)	**(2 to 8°C) Cold storage**	**40 ± 2°C/75 ± 5%RH Accelerated condition**	**(2 to 8°C) Cold storage**	**40 ± 2°C/75 ± 5%RH Accelerated condition**	**(2 to 8°C) Cold storage**	**40 ± 2°C/75 ± 5%RH Accelerated condition**
4 Vials	1st and 2nd day	3rd and 4th day	5th and 6th Day	7th and 8th day	9thand 10th Day	11th and 12th day
	← Cycle I →		← Cycle II →		← Cycle III →	

Thermal cycle (Freeze thaw & Cool thaw cycle) study

Cycle-I: Charge the samples in upright orientation in the freezer maintained at temperature between -10ºC to -20°C for 2 days. On 3rd day remove all vials from the freezer. Place the above samples in the 40 ± 2°C/75 ± 5 % RH chamber s for 2 days.

Cycle-II: On 5th day remove all the vials from the 40 ± 2°C/75 ± 5 %RH stability chamber. Store them in freezer maintained at temperature between -10ºC to -20°C for 2 days. On 7th day remove all vials from the freezer. Place them in the 40 ± 2°C/75 ± 5 %RH chamber for 2 days.

Cycle-III: On 9th day remove all the vials from the 40 ± 2°C/75 ± 5 %RH stability chamber. Store them in freezer maintained at temperature between -10ºC to -20°C for 2 days. On 11th day remove all vials from the freezer. Place them in the 40 ± 2°C/75 ± 5 %RH chamber for 2 days.

Upon completion of Cycle-III, remove all samples from the 40 ± 2°C/75 ± 5 % RH chamber s. Analyze the samples as per test parameters.

Thermal cycle (Freeze thaw & Cool thaw cycle) study (Study-II)

Samples (Quantity)	(-10 to -20°C) Freezer	40± 2°C/75 ± 5%RH Accelerated condition	(-10 to -20°C) Freezer	40± 2°C/75 ± 5%RH Accelerated condition	(-10 to -20°C) Freezer	40± 2°C/75 ± 5%RH Accelerated condition
4 Vials	1st and 2nd day	3rd and 4th day	5th and 6th day	7th and 8th day	9thand 10th day	11th and 12th day
	← Cycle I →		← Cycle II →		← Cycle III →	

The analytical results are given in the Table 7.

Photostability study:

The study was carried out in Photostability chamber with samples as follows:

Test Sample: Product filled in clear glass vials.

Control Sample: Product filled in clear glass vials wrapped by aluminium foil.

Carton Pack: Product filled in clear glass vials and packed in a carton.

The vials were exposed to light for an overall illumination of not less than 1.2 million lux hours

and an integrated near ultraviolet energy of not less than 200 watt hours/square meter. The analytical results of various tests performed in the Photostability studies are presented in the table 8.

Filter validation study

Bubble point test

A bubble point test is a test designed to determine the pressure at which a continuous stream of bubbles is initially seen downstream of a wetted filter under gas pressure. The point at which the first stream of bubbles emerges is the largest pore. Therefore, the bubble point value can be used to obtain a relative measure of the size of the single largest pore in a filter element. The purpose of this study was to determine the minimum product bubble point value for the sterilizing grade hydrophilic Durapore membrane wetted with Palonosetron. The bubble point of the filter was detected at 42.6 psi and the limit of the filter was 50 psi.

Leachable and Extractable test

Leachables are compounds that migrate into a drug product from the sample container closure (SCC) system under normal storage conditions. Both the primary SCC in direct contact with the drug product and the secondary SCC, which does not contact the drug product, can be sources of leachables. Extractables are the compounds that can be extracted from the SCC that might become leachables. The conditions of an extraction study are selected based upon the drug product and are designed to mimic a worst-case-scenario for then intended drug product. In the present study no leachable and extractable were found after analyzing the solution with FTIR and RP-HPLC.

Bacterial Retention study

Bacterial retention study was performed to check the sterility and integrity of filter. Performance of sterilizing grade filter has been demonstrated to be acceptable as the membrane retained the B. diminuta challenge concentration equal to or greater than $1*10^7$ cfu per cm2 of effective filtration area. So it was concluded that the challenge test was passed.

Stability study on development batch

To assess the stability of Palonosetron Injection; development batches, were kept at accelerated (40°C ± 2°C / 75 ± 5 % RH), intermediate (30°C ± 2°C / 65 ± 5 % RH) & long term (25°C ± 2°C / 60 ± 5 % RH) condition. The analytical results are presented in Table 9 & 10.

RESULTS AND DISCUSSION

Palonosetron Hydrochloride is an antiemetic and antinauseant agent. The main objective of the present study was to formulate a stable formulation of Palonosetron Hydrochloride Injection

Table 2: Metal (SS316L) compatibility data at room temperature (~20-25°C)

Test	Specification	Initial	24 hrs	48 hrs
pH	Between 4.5 and 5.5	5.0	5.0	5.0
Related Substances (by HPLC)				
Related compound A	NMT 1.0 %	0.07 %	0.07 %	0.05 %
Disteriomer	NMT 0.5 %	0.02 %	0.02 %	0.02 %
Any individual Unspecified unidentified impurity	NMT 0.5 %	0.01 %	0.02 %	0.02 %
Total Impurity	NMT 2.0 %	0.13 %	0.16 %	0.13 %
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount.	100.3 %	100.2%	99.9 %

Table 3: Platinum cured silicone tube compatibility data at room temperature (~20-25°C)

Test	Specification	Initial	24 hrs	48 hrs
pH	Between 4.5 and 5.5	5.0	5.0	5.0
Related Substances (by HPLC)				
Related Compound A	NMT 1.0 %	0.07 %	0.06 %	0.06 %
Disteriomer	NMT 0.5 %	0.02 %	0.02 %	0.02 %
Any individual Unspecified unidentified impurity	NMT 0.5 %	0.01 %	0.05 %	0.06 %
Total Impurity	NMT 2.0 %	0.13%	0.18%	0.18%
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount	100.3 %	99.3 %	98.0 %

Table 4: PVDF membrane filters compatibility data at room temperature (~20-25°C)

Test	Specification	Initial	24 hrs	48 hrs
pH	Between 4.5 and 5.5	5.0	5.0	5.0
Related Substances (by HPLC)				
Related compound A	NMT 1.0 %	0.07 %	0.07 %	0.06 %
Disteriomer	NMT 0.5 %	0.02 %	0.02 %	0.02 %
Any individual Unspecified unidentified impurity	NMT 0.5 %	0.01 %	0.01 %	0.01 %
Total Impurity	NMT 2.0 %	0.13 %	0.13 %	0.13 %
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount.	100.3 %	98.8 %	96.3 %

Table 5: Analytical Results of Stopper compatibility study:For 0.075 mg/1.5 mL

Tests	Specification	Initial	40°C ± 2°C/ 75 ± 5 % RH			30°C ± 2°C/ 65 ± 5 % RH	25°C ± 2°C/ 60 ± 5 % RH
			1 M	2 M	3 M	3 M	3 M
pH	Between 4.5 and 5.5	4.9	4.9	4.9	4.9	4.9	4.9
Related Substances (by HPLC)							
Related Compound A	NMT 1.0 %	BLQ	ND	ND	ND	ND	ND
Diasteriomer	NMT 1.0 %	0.24%	0.23 %	0.23 %	0.24 %	0.21%	0.21 %
Individual Unspecified unidentified impurity	NMT 1.0 %	BLQ	0.11%	BLQ	BLQ	BLQ	BLQ
Total Impurity	NMT 2.0 %	0.25 %	0.37 %	0.23 %	0.24 %	0.21 %	0.21 %
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount.	100.9 %	98.9 %	99.0 %	98.9 %	98.7 %	99.0 %

Table 6: Analytical Results of Stopper compatibility study:For 0.25 mg/5 mL

Tests	Specification	Initial	40°C ± 2°C/ 75 ± 5 % RH			30°C ± 2°C/ 65 ± 5 % RH	25°C ± 2°C/ 60 ± 5 %RH
			1 M	2 M	3 M	3 Month	3 Month
pH	Between 4.5 and 5.5	4.9	4.9	4.9	4.9	4.9	4.9
Related Substances (by HPLC)							
Related Compound A	NMT 1.0 %	BLQ	ND	ND	ND	ND	ND
Diasteriomer	NMT 1.0 %	0.24%	0.25 %	0.22 %	0.23%	0.23 %	0.23 %
Individual Unspecified unidentified impurity	NMT 1.0 %	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
Total Impurity	NMT 2.0 %	0.24 %	0.25 %	0.22 %	0.23 %	0.23 %	0.23 %
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount.	100.4 %	100.1 %	98.6 %	98.5 %	98.8 %	98.7 %

Table 7: Analytical results of Freeze thaw & Cool thaw cycle study:

Test	Specification	Initial	Study I	Study II
pH	Between 4.5 and 5.5	5.0	4.9	4.9
Related Substances (by HPLC)				
Related Compound A	NMT 1.0 %	Not Detected	Not Detected	Not Detected

Test	Specification	Initial	Study I	Study II
Disteriomer	NMT 1.0 %	0.24 %	0.23 %	0.23 %
Individual Unspecified unidentified impurity	NMT 1.0 %	BLQ	ND	ND
Total Impurity	NMT 2.0 %	0.24 %	0.23 %	0.23 %
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount	100.4 %	101.7 %	98.0 %

Table 8: Analytical results of Photo stability study:

Test	Specification	Initial	Test sample	Control sample	Carton pack
pH	Between 4.5 and 5.5	4.9	4.9	4.9	4.9
Related Substances (by HPLC)					
Related Compound A	NMT 1 %	0.24%	BLQ	0.19 %	0.20%
Disteriomer	NMT 1 %	ND	Not Detected	Not Detected	Not Detected
Individual Unspecified unidentified impurity	NMT 1 %	BLQ	0.03 %	0.03 %	0.03 %
Total Impurity	NMT 2.0 %	0.24%	BLQ	0.19 %	0.20%
Assay (by HPLC)	Not less than 90.0% and not more than 110.0% of labelled amount	100.4	99.6 %	98.7 %	99.5 %

Table: 9. Stability study for 0.075 mg/1.5 mL

Tests	Specification	Initial	40°C ± 2°C/ 75 ± 5 % RH			30°C ± 2°C/65 ± 5 % RH	25°C ± 2°C/60 ± 5 % RH
			1 M	2 M	3 M	3 M	3 M
pH	Between 4.5 and 5.5	4.9	4.9	4.9	4.9	4.9	4.9
Related Substances (by HPLC)							
Related Compound A	NMT 1.0 %	BLQ	ND	ND	ND	ND	ND
Diasteriomer	NMT 1.0 %	0.24%	0.23 %	0.23 %	0.24 %	0.21%	0.21 %
Individual Unspecified unidentified impurity	NMT 1.0 %	BLQ	0.11%	BLQ	BLQ	BLQ	BLQ
Total Impurity	NMT 2.0 %	0.25 %	0.37 %	0.23 %	0.24 %	0.21%	0.21 %
Assay (by HPLC)	NLT 90.0% and NMT 110.0% of labelled amount.	100.9 %	98.9 %	99.0 %	98.9 %	98.7 %	99.0 %

Table: 10. Stability study for 0.25 mg/5 mL

Tests	**Specification**	**Initial**	**40°C ± 2°C/ 75 ± 5 % RH**			**30°C ± 2°C/65 ± 5 % RH**	**25°C ± 2°C/60 ± 5 % RH**
			1 M	**2 M**	**3 M**	**3 M**	**3 M**
pH	Between 4.5 and 5.5	4.9	4.9	4.9	4.9	4.9	4.9
Related Substances (by HPLC)							
Related Compound A	NMT 1.0 %	BLQ	ND	ND	ND	ND	ND
Diasteriomer	NMT 1.0 %	0.24%	0.25 %	0.22 %	0.23 %	0.23 %	0.23 %
Individual Unspecified unidentified impurity	NMT 1.0 %	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
Total Impurity	NMT 2.0 %	0.24 %	0.25 %	0.22 %	0.23 %	0.23%	0.23 %
Assay(by HPLC)	NLT 90.0% and NMT 110.0% of labelled amount.	100.4 %	100.1%	98.6 %	99.5 %	98.8 %	98.7 %

0.05mg/mL in compliance with the reference drug product. Preformulation study was performed to evaluate the compatibility of drug product with different contact materials. Compatibility study of Palonosetron Injection with platinum cured silicon tubes, metal (SS316 L), PVDF membrane filters and stoppers were performed. Compatibility study results indicates that there was no significant degradation in Palonosetron Injection in contact with platinum cured silicon tubes, metal (SS316 L), and PVDF membrane filters at room temperature (~20-25 ^{0}C) over a period of 24 hours and 48 hours respectively (table 1, 2, and 3). Compatibility study of drug product with stopper was also studied at different time periods and results were found well within the specified limits (table 4 and 5). Thermal cycling and Photostability study was conducted on the drug product. Results obtained from Freeze thaw and Cool thaw studies indicate that the product was stable at the extreme of temperature conditions. It can withstand thermal excursions in the range of -10°C to 40°C ± 2°C/75 ± 5 % RH (table 6). In Photostability study no significant degradation was observed on Palonosetron Injection vials upon exposure to light so the product was photostable when stored in clear glass vials (table 7). Formulation was developed according to the reference drug product. The excipients used in the drug product were similar to the reference drug product and found compatible with the API. All excipients used in the formulation were well documented in different Pharmacopoeias. Accelerated stability study was also performed on Palonosetron Injection as they are packed in clear glass vials stoppered with rubber stoppers and sealed with aluminum seal. These batches are kept at accelerated (40°C ± 2°C / 75 ± 5 % RH), for 1, 2, and 3

month, and intermediate (30°C ± 2°C / 65 ± 5 % RH) & long term (25°C ± 2°C / 60 ± 5 % RH) for 3 month. All results obtained from stability studies were found to be well within the specified limits. Microbial study was also conducted on the drug product such as Bacterial endotoxin test, Sterility test, and Bioburden test and results were found satisfactory.

CONCLUSION

In the present investigation formulation of two different strength of Palonosetron Injection 0.075 mg/1.5 mL and 0.25 mg/5 mL were done. Compatibility study of drug product with product contact material was performed. Based on the results obtained it was concluded that Palonosetron Injection was found compatible with platinum cured silicon tubes, metal (SS316 L), PVDF membrane filters and stoppers. Results obtained from Thermal cycling and Photostability study also conclude that the dug product is stable at the extreme temperature and photostable. Accelerated stability studies at different conditions were performed and results were well within limits.

REFERENCES

1. Jian Huang, Xiao-Jia Wang, Ding Yu, Ye-Ning Jin, Lei-Zhen Zhen, Nong Xu, Wei Liu, Yong-Chuan Deng, Shi-Xiu Wu and Jia He, The effect of Palonosetron hydrochloride in the prevention of chemotherapy-induced moderate and severe nausea and vomiting, Experimental and Therapeutic Medicine , 20135 1420 : 1418-1426.
2. Miriam P. Rogers, and Linda Blackburn, Use of Neurokinin-1 Receptor Antagonists in Patients Receiving Moderately or Highly Emetogenic Chemotherapy, Clinical Journal of Oncology Nursing,August 2010, Volume 14, Number 4, 500-504.
3. Miller A D and Leslie R A: The area postrema and vomiting. Front Neuroendocrinol. 1994; 15 (4): 301-20.
4. Cubeddu L X: Mechanisms by which cancer chemotherapeutic drugs induce emesis. Semin Oncol, 1992, 19 (6 Suppl 15); 2-13.
5. Howard S. Smith, Lorraine R. Cox, Eric J. Smith, 5-HT3 receptor antagonists for the treatment of nausea/vomiting, Ann Palliat Med 2012;1(2):115-120.
6. Yogendra K. Gupta, Saravana P. Shanmugam, Biswa M. Padhy & Aman Goyal, Palonosetron induced anaphylaxis in an adult female, British Journal of Clinical Pharmacology, 70:1, 149–150.
7. Pawar Prashant B, Rawat SS, Mahajan YY, Galgatte UC, Maheshwari R K, Formulation development and evaluation of aqueous injection of poorly soluble drug made by novel

application of mixed solvency concept, International Journal of Drug Delivery, (2013) 5 152-166.

8. Rakesh P. Patel, Kaushal P. Patel,Kushal A. Modi, Chirayu J. Pathak, Formulation, development and evaluation of injectable formulation of Aspirin, Drugs and Therapy Studies 2013; 3(2):6-12.

AJPTR is

- **Peer-reviewed**
- **bimonthly**
- **Rapid publication**

Submit your manuscript at: editor@ajptr.com