No.31015/14/2016-PI.I
Government of India
Ministry of Chemicals & Fertilizers
(deptt. of Pharmaceuticals)
****

Janpath Bhavan, New Delhi

O R D E R BY REVIEWING AUTHORITY UNDER PARA.31 OF DPCO, 2013

Subject: **The review application of M/s Claris Injectables Ltd. under para 31 of DPCO against NPPA order No. S.O. 1405(E) dated 12/04/2016 for price fixation of Fluconazone Injection (200mg/100ml)**

Ref: **1) Applicant's Review application dated 26/4/2016**
2) NPPA Notification under review SO No.1405(|E), dated 12/4/2016
3) Record Note of discussions dated 18/5/2016

Whereas National Pharmaceuticals Pricing Authority (NPPA), Government of India, vide S.O. No 1405(E) dated 12/04/2016, fixed/revised ceiling price of Fluconazone Injection (200mg/100ml).

2. And whereas aggrieved by the above notification, M/s Claris Injectables Ltd. (hereinafter referred to as "Petitioner") submitted review application dated 26/4/2016 under para 31 of DPCO, 2013 for review of NPPA Price Fixation Order SO No.1405(E) dated 12/4/2016 fixing ceiling price of Fluconazone Injection (200mg/100ml) under DPCO 2013.

3. The grievance of the petitioner raised in their review application dated 26.4.2016 were sent to NPPA and the comments of NPPA were given to the Petitioner through the Record Note of Discussions held in the Review Hearing on 18.5.2016. Record Note of discussions is made part of the review order. After considering the comments of NPPA, the Petitioner has raised following points on which comments given by NPPA representative, during the hearing and Government's comments on the issue is recorded subsequently against each point:

Petitioner:

The Petitioner stated that vide S.O NO. 1405(E), NPPA has fixed a common price for all types of delivery systems for Fluconazole Injection 200mg/100ml i.e. Plastic Bottle, Glass Bottle and Non-PVC bags. They manufacture Fluconazole Injection 200mg/100ml in Non-PVC bag which has various therapeutic advantages against all the other conventional delivery systems. Glass Bottles can be sterilized at 121 degree as per international standards. Plastic bottle are sterilized at only at 109 Degree (only 3-4 log sterilization). It also requires Air Vent thereby possibility of nosocomial infection. It may not be self-collapsible, whereas Polypropylence Bottles can be sterilized at 121 degree as per international standards. It is leach free and there is no shedding of particulate matter.

In its written submission, the company stated the Pros and Cons of the various delivery systems from generation to generation i.e. from Glass Bottles to Non-PVC bags as under:-

a) <u>Glass Bottle</u> -

Pros - Glass Bottles can be sterilized at 121 degree as per international standards.

Cons - It involves 23 manuals steps of manufacturing, resulting in high chances of human contamination. Also due to the open technology manufacturing process, there are high chances of particulate contamination. It may also shed particles from rubber closures, and there is a possibility of leaching of Alkali from glass in the solution. It also requires Air Vent which increases the chances of nosocomial infection. Altleast 10-30% of the patients acquire Nosocomial infections and the figure rises to 28% for patients in ICU. It is heavy in weight and hence there is difficulty in transportation including chances of breakage of the same. It is also not self collapsible.

b) **<u>Plastic Bottles (Polypropylene bottles - BFS technology)</u> –**

Pros - Polypropylence Bottles can be sterilized at 121 degree as per international standards. It is leach free and there is no shedding of particulate matter.

Cons - It uses the semi-closed technology during manufacturing as filling and sterilization is done through separate process. Thus, there are high chances of contamination. Also due to High Moistuer Vapor Tranmission Rate (MVTR), there is a possibility of change in concentration of solution. It also requires Air Vent which increases the chances of nosocomial infection.

c) **<u>Plastic Bottles (Poly Ethylene bottles - AFFS technology)</u> –**

Pros - There is no human touch involved and no concern about alkali generated from glass. There are no chances of particulate matter except plastic bottle with rubber closures. It has a Low Moistuer Vapor Tranmission Rate (MVTR), hence the physico-chemical properties remain stable during shelf life.

Cons - Plastic bottle are sterilized at only at 109 Degree (only 3-4 log sterilization). It also requires Air Vent thereby possibility of nosocomial infection. It may not be self-collapsible.

d) **<u>Plastic Bottles with Eurohead</u>** -

Pros – Euorhead pack makes easy to administer co-medication, hence there is no air-vent required which reduces the chances of nosocomial infection.

Cons - There are chances of leaching of rubber and other particulate matters in the same.

The company representative also submitted the following advantages of using polypropylence bottle :-

1) Non-PVC Bag is sterilized at 121 degree Celsius for 15 minutes thus achieving more than 12 log sterilization. Hence, SAL objective is attained before doubling the time. Only at 121 degree Celsius, Spore forming bacteria like Bacillus Stearothermophilus, CL.Botulinium & CL.Sporogenes can be destroyed & thus Non-PVC bag ensures the Over kill model approach.

2) Non-PVC bag is multi-layered due to which there is no change in the physico – chemical properties of solution over a period of time. The outer layer protects against high MVTR (Moisture Vapour Transmission Rate). The middle layer provides strength & flexibility over wide range of temperature and the inner layer provides protection against chemical contamination & stability at different pH of solution.

3) The outer surface of this plastic container is sterile & the container is covered with a thick over pouch to protect sterility to ensure greater protection against infection.

4) Non-PVC bag have closed infusion delivery system. hence it does not require an air vent during administration due to which there is no air embolism, no air contamination & it prevents the chances of nosocomial infection, therefore, reduces the duration of Hospital stay & saves cost.

5) Non-PVC Bag is Di-ethyl Hexyl Pthalate (DEHP) free & hence it is non-carcinogenic. It is also environment friendly and there is no leaching of chemicals. Since it does not contain any plasticizers & adhesives, there is no chance of hazardous chemical contamination and particle contamination (which reduces the risk of circulatory blockage /pulmonary embolism). Hence, Non-PVC bag is a safe delivery system.

6) Non-PVC Bag is self-collapsible in nature due to which is there is proper utilization of the medicine. It also has higher adaptability which makes easier to handle, store and administer thereby reducing chances of transportation loss. Its higher flexibility allows it easily fit into pressure pump and also can be squeezed easily for quick infusion in emergency condition i.e enabling to use directly in Operation Theatre. Non-PVC bag has higher transparency, enabling higher visual inspection before administration.

7) Non-PVC Bag has an Extra Medication Port which is leach free rubber and makes easy to administer co-medication.

He further mentioned that amendment in DPCO 2013 vide S.O no. 1192(E) dated 22/03/2016, clearly states that the Government may notify a separate price considering the type of packaging with specific therapeutic rationale. **They**

requested that a separate price should be fixed for the different pack type of product.

4. NPPA Comments:

NPPA representative stated that section 6.3.3.6 of DPCO, 2013 and NLEM 2015 does not differentiate between the type of various packing material used for Parenteral preparation.

Company has requested for a separate price for their pack in non- PVC bag based on S.O. 1192(E) dated 22.3.2016. In this regard, he mentioned that NPPA has constituted committee of experts under Para 11(3& 4) of DPCO, 2013 for fixation for ceiling price/Retail price considering type of packaging. Company has not submitted representation under para 11(3&4) of DPCO, 2013 along with required information/documents for separate price. Company may submit representation if required so to NPPA indicating the therapeutic advantages and other physio-chemical properties of the polymer used in the packing etc. for consideration and approval of the Competent Authority. Company representative assured to submit supporting information/document for separate price to the NPPA with a copy to this office by 27.5.2016 for consideration.

5. Examination:

The view points of the applicant as well as the NPPA were heard and discussed with reference to various aspects of the matter. It was brought out by NPPA that as per the latest amendment in the DPCO,2013, an Expert Committee has been constituted in the NPPA to look into the veracity of the claims made by the Petitioner. Accordingly, the applicant company was advised to submit a formal representation to NPPA along with other necessary supporting documents and other material including scientific literature about the plyometric identity of so-called non-PVC bags.

6. Decision of the Government:

In view of the above, the Government has decided that the matter may be referred by NPPA to the Expert Committee constituted under para 11(4) to be examined on merits in the light of para 11(3) and 11(4) of DPCO, 2013, within a period of one month of the issue of this Order and to re-fix the prices of the formulation “Fluconazole Injection (200 mg/100 ml)”.

Issued on this date, the 7th day of September, 2016.

(M.K. Bhardwaj)
Deputy Secretary
For and on behalf of the President of India

To

1. M/s Claris Injectables Ltd., Claris Corporate Headquarters, Nr. Parimal Rly. Crossing, Ellisbridge, Ahmedabad-130 008.
2. The Member Secretary, NPPA, YMCA Cultural Centre Building, New Delhi 110 001.

Copy to:

(i) PS to Hon'ble Minister (C&F), Shastri Bhavan, New Delhi for information.
(ii) PSO to Secretary (Pharma), Shastri Bhavan, New Delhi for information.
(iii) Technical Director (NIC) for uploading the order on Department's Website.