No. 31015/30/2017-Pricing
GOVERNMENT OF INDIA
MINISTRY OF CHEMICALS & FERTILIZERS
DEPARTMENT OF PHARMACEUTICALS
……..

A- Wing, Shastri Bhawan,
New Delhi 110 001

Subject: **Review application of M/s Dr. Reddy's Laboratories Limited against price fixation of "Omeprazole Powder for Injection 20mg" vide NPPA order No. S.O. 247(E), dated 24.01.2017 issued under Drugs (Prices Control) Order, 2013 (DPCO 2013).**

Ref: **1) Review application dated 21.02.2017**
2) NPPA notification under review S.O. 247(E), dated 24.01.2017
3) Record Note of discussions held in the personal hearing held in the matter on 22.08.2017.

1. This is a petition under paragraph 31 of the Drugs (Prices Control) Order, 2013 (hereinafter called the DPCO) filed by M/s Dr. Reddy's Laboratories Limited (hereinafter called the petitioner) against notification S.O. No.247(E), dated 24.01.2017 issued by the National Pharmaceutical Pricing Authority (hereinafter called the NPPA) fixing the ceiling price of Omeprazole Powder for Injection 20mg

2. The petitioner has contended as under :-

(i) NPPA has erred in stating the correct dosage form and notified the Non-Scheduled formulation OMEPRAZOLE 20 MG POWDER FOR INJECTION instead of the scheduled formulation OMEPRAZOLE 20MG POWDER FOR ORAL LIQUID.

(ii) AND WHEREAS, the worksheet for calculation of ceiling price of formulations notified vide S.O. 247(E) dated 24th January, 2017 wrongly considered the Product as a Scheduled Formulation. Company submitted that the Product is a Fixed Dose Combination (FDC) of two distinct API's as mentioned in S.O.701 (E) dated 10th March, 2016 namely: Omeprazole Powder for oral liquid 20 mg at Sr. No.20.1.1 and Sodium Bicarbonate Injection (as per IP) at Sr. No. 29.6 and since the combination is not mentioned under Drugs (Prices Control) Amendment Order, 2016 (hereinafter referred to as DPCAO, 2016), company's formulation is a Non Scheduled Formulation. The Product is also notified by Drug Controller General of India (DCGI) as a FDC in the latest available list of approved FDCs.

(iii) AND WHEREAS, the Product is an advanced formulation as immediate release oral Proton Pump Inhibitor (PPI). PPI is a differentiated dosage form with an additional therapeutic value with significantly improved pharmacokinetic profile over its Powder for Oral Suspension counterparts.

(iv) AND WHEREAS, the PPI reduces the intragastric acidity (acid concentration in stomach) by 78% within first 30 mins of ingestion. Since the GI transit time is low for powders and especially effervescent powders, the Product passes through the stomach

quickly and further the micro-environmental alkaline pH protects the Omeprazole from degradation in stomach with simultaneous release of carbon dioxide that enhances the motility thereby reducing the GI transit time. The Product fills the gap which was present in the PPI market by offering a PPI formulation available in drinkable form.

(v) AND WHEREAS, company's formulation is an innovative powder formulation that offers instant in acute gastritis and is also ideal for critically ill patients on Ryle's tube feeding, enhancing patient compliance. Brief mode of action of Omez Insta:

a. The Product raises intragastric pH and thereby protects Omeprazole from acid degradation. This leads to fast and effective absorption of Omeprazole resulting in rapid inhibition of acid secretion.

b. Buffer present in the Product stimulates gastrin release which in turn stimulates parietal cells and switch on the proton pumps which enable Omeprazole to block them more effectively.

c. It provides instant relief with a lasting effect by bringing up the pH level to > 6 within a minute.

d. Xanthan gum acts as a suspending agent and its solution are stable in presence of enzymes, acids and bases provide stability in acidic environment.

e. Xylitol provides distant cooling effect upon dissolution of its crystals which aids a cooling effect along with peppermint with rapid inhibition of acid secretion leads to better patient compliance.

f. Sucrose along with sucralose and Xylitol takes good care of palatability especially for the patients with difficult in swallowing.

2. AND WHEREAS, Company has further submitted papers from various independent authorities satisfying the aforesaid claims.

3. AND WHEREAS, NPPA has erred in considering the Product as a Scheduled formulation and has wrongly considered the same for calculation of ceiling price of Omeprazole Powder for Injection 20 Mg under the provisions of Para 6 of DPCO, 2013.

Under the circumstances:

a. The Product is a Non-Scheduled Formulation as per the provisions of the DPCO as the composition is not mentioned in the National List of Essential Medicines, 2015 and subsequently also in the First Schedule of DPCO, 2013.

b. Further, the dosage of the Product is not 'powder for injection' as notified by NPPA but an innovative "immediate release oral Proton Pump Inhibitor (PPI) powder for suspension", considering the explanation note 2 of DPCAO, 2016, the Product is again to be classified as a Non-Scheduled Formulation.

c. Thus, NPPA must not consider the Product in calculation of the ceiling price of the aforesaid formulation as it is a Non Scheduled Formulation as per the provisions of

DPCO, 2013.

d. Since, company's formulation is Non-Scheduled, ceiling price under Para 4 or Para 6 cannot be made applicable and NPPA must withdraw the notified ceiling price for aforesaid mentioned formulation namely: OMEPRAZOLE 20MG POWDER FOR SUSPENSION / INJECTION.

4. Having been aggrieved by the fact that the Product was considered in calculation of ceiling price under Para 6, NPPA has committed an error of principal and to maintain equity of justice, the notified ceiling price of Omeprazole 20Mg Powder for Injection should be set aside and the Product should be deemed as a Non-Scheduled.

5. In view of the above, company requested this Department as under:-

a. To consider and conclude that NPPA had erred in pricing of OMEPRAZOLE 20 MG Powder for injection under Sr. 11 of S.O 247(E) dated 24th January, 2017.

b. To consider and conclude that the Product is a non-scheduled formulation and cannot be priced under para 4 or para 6 of DPCO, 2013.

c. Pass a speaking order in respect hereof.

d. Any other order in interest of this manufacturer.

3. **Comments of NPPA:**

In this regard, it is mentioned that ceiling price of **Omeprazole Powder for Oral Liquid 20mg** was notified as Rs. 1.14/gram vide S.O. 247(E) dated 24.01.2017 and revised to Rs. 1.11/gram vide S.O. 2058(E) dated 30.06.2017 as per para 4, 6, 10, 11, 14, 16, 17, & 18 of DPCO, 2013.

II. The company has stated that correct methodology was not followed in arriving at the ceiling price of **Omeprazole Powder for Oral Liquid 20mg**. The points raised by the company are not relevant. Price fixation has been done strictly in accordance with the provisions of DPCO, 2013. Details are as follows:**-**

Sl. No.	Company's Grievances	NPPA's comments
1.	Company pointed out that NPPA has erred in stating the correct dosage form and notified the non-scheduled formulation **Omeprazole 20mg Powder for Injection** instead of the scheduled formulation **Omeprazole 20mg Powder for oral liquid.**	NPPA fixed the ceiling price of **Omeprazole Powder for Oral Liquid 20mg** as Rs. 1.14/gram as per S.O. 247(E) dated 24.01.2017 based on the working sheet uploaded in NPPA website. In the notification due to typographical mistake, it came as Omeprazole powder for injection 20 mg. The same was rectified while giving WPI impact (S.O. 1039(E) dated 01.04.2017) and while giving GST impact (S.O. 2058(E) dated 30.06.2017).

2.	Company claimed that work sheet for calculation of ceiling price of formulation notified by S.O. 247(E) dated 24.01.2017 is wrongly considered their product as a scheduled formulation. Company has also stated that their product is a fixed dose combination (FDC) of 2 distinct API i.e. Omeprazole + Sodium Bicarbonate. Since, the combination is not mentioned under Drugs (Prices Control) Amendment Order, therefore, their formulation is a non-scheduled formulation. Company enclosed the manufacturing license copy of their formulation. Formulation under reference is also notified by Drug Controller General of India as a FDC in the latest available list of approved FDCs.	The ceiling price was fixed based on the data provided by AIOCD-AWACS for the month of August 2015. DOP vide letter no. F. No. 31015/44/2016-PI.I dated 11.07.2016 gave the following, directions: "NPPA to henceforth place a draft version of the Price Calculation Sheets for the proposed revised price notification, including wherever applicable, the Price to Retailer (PTR) and Moving Annual Turnover (MAT) values adopted for calculations, on the website of NPPA for 10 clear working days to invite comments from the affected pharmaceuticals firms. Only after taking into account the comments or any additional data thus received within the given time period, the NPPA shall finalize the Ceiling and the Retail Prices. This issues with the approval of Hon'ble Minister (Chemicals & Fertilizers)". Accordingly, NPPA uploaded draft working sheet of proposed ceiling price of this formulation also on its website. This was on the website of NPPA for 10 clear working days. Dr. Reddy's Laboratories did not submitted any representation against the proposed retail price uploaded on NPPA's website.
3.	In view of the Company, their product is an advance formulation as immediate release oral Proton Pump Inhibitor (PPI) and PPI is a differentiated dosage for with an additional therapatic value with significantly improved pharmacokinetic profile over its powder for Oral suspension counterparts.	As decided in Authority Meeting, all variants of the product is to be taken while calculating the ceiling price of the formulation unless different variants of the formulation are specifically mentioned against any formulation in the NLEM 2015. Therefore, the representation of the company is not tenable.
4.	Company reiterated that PPI reduces the intragastric acidity (acid concentration in stomach) by 78% within first 30 minutes of ingestion. Since, the GI transit time is low for powders and specially effervescent powders, the product passes through stomach quickly and further the micro-environmental alkaline pH protects the Omeprazole from	As decided in Authority Meeting, all variants of the product is to be taken while calculating the ceiling price of the formulation unless different variants of the formulation are specifically mentioned against any formulation in the NLEM 2015. Therefore, the representation of the company is not tenable.

	degradation in stomach with simultaneous release of the carbon dioxide that enhances the motility thereby reducing the GI transit time. The product fills the gap which was present in the PPI market by offering a PPI formulation in drinkable form.	
5.	The mode of action of their product Omez Insta sachet are as follows: a. Omez Insta sachet raises intragastric pH and thereby protects Omeprazole from acid degradation. This lead to fast and effective absorption of Omeprazole resulting in rapid inhibition of acid secration. b. Buffer present in the product stimulate gastrin release which in turn stimulate parietal cells and switch on the proton pumps which enable Omeprazole to block them more effectively. c. It provides instant relief with a lasting effect by bringing up the pH level to > 6 within a minute. d. Xanthan gum acts as a suspending agent and its solution are stable in presence of enzymes, acids and basis provide stability in acidic environment. e. Xylitol provides distant cooling effect upon dissolution of its crystals which aids a cooling effect along with peppermint with rapid inhibition of acid secretion leads to better patient compliance. f. Sucrose along with sucralose and Xylitol takes good care of palatability especially for the patients with difficult in swallowing.	As decided in Authority Meeting, all variants of the product is to be taken while calculating the ceiling price of the formulation unless different variants of the formulation are specifically mentioned against any formulation in the NLEM 2015. Therefore, the representation of the company is not tenable.
6.	Company again reiterated that NPPA has erred in considering the product as a scheduled formulation and has wrongly considered the same for calculation of ceiling price of Omeprazole powder for injection 20 mg under the provisions of para 6 of DPCO, 2013.	As decided in Authority Meeting, all variants of the product is to be taken while calculating the ceiling price of the formulation unless different variants of the formulation are specifically mentioned against any formulation in the NLEM 2015. Therefore, the representation of the company is not tenable.

III. Company has not challenged in any Court in respect of ceiling price fixation for **Omeprazole Powder for Oral Liquid 20mg** vide S.O. No. 247(E) dated 24.01.2017.

4. **Examination:**

The Drug Manufacturing Licence (DML), No.HFW-H(Drugs)471/05(Vol.II), dated 4.4.2016, issued by Health and Family Welfare Department, Baddi, Himachal Pradesh, to the company for **the product OMEZ INSTA contains the formulation 'Omeprazole powder for Oral suspension' and each sachet contain Omeprazole BP 20mg., which is a scheduled drug as per Section 20.1.1 of Schedule I.** As per DML, Sodium bicarbonate is used as **"buffer"**.

4.2 The medicinal usage of sodium bicarbonate emanate from its mild alkaline nature. In medicines, it primarily acts as **antacid** to treat indigestion. As evident from NLEM, it is also classified as API under serial No.29.6 for injectable usage for correcting electrolyte and acid-base disturbances. As such, **technically Sodium bicarbonate can be used either as API or an excipient.**

4.3 An excipient is a substance added along with the API for the purpose of long-term stabilization, bulking up solid formulation that contain API in small amounts (thus often referred to an "bulking agents", "fillers" or "diluents"). The excipients also generally confer a therapeutic enhancement on the active ingredient in the final dosage form.

4.4 In the instant case, the product has been licensed to be manufactured with main API Omeprazole and Sodium Bicarbonate as **buffer.** The buffering agents are weak acids or bases used to maintain the acidity (pH) of a solution near the desired level after the addition of another acid or base. The function of the buffering agents is to prevent a rapid change in pH or acidity level or any solution. **As such, the buffering agent is used in the instant case as an excipient and not as an API.** The applicant has tried to prove that their product is similar to an Fixed Dose Combination (FDC), approved by DCG(I), fact remains that the DML do not reflect that OMEZ INSTA is a combination of two APIs. **Therefore, the subject formulation does not qualify to be treated as 'non-scheduled formulation'**. While fixing the ceiling price of the formulation, all variants of the product is to be taken unless different variants of the formulation are specifically mentioned against any formulation in the NLEM, 2015. Since, the APIs used in the drug are scheduled formulations, the representation of the company is not tenable.

4.5 It is worth mentioning here that the company has not complied with the ceiling price notified by NPPA. Para 31 of DPCO, 2013 states that "***……pending a decision by the Government on the application submitted under the above paragraph, no manufacturer shall sell a scheduled formulation or a new drug, as the case may be, at a price exceeding the ceiling price or retail price, as the case may be, fixed by the Government of which a review has been applied for."*** Since the company has not complied with the notified price, the review application may be rejected.

5. **Government Decision:**

"The Drug Manufacturing Licence does not reflect that OMEZ INSTA is a combination of two APIs. Omeprazole is the API and Sodium Bicarbonate is a buffer. Therefore, the formulation does not qualify to be treated as 'non-scheduled formulation'."

"The company has not complied with the price notified vide SO 247(E), dated 24.01.2017 before filing the review application, as provided under para 31 of DPCO, 2013. Therefore, the review petition stands rejected"

Issued on this date, the 28th day of November, 2017.

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

To

1. M/s. Dr. Reddy's Laboratories Limited,
   Global Generics – India,
   7-1-27, Ameerpet,
   Hyderabad – 500016.

2. The Member Secretary,
   National Pharmaceutical Pricing Authority,
   YMCA Cultural Centre Building, New Delhi-110001

Copy to :

1. PS to Hon'ble Minister (C&F), Shastri Bhawan, New Delhi for information.
2. PSO to Secretary (Pharma), Shastri Bhawan, New Delhi for information.
3. T.D., NIC for uploading the order on Department's Website