No. 31015/13/2017-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 Sun Pharma Laboratories Ltd. against price fixation of "Methylprednisolone Injection 40mg/ml" vide NPPA order No. S.O. 248(E), dated 24.01.2017 issued under Drugs (Prices Control) Order, 2013 (DPCO 2013).**

Ref: **1) Review application dated 20.02.2017**
2) NPPA notification under review S.O. 248(E), dated 24.01.2017
3) Record Note of discussions held in the personal hearing held in the matter on 30.05.2017.

1. This is a petition under paragraph 31 of the Drugs (Prices Control) Order, 2013 (hereinafter called the DPCO) filed by M/s Sun Pharma Laboratories Ltd.(hereinafter called the petitioner) against notification S.O. No.248(E), dated 24.01.2017 issued by the National Pharmaceutical Pricing Authority (hereinafter called the NPPA) fixing the ceiling price of Methylprednisolone Injection 40mg/ml.

2. The petitioner has contended as under:-

I. NPPA has displayed the draft working sheet of 31 formulations including captioned formulation on NPPA website on 26.10.2016. The sheet captured 3 packs of company, out of which PTR of 2 packs viz. DEPOPRED 40 MG INJECTION 1 ML, and DEPOPRED 40 MG INJECTION 2 ML were erroneously captured than actual data of August 2015. Company had submitted their representation dated 07.11.2016 along with necessary documents within 10 working days of draft working sheet display on NPPA website, and subsequently on 22.11.2016, and 02.12.2016. Moreover, 1 pack DEPO MEDROL 40 MG INJECTION 5 ML of M/S PFIZER with MAT MS less than 1% has been included in the ceiling price calculation, which is not as per provision of DPCO 2013.

II. Company further submitted that IVEPRED 40 MG INJECTION 1 ML pack, being a lyophilized version of Methylprednisolone Inj 40 mg/ml is a non-scheduled formulation, hence should be excluded from ceiling price calculation, as per explanation note (2) of Department of Pharmaceuticals notification No. 701 (E) dated 10.03.2016. Company had presented this fact in their representation to the good office of NPPA. They submitted the sample pack of IVEPRED 40 MG INJECTION 1 ML to confirm its composition.

III. Further, they had duly submitted supporting documents as required under NPPA Office Memorandum F. No. 8(35)/2016/DP/NPPA- DIV.II, dated 26.10.2016, and NPPA letter F.No.7(49)/2016/DP/NPPA/Div.II dated 16.11.2016.

IV. In view of the above, company requested this Department to issue necessary directives to NPPA to consider their representation and to recalculate the ceiling price of the said formulation.

3. **Comments of NPPA:**

(i) Ceiling price of Rs. 44.53 per ml for **Methylprednisole 40mg/ml Injection** was notified vide S.O. 248(E) dated 24.01.2017 as per para 4, 10, 11, 14, 16, 17 & 18 under DPCO 2013.

(ii) Company has stated that correct methodology was not followed in arriving at the ceiling price for **Methylprednisole 40mg/ml Injection**. The points raised by the company are not relevant. Price fixation has been done strictly in accordance with the provisions of DPCO, 2013 and as per the decisions of 27th Authority meeting held on 29.3.2016. Details are as follows:**-**

Sl. No.	Company's Grievances	NPPA's comments
1.	Company has pointed out PTR of (a) its product Depopred 40mg injection 1ml & Depopred 40mg injection 2ml was taken incorrectly in the working sheet while computing the ceiling price company has also pointed out that PTR of Deepo Medrol 40mg Injection 5ml has included in the working sheet having less than 1% market shear (b) Company has challenged the inclusion of their product Ivepred 40mg Injection in working sheet being a Lyophilized version of Methylprednisole 40mg/ml Injection.	NPPA has fixed the ceiling price for **Methylprednisole 40mg/ml Injection** as per the data provided by pharmatrac for the month of August, 2015. M/s Intas Pharmaceuticals Limited, M/s Pfizer Limited & M/s Neon Laboratories also submitted representation prior to notification. The representation of M/s Sun Pharma Laboratories Ltd. alongwith the representation of other companies were examined and the same were not considered in the Authority meeting.

(iii) Company has not challenged any notification in respect of **Methylprednisole 40mg/ml Injection** in the Court.

4. During the personal hearing, the representatives of the company made following further submissions -

1. The comment of NPPA that "the applicant's representation was examined and the same was not considered in the Authority meeting" is without specifying any reasons or basis for not considering the representation.
2. Company requested that in case the representation filed by the company against the draft calculation sheet is not being considered by NPPA, same should be communicated to the company along with the reasons.
3. Revised ceiling price should be notified after
    a. Considering correct PTR of our 2 products viz. DEPOPRED 40 MG INJECTION 1 ML, and DEPOPRED 40 MG INJECTION 2 ML for which company has duly submitted supporting documents as required under

NPPA OM F. No. 8(35)/2016/DP/NPPA-Div-II dated 26.10.2016, and NPPA letter F. No. 7(49)/2016/DP/NPPA/Div-II dated 16.11.2016.

b. Excluding 1 pack namely DEPO MEDROL 40 MG INJECTION 5 ML of M/S PFIZER with MAT MS less than 1%.

IVEPRED 40 MG INJECTION 1 ML qualifies for exclusion from ceiling price calculation as per provisions made in the applicable law as incorporated vide explanation no. 2 of SO 701 (E) dated 10.03.2016, issued in DPCO amendment 2016, on the recommendations of NLEM Committee, and this Hon'ble Reviewing Authority's order dated 29.11.2016 in Ciprofloxacin 250/500 mg tablet matter, which read as **"The existing Schedule-I of DPCO 2013 is very clear that "the formulations developed through incremental innovation or novel drug delivery systems like lipid/liposomal formulations, sustained release/controlled release etc. should be considered as included only if specified in the list against any medicine". NPPA may also be directed to comply with these provisions of Schedule-I."**

A. IVEPRED 40 MG INJECTION 1 ML is parenteral (Intramuscular and Intravenous) form of methylprednisolone sodium succinate, particularly suitable for the treatment of clinical conditions, in which **effective and rapid** glucocorticoid activities are required. Through Ivepred product, we cater to the patient segment wherein rapid glucocorticoid activities are required, sometimes in initial emergency use, which cannot be met with our other products like Depopred -1 ml, Depopred-2ml.

B. IVEPRED 40 MG INJECTION 1 ML contains methylprednisolone sodium succinate 40 mg, and administered by Intravenous/ Intramuscular route. DEPOPRED 40 MG INJECTION 1 ML and DEPOPRED 40 MG INJECTION 2 ML contains methylprednisolone sodium acetate 40 mg, and administered by Intra-arterial/intramuscular route. It is pertinent to be noted that Intramuscular injections give lower peak values than intravenous injections, thus IVEPRED 40 MG INJECTION 1 ML when administered through I/V route provides better bioavailability than to DEPOPRED 40 MG INJECTION 1 ML, and DEPOPRED 40 MG INJECTION 2 ML.

C. The NLEM Committee has given thrust on three parameters, while discussing the need of affordable medicines in the Country i.e. Safety, Efficacy & Cost Effectiveness of the drugs. It is apparent from the current scenario NPPA is leaving behind the two important aspects i.e. Safety and Efficacy of the medicines and just focusing in the cost part, which is probably incorrect and will ultimately force the manufacturer to discontinue the innovative parameters and will deprive the public at large from getting the advantage of these more safer and efficient formulations. Deviating from any one of outlined 3 principles would be like deviating from very essence of NLEM-2015, and schedule-I of DPCO 2013. While we optimize the price in order to bring cost effectiveness, at the same time we brought higher efficacy and safety profile with our lyophilized formulation.

Few advantages of lyophilized formulation vs. conventional formulation are outlined for ready reference.

Sr. No.	Lyophilized formulation of Methylprednisolone	Conventional formulation of Methylprednisolone
1	Lyophilized formulation of Methylprednisolone is available as Methylprednisolone Sodium Succinate for Injection.	Conventional formulation of Methylprednisolone is available as Methylprednisolone Acetate Injectable Suspension.
2	It can be given by intravenous route as Methylprednisolone sodium succinate is water soluble and forms a solution after reconstitution with diluent.	It cannot be given by intravenous route as Methylprednisolone acetate is water insoluble and forms a suspension in water.
3	Bioavailability is high as it can be given by intravenous injection and is a solution product.	Bioavailability is comparatively less as it cannot be given by intravenous route and is a suspension product.
4	Onset of action is fast as it does not form depo after injection.	Slow onset of action as it forms a depo at injection site and releases slowly from site into systemic circulation.
5	Less painful when given by intramuscular route as it forms a solution when reconstituted with a diluent.	More painful when given by intramuscular route as it is a suspension injection.

It is apparent form the above table that lyophilised formulation (IVEPRED 40 MG INJECTION) has significant therapeutic advantages over conventional formulation (DEPOPRED 40 MG INJECTION 1 ML, DEPOPRED 40 MG INJECTION 2 ML) of methylprednisolone 40 mg Injection.

NPPA representative submitted that ceiling price for the captioned formulation has been fixed as per the provisions of DPCO, 2013.

5. Examination:

The petitioner company has challenged the NPPA Order S.O. 248(E), dated 24.01.2017 for price fixation of their formulation **Methylprednisolone Injection 40 mg/ml** on the following grounds –

(i) NPPA has erroneously captured PTR of two formulations, viz. Depopred 40MG Injection 1ml and Depopred 40mg injection 2ml.

(ii) 1 pack Depo Medrol 40mg Injection 5 ml with less than 1% market share has been considered.

(iii) Ivepred 40mg injection 1ml pack, being a lyophilized version of Methylprednisolone Inj 40 mg/ml is a non-scheduled formulation and should be excluded from ceiling price calculation. The company stated that they submitted supporting documents in support of their claim to NPPA.

As regards (i) above, viz. PTR of two formulations - Depopred 40MG Injection 1ml and Depopred 40mg injection 2ml, being wrongly considered by NPPA, it is opined that NPPA may be directed to examine the documents submitted by the petitioner company and after getting confirmation of Pharmatrac, revise the ceiling price of the subject formulation, on merit.

Regarding (ii) above that 1 pack Depo Medrol 40mg Injection 5 ml with less than 1% market share has been considered, on going through the calculation sheet, it is found that NPPA has erred in considering the PTR of this formulation by combining the total market share of this brand of M/s Pfizer Ltd. DPCO does not recognize a company for average PTR but only medicines/formulations. Hence, NPPA may be directed to refix the ceiling price of subject formulation by excluding the PTR of Depo Medrol 40mg Injection 5ml having market share of only 0.11% (less than 1%).

In regard to point (iii) above, the company stated that Ivepred 40mg injection 1ml pack, being a lyophilized version of Methylprednisolone Inj 40 mg/ml is a non-scheduled formulation and should be excluded from ceiling price calculation. In support of their claim, the company submitted sample pack of Ivepred 40mg Injection 1ml to confirm its composition. The company further stated that IVEPRED 40 MG INJECTION 1 ML is parenteral (Intramuscular and Intravenous) form of methylprednisolone sodium succinate, particularly suitable for the treatment of clinical conditions, in which **effective and rapid** glucocorticoid activities are required. Through Ivepred product, cater to the patient segment wherein rapid glucocorticoid activities are required, sometimes in initial emergency use, which cannot be met with their other products like Depopred -1 ml, Depopred-2ml. IVEPRED 40 MG INJECTION 1 ML contains methylprednisolone sodium succinate 40 mg, and administered by Intravenous/ Intramuscular route. DEPOPRED 40 MG INJECTION 1 ML and DEPOPRED 40 MG INJECTION 2 ML contains methylprednisolone sodium acetate 40 mg, and administered by Intra-arterial/intramuscular route. It is pertinent to be noted that Intramuscular injections give lower peak values than intravenous injections, thus IVEPRED 40 MG INJECTION 1 ML when administered through I/V route provides better bioavailability than to DEPOPRED 40 MG INJECTION 1 ML, and DEPOPRED 40 MG INJECTION 2 ML.

In view of the specified therapeutic rationale of the formulation IVEPRED 40 MG INJECTION 1 ML, it is proposed that the NPPA may be directed to take the opinion of Expert Committee for including / excluding of this formulation while fixation of ceiling price of Methylprednisolone Inj 40 mg/ml.

6. <u>Government Decision:</u>

"NPPA is hereby directed to examine the documents submitted by the petitioner company about the actual PTR of two formulations - Depopred 40MG Injection 1ml and Depopred 40mg injection 2ml and after getting confirmation of Pharmatrac under intimation to the petitioner, examine the ceiling price of the subject formulation, on merit."

"NPPA is also directed to refix the ceiling price of subject formulation by excluding the PTR of Depo Medrol 40mg Injection 5ml having market share of

only 0.11% (less than 1%), as DPCO does not recognize a company for average PTR but only medicines/formulations."

"NPPA is further directed to take the opinion of Expert Committee on whether formulation IVEPRED 40 MG INJECTION 1 ML is a scheduled drug or not and fix the ceiling price of Methylprednisolone Inj 40 mg/ml accordingly."

Issued on this date, the 24th day of August, 2017.

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

To

1. M/s. Sun Pharma Laboratories Limited,
   Sun House, Plot No.201 B/1,
   Western Express Highway,
   Goregaon (E), Mumbai-400 063.
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