File No. 4-01/2013-DC (Misc. 13-PSC) (Pt. II) (Sub Part-1)
Govt. of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

Dated: 11 JAN 2024

NOTICE

Subject: Evaluation of certain pre 1988 permitted Fixed Dose Combinations (FDCs) de novo for manufacture for sale in the country without due approval from Central Licensing Authority -regarding.

This is with reference to this office letter dated 15.01.2013 whereby all the State/UT Drugs Controllers were requested to ask the concerned manufacturers in their State to prove the safety and efficacy of FDCs within 18 months which were permitted by State Licensing Authorities without due approval from the office of DCG(I).

In continuation to Hon'ble Supreme Court order dated 15.12.2017 and 14.02.2019, Ministry of Health & Family Welfare accordingly, vide order No. X11035/53/2014-DFQC (Part-IV) dated 02.02.2021 constituted an Expert Committee under the Chairmanship of Dr. M. S. Bhatia, Professor & Head, D/o Psychiatry, University College of Medical Sciences, New Delhi for examining 19 pre-1988 FDCs denovo licensed for manufacturing for sale in the country without due approval from Central Licensing Authority.

The Expert Committee submitted its report on these 19 FDCs claimed to be pre-1988 after holding a series of meetings as well as by providing hearing to the stakeholders wherein, the Committee after detailed deliberation considered following 02 FDCs as rational with certain conditions: -

Sr. No.	Name of FDC as per the public notice	Recommendations
1.	Imipramine Hydrochloride IP + Diazepam IP (25mg + 2mg & 25mg + 5mg) tablets	The committee recommended for continued manufacturing and marketing of the FDC. FDC shall be indicated for co-morbid anxiety conditions and duration of the treatment should not exceed 6 to 8 weeks.
2.	Chlorpheniramine Maleate IP + Ammonium Chloride IP + Sodium Citrate IP (2mg + 100mg + 50mg/5ml & 2.5mg + 125mg + 55mg/5ml Syrup	The committee noted that the firms are manufacturing the FDC in different strengths. The committee also noted that as per liierature available, Sodium Citrate is administratered 0.3gm to 1gm in divided doses in a day and Chlorpheniramine Maleate is administratered 4mg to 16mg in divided doses in a day. After detailed deliberation, the Committee recommended for continued manufacturing and marketing of the FDC with the condition that the firm should modify the prescribing information/label by clearly mentioning the dose schedule for adults and children keeping in view of the above stated dose range without exceeding the maximum permissible dose.

Accordingly, with the approval of the Ministry of Health and Family Welfare, it has been now decided to follow the following pathway for grant of product license by SLAs for these FDCs:

1. Applicants shall submit the requisite fees preferably through Bharatkosh for each FDC to CDSCO as specified under Drugs and Cosmetics Act, 1940 and existing Rules thereunder.
2. The applicant shall submit application to the concerned SLA as per the provisions of Drugs and Cosmetics Rules 1945 for grant of product manufacturing license giving the details of FDCs, stability studies data (06 months accelerated), Test Specification of the FDC alongwith Method of Analysis as well as label and other documents as required for grant of product license under Drugs and Cosmetics Rules.
3. State Licensing Authority shall grant the product license of such FDCs without NOC from DCG (I), if conditions of license under the Drugs and Cosmetics Rules, which need to be verified by SLA, are found to have been fulfilled. The SLAs shall verified the quality of such FDCs of each applicant/manufacturer, before grant of license.
4. Every manufacturer permitted to manufacture these FDCs shall submit the periodic safety update reports (PSURs) as per New Drugs and Clinical Trial Rules, 2019 to the Central Licensing Authority as defined in Rule '3' i.e. DCG(I). Failure to submit the PSURs shall be considered as contravention of these Rules.
5. Manufacturers shall comply with the recommendation of the expert committee w.r.t. revision of the prescribing information/label.

In view of above, you are requested to ask the concerned stakeholders to follow the above procedure for obtaining the manufacturing license w.r.t. FDCs declared as rational by Dr. M. S. Bhatia Committee.

Yours faithfully,

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

To:-
All State/UT Drugs Controllers/All Zonal/Sub Zonal offices of CDSCO.

Copy to:-
1. PPS to Secretary/AS(F&D)/JS(R), Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi.

F. No. 04-01/2013-DC (Misc. 13-PSC) (Pt. II) (Sub Part-1)
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

FDA Bhawan, Kotla Road,
New Delhi

Dated:
24 FEB 2025

To
All State/UT Drugs Controllers,

Subject:- Evaluation of certain pre 1988 permitted Fixed Dose Combinations (FDCs) de novo for manufacture for sale in the country without due approval from Central Licensing Authority -regarding.

Sir,

This is in continuation to this Directorate notice of even number dated 11.01.2024. As per this said letter, manufacturers who are already holding licenses from State Licensing Authorities for such FDCs before 01.10.2012 and did not apply to DCG (I) were required to submit their applications for Phase IV Clinical Trial protocol / Active Post Marketing Surveillance to this Directorate. The date for filing such applications expired on 11.07.2024 and already passed approximate 12 months from the date of above mentioned notice.

However, it is observed that most of the firms have not submitted their application to this Directorate. It has been decided that the manufacturers/stakeholders who were holding license prior to 01.10.2012 may submit their applications w.r.t category 'd' FDCs within 03 months from the date of issuance of this letter.

In view of above, without prejudice to legal validity of such product licenses, all the concerned manufacturers/stakeholders may be requested to submit their application within 03 months from the date of issuance of this letter, failing which appropriate regulatory action will be recommended from CDSCO.

Yours faithfully

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

Copy to:-

1. PS to JS(R), Ministry of Health and family Welfare, Nirman Bhawan, New Delhi
2. CDSCO Zonal and Sub-Zonal offices
3. Indian Drug/Pharmaceuticals Association Forum
4. Website of CDSCO