Editorial

Greetings from Drug Information Bulletin!

Government of India, for the first time has proposed to introduce over-the-counter (OTC) drugs in India through an amendment in the Drugs and Cosmetics Rules vide GSR. 393 (E) dated 25th May 2022 and allow their sale in the retail market without doctors’ prescription with several conditions like-(i) The maximum duration of treatment/use should not exceed five days. (ii) If the symptoms do not resolve the patient should consult Registered Medical Practitioner. (iii) Pack size may not exceed the maximum doses recommended for five days. (iv) Each pack of the drug may be accompanied with Patient Information Leaflet (PIL). (v) The indication claimed should be same as already approved by the Licensing Authority. This list contains 16 drugs used for treatment of minor symptoms. Stake holders of the health care of the country is demanding for creating an OTC policy of India and framing a suitable legislation since long back. Experts said that the demand is not fulfilled but Govt. has initiated this process through this draft notification. There are mixed reactions in the pharma industry and professionals like- this list is too small, some other categories have been left out etc. Some experts said that it was better to release list of “Pharmacists only medicines” providing prescription right to pharmacist for minor ailments like-nurses only medicines already existing in different developed countries. Hope this is an historical step to initiate releasing an OTC policy and release of a complete list of OTC products.
MINISTRY OF HEALTH AND FAMILY WELFARE
(Department of Health and Family Welfare)

NOTIFICATION
New Delhi, the 18th May, 2022

G.S.R. 356(E).—Whereas a draft of certain rules further to amend the Medical Devices Rules, 2017, was published as required under sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) vide notification of the Government of India in the Ministry of Health and Family Welfare (Department of Health and Family Welfare) number G.S.R. 23(E), dated the 18th January, 2022, in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), inviting objections and suggestions from persons likely to be affected thereby, before the expiry of a period of forty-five days from the date on which the copies of the Official Gazette containing the said notification were made available to the public;

And whereas, copies of the said Official Gazette were made available to the public on the 19th January, 2022;

And whereas, objections and suggestions received from the public on the said draft rules have been considered by the Central Government;

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Medical Devices Rules, 2017, namely:

1. (1) These rules may be called the Medical Devices (Third Amendment) Rules, 2022.

   (2) They shall come into force on the date of their publication in the Official Gazette.

2. In the Medical Devices Rules, 2017, after rule 43, the following rule shall be inserted, namely:

   “43A. Suspension and cancellation of licence.—(1) If the manufacturer or licensee fails to comply with any of the conditions of an import license, or any provisions of the Act and these rules, the Central Licensing Authority may after giving the manufacturer or licensee an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons thereof, cancel a license issued under rules, or suspend it for such period as it may thinks fit either wholly or in respect of any of the part of medical device to which it relates or direct the licensee to stop import, sale or distribution of the said medical device and, thereupon, order the destruction of medical device and the stock thereof in the presence of an officer authorised by the Central Licensing Authority, if in its opinion, the licensee has failed to comply with any of the conditions of the licence or with any provisions of the Act or the rules made thereunder:

   Provided that a person who is aggrieved by the order passed by the Central Licensing Authority under this rule may, within thirty days of the serving of the order, file an appeal to the Central Government, and the Central Government may, after such enquiry into the matter, as it considers necessary and after giving the said appellant an opportunity of being heard, pass such order as it thinks fit.”

[F. No. X.11014/4/2019-DR]

Dr. MANDEEP K. BHANDARI, Jr. Secy.

**New Drug: Pralsetinib Capsules**

Gavreto (Genentech)

**INDICATIONS AND USAGE:** GAVRETO is a kinase inhibitor indicated for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive nonsmall cell lung cancer (NSCLC) as detected by an FDA approved test. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

**DOSAGE AND ADMINISTRATION:** Select patients for treatment with GAVRETO based on the presence of a RET gene fusion. The recommended dosage in adults is 400 mg orally once daily on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking GAVRETO).

**DOSAGE FORMS AND STRENGTHS:** Capsules: 100 mg.

**CONTRAINDICATIONS:** None.

**WARNINGS AND PRECAUTIONS:**
- **Interstitial Lung Disease (ILD)/Pneumonitis:** Withhold GAVRETO for Grade 1 or 2 reactions until resolution and then resume at a reduced dose. Permanently discontinue for recurrent ILD/pneumonitis. Permanently discontinue for Grade 3 or 4 reactions.
- **Hypertension:** Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure (BP) prior to initiating GAVRETO. Monitor BP after 1 week, at least monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue GAVRETO based on severity.
- **Hepatotoxicity:** Monitor ALT and AST prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue GAVRETO based on severity.
- **Hemorrhagic Events:** Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.
- **Risk of Impaired Wound Healing:** Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.
- **Embryo-Fetal Toxicity:** Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective non-hormonal contraception.

**ADVERSE REACTIONS:** The most common adverse reactions (≥25%) were fatigue, constipation, musculoskeletal pain, and hypertension. The most common Grade 3-4 laboratory abnormalities (≥2 %) were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected), and increased alanine aminotransferase (ALT).

To report SUSPECTED ADVERSE REACTIONS, contact Blueprint Medicines Corporation at 1-888-258-7768 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS:**
- **Strong CYP3A inhibitors:** Avoid coadministration.
- **Combined P-gp and Strong CYP3A inhibitors:** Avoid coadministration. If coadministration cannot be avoided, reduce the dose of GAVRETO.
- **Strong CYP3A inducers:** Avoid coadministration. If coadministration cannot be avoided, increase the dose of GAVRETO.

**USE IN SPECIFIC POPULATIONS:**
- **Lactation:** Advise not to breastfeed.

Ref. USFDA

**Status in India:** Pralsetinib Capsule 100mg, approved by CDSCO

- Indicated for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer who require systemic therapy.

- Indicated for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer who require systemic therapy.

- Indicated for the treatment of advanced or metastatic RET-fusion positive thyroid cancer who require systemic therapy and who are radioactive iodine refractory (if radioactive iodine is appropriate) on 26.05.2022.

Industry source revealed that price of 60 capsules of 100 mg Pralsetinib (Gavreto) is about Rs. 2.5 lakhs. It is expected that this may be available at a lower price when this will be manufactured by Indian Manufacturers as it has been approved by CDSCO recently.
**Pregabalin Risk of severe respiratory depression**
The Health Products Regulatory Authority (HPRA) has announced that the product information for pregabalin-containing medicinal products will be updated to include a warning on respiratory depression and to add it as a possible adverse reaction with unknown frequency, following the conclusions of the PRAC. Pregabalin-containing medicinal products are indicated for the treatment of neuropathic pain in adults, as adjunctive therapy in adults for specific forms of epilepsy and for generalized anxiety disorder in adults. The PRAC reviewed safety data and concluded that pregabalin is associated with reports of respiratory depression in the absence of concomitant therapy with opioids or other central nervous system (CNS) depressants, in patients with and without other risk factors for respiratory depression. Healthcare professionals should be advised that patients with risk factors (compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of CNS depressants and older age (>65 years)) may be at higher risk of experiencing respiratory depression with pregabalin and dose adjustment may be necessary. Patients taking the medicine should be advised to contact their doctor if they experience trouble breathing or have shallow breaths and not to drink alcohol while taking pregabalin.

Reference: Newsletters and Reports, HPRA, 16 September 2021 (link to the source within www.hpra.ie)
(See also WHO Pharmaceuticals Newsletter No.2, 2021: Risk of severe respiratory depression in UK)

**Remdesivir Potential risk of sinus bradycardia**
Health Canada has announced that it will work with the manufacturer of remdesivir (Veklury®) to update the product information to include a warning on the potential risk of sinus bradycardia. Sinus bradycardia occurs when the heart beats slower than normal. Remdesivir is indicated to treat COVID-19 in adults with pneumonia who require oxygen. Health Canada assessed case reports of sinus bradycardia in patients receiving remdesivir in their database and in the literature and concluded that a link between the use of remdesivir and the risk of sinus bradycardia is possible.

Reference: Summary Safety Review, Health Canada, 18 August 2021 (link to the source within www.hc-sc.gc.ca) (See also WHO Pharmaceuticals Newsletter No.4, 2021: Risk of sinus bradycardia in Europe)

**Tinidazole Risk of fixed eruption**
The National Coordination Centre – Pharmacovigilance Programme of India (NCC-PvPI), Indian Pharmacopoeia Commission (IPC) has advised the Central Drugs Standard Control Organization (CDSCO) to revise the prescribing information leaflet (PIL) for tinidazole to include fixed eruption as an adverse drug reaction. Tinidazole is indicated for the treatment of intestinal amoebiasis, giardiasis, trichomoniasis and anaerobic infections. NCC-PvPI, IPC reviewed 71 case reports of tinidazole associated fixed eruption and a strong causal relationship between them was found. Reference: Based on the communication from IPC, India, November 2021 (ipc.gov.in)

**Tramadol Risk of urinary retention**
The NCC-PvPI, IPC has advised the CDSCO to revise the PIL for tramadol to include urinary retention as an adverse drug reaction. Tramadol is indicated for the treatment of moderate to severe pain, diagnostic procedures and surgical pain. NCC-PvPI, IPC reviewed seven reports of tramadol-associated urinary retention and a causal relationship between them was found.

Reference: Based on the communication from IPC, India, November 2021 (ipc.gov.in)

**DISCLAIMER:**
The Newsletter intends to provide updated and reliable information on medicines and other related issues in an attempt to equip healthcare professionals to take informed decision in recommending medicines to the patients. However, they are encouraged to validate the contents. None of the people associated with the publication of the Newsletter nor the organization shall be responsible for any liability for any damage incurred as a result of use of contents of this publication. The brand names of medicines, if mentioned, are for illustration only and the Newsletter does not endorse them.