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.

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**New Drug: Nirmatrelvir and Ritonavir for COVID-19**

Approved indication: COVID-19

Paxlovid (Pfizer)
Nirmatrelvir 150 mg film-coated tablets, Ritonavir 100 mg film-coated tablets

Viral proteases are feasible targets for antiviral drugs. The main protease of SARS-CoV-2 plays a pivotal role in viral replication so inhibiting it could be an effective treatment for COVID-19. The antiviral drug nirmatrelvir, given with ritonavir, has been provisionally approved for the treatment of COVID-19 in adults who have an elevated risk of progressing to hospitalisation or death but do not require supplemental oxygen. This approval is based on incomplete data and may be revised with the publication of peer-reviewed results. The efficacy of the combination against the Omicron variant is not yet established. The combination is not approved for patients requiring hospitalisation for severe or critical COVID-19.

Nirmatrelvir works by binding to the SARS-CoV-2 3CL protease to prevent viral replication. To boost plasma concentrations, it is taken with ritonavir, an inhibitor of cytochrome P450 (CYP) 3A4 that blocks the metabolism of nirmatrelvir. Ritonavir itself is inactive against SARS-CoV-2.

The recommended regimen is two nirmatrelvir 150 mg tablets and one ritonavir 100 mg tablet taken together every 12 hours for five days, starting as soon as possible after a diagnosis of COVID-19 and within five days of the onset of symptoms. The tablets should be swallowed whole, with or without food, and not chewed, broken or crushed. As its metabolism by CYP3A4 is blocked by ritonavir, nirmatrelvir is mainly excreted unchanged in the urine and faeces. The mean half-life of nirmatrelvir with ritonavir is about seven hours. In patients with moderate renal impairment, a reduced dose of nirmatrelvir is recommended, but this adjusted regimen has not been clinically tested. The combination is contraindicated in patients with severe renal or hepatic impairment.

Nirmatrelvir and ritonavir are also contraindicated in patients who are taking drugs that are highly metabolised by CYP3A and drugs that are strong CYP3A inducers. There are many potential drug interactions.

A phase II/III double-blind, randomised controlled trial investigated the efficacy of the combination in unvaccinated patients at high risk of hospitalisation or death. This trial enrolled 2246 adults with COVID-19, mainly (98%) the Delta variant.

Among those who were treated within three days of symptom onset, 0.7% (5/697) of the patients in the treatment group and 6.5% (44/682) of the placebo group were hospitalised within 28 days following randomisation. There were no deaths in the treatment group whereas nine patients in the placebo group died. When treated within five days of symptom onset, 0.8% (8/1039) of the treatment group and 6.3% (66/1046) of the placebo group were hospitalised within 28 days following randomisation. There were no deaths in the treatment group whereas 12 patients in the placebo group died. In this trial, up to 34 days after the last dose, 22.6% (251/1109) of the patients in the treatment group and 23.9% (266/1115) of the patients in the placebo group experienced treatment-emergent adverse reactions, which were usually mild in intensity. The most common adverse reactions were dysgeusia, diarrhoea, headache and vomiting. Nine (0.8%) patients in the treatment group and seven (0.6%) patients in the placebo group discontinued treatment due to an adverse event considered to be related to the drug or placebo.

The safety and efficacy of nirmatrelvir and ritonavir in children and pregnant women are unknown. Breastfeeding should be discontinued during and for seven days after treatment. Ritonavir is likely to reduce the efficacy of combined hormonal contraceptives, so women are advised to use additional or alternative contraceptives during treatment and during a menstrual cycle after treatment.

Nirmatrelvir boosted with ritonavir should be used with caution for COVID-19 because of the potential for drug–drug interactions. The safety and efficacy of this treatment in vaccinated people have yet to be established.

References:
Source: Australian Prescriber.

**Status in India:** Nirmatrelvir bulk and Combi-pack of Nirmatrelvir 300mg tablets (2x150mg tablets) and Ritonavir tablets 100mg has been approved for treatment of adult patients with Covid-19, with SpO2 >93% and who have high risk of progression of the disease including hospitalization or death, in light of Covid 19 outbreak for restricted emergency use in the country on 21.04.2022. Few companies like Hetero, Granules India etc. got licence for manufacturing and marketing. It is expected that this product may be available in Indian market very soon.

**Monkeypox and Smallpox Vaccine Guidance**

When properly administered before exposure to monkeypox vaccines are effective at protecting people against monkeypox.

ACAM200 and JYNNEOS™ (also known as Imvamune or Imvanex) are the two currently licensed vaccines in the United States to prevent smallpox. JYNNEOS is also licensed specifically to prevent monkeypox.

ACAM2000 is administered as a live virus preparation that is inoculated into the skin by pricking the skin surface. Following a successful inoculation, a lesion will develop at the site of the vaccination. The virus growing at the site of this inoculation lesion can be spread to other parts of the body or even to other people. Individuals who receive vaccination with ACAM2000 must take precautions to prevent the spread of the vaccine virus.

JYNNEOS™ is administered as a live virus that is non-replicating. It is administered as two subcutaneous injections four weeks apart. There is no visible “take” and as a result, no risk for spread to other parts of the body or other people. People who receive JYNNEOS™ are not considered vaccinated until they receive both doses of the vaccine.

CDC, in conjunction with the Advisory Committee on Immunization Practices (ACIP), provides recommendations on who should receive smallpox vaccination in a non-emergency setting. At this time, vaccination with ACAM2000 is recommended for laboratorians working with certain orthopoxviruses and military personnel. The ACIP is currently evaluating JYNNEOS™ for the protection of people at risk of occupational exposure to orthopoxviruses in a pre-event setting.

**Vaccine Effectiveness**

Because monkeypox virus is closely related to the virus that causes smallpox, the smallpox vaccine can protect people from getting monkeypox. Past data from Africa suggests that the smallpox vaccine is at least 85% effective in preventing monkeypox. The effectiveness of JYNNEOS™ against monkeypox was concluded from a clinical study on the immunogenicity of JYNNEOS and efficacy data from animal studies. Smallpox and monkeypox vaccines are effective at protecting people against monkeypox when given before exposure to monkeypox. Experts also believe that vaccination after a monkeypox exposure may help prevent the disease or make it less severe.

**Receiving Vaccine After Exposure to Monkeypox Virus**

Vaccination after exposure to monkeypox virus is still possible. However, the sooner an exposed person gets the vaccine, the better.

CDC recommends that the vaccine be given within 4 days from the date of exposure in order to prevent onset of the disease. If given between 4–14 days after the date of exposure, vaccination may reduce the symptoms of disease, but may not prevent the disease.

Smallpox and monkeypox vaccines are effective at protecting people against monkeypox when given before exposure to monkeypox. Experts also believe that vaccination after a monkeypox exposure may help prevent the disease or make it less severe.

For details: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP)
MINISTRY OF HEALTH AND FAMILY WELFARE
(Department of Health and Family Welfare)

NOTIFICATION
New Delhi, the 25th May, 2022

G.S.R. 399(E).—The following draft of certain rules further to amend the Drugs Rules, 1945, which the Central Government proposes to make, in exercise of the powers conferred by sub-section (1) of section 12 and sub-section (1) of section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) and in consultation with the Drugs Technical Advisory Board is hereby published for information of all persons likely to be affected thereby and notice is hereby given that the said draft rules shall be taken into consideration on or after the expiry of a period of thirty days from the date on which the copies of the Gazette of India containing these draft rules are made available to public;

Objections and suggestions which may be received from any person within the period specified above will be considered by the Central Government;

Objections and suggestions, if any, may be addressed to the Under Secretary (Drugs), Ministry of Health and Family Welfare, Government of India, Room No. 434, C Wing, Nirman Bhavan, New Delhi - 110001 or emailed at drugsiv-mohfw@gov.in.

DRAFT RULES

1. (1) These rules may be called the Drugs (…… Amendment) Rules, 2022.
   (2) These rules shall, unless specified otherwise, come into force on the date of their final publication in the Official Gazette.

2. In the Drugs Rules, 1945, in Schedule K after serial no. 39 and entries relating thereto, the following serial number and entries shall be inserted, namely:—

<table>
<thead>
<tr>
<th>Class of Drugs</th>
<th>Extent and conditions of Exemption</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;40. The following drugs to be sold Over-The-Counter (OTC) by retail under the valid license: (1)</td>
<td>The provisions of Chapter IV of the Act and Rules thereunder to provide that these drugs can be sold by retail Over-The-Counter without prescription of a Registered Medical Practitioner (RMP), subject to the following conditions, namely:—</td>
</tr>
<tr>
<td>Povidone Iodine 5% w/v solution Composition: Povidone Iodine 5% w/v (Antiseptic and disinfectant agent)</td>
<td>(a) The maximum duration of treatment/usage should not exceed five days.</td>
</tr>
<tr>
<td>Chlorhexidine Mouth wash Composition: Chlorhexidine Gluconate 0.2% (For the treatment of gingivitis)</td>
<td>(b) If the symptoms do not resolve the patient should consult a Registered Medical Practitioner.</td>
</tr>
<tr>
<td>Clotrimazole cream Composition: Clotrimazole 1% w/w cream (Fungal)</td>
<td>(c) Pack size may not exceed the maximum doses recommended.</td>
</tr>
<tr>
<td>Clotrimazole dusting powder Composition: Clotrimazole 1% w/w powder (Antifungal)</td>
<td>(d) Each pack of the drug may be accompanied with Patient Information Leaflet (PIL).</td>
</tr>
<tr>
<td>Dextroxypropanol Hydrobromide Lozenges (5mg)</td>
<td>(e) The indication claimed should be same as already approved by the Licensing Authority under Rule 21(b) for the categories mentioned.</td>
</tr>
<tr>
<td>Cough</td>
<td></td>
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<tr>
<td>Diclofenac ointment/cream/gel Each gram of gel contains 10 mg of diclofenac sodium (equivalent to 1.16 mg of diclofenac diethylammonium) (Analgesic)</td>
<td></td>
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<tr>
<td>Diphenhydramide Capsules 25 mg</td>
<td></td>
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<tr>
<td>(Antihistaminic/Antiallergic)</td>
<td></td>
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<tr>
<td>Paracetamol tabs 500 mg (Antipyretic)</td>
<td></td>
</tr>
<tr>
<td>Sodium Chloride Nasal spray – 0.9% (Nasal Decongestant)</td>
<td></td>
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<tr>
<td>Osymetazoline nasal solution 0.05%</td>
<td></td>
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<tr>
<td>(Nasal Decongestant)</td>
<td></td>
</tr>
<tr>
<td>Ketocozaol shampoo 2% w/v (Anti dandruff)</td>
<td></td>
</tr>
<tr>
<td>Lactulose solution 10gm/15ml (Laxative)</td>
<td></td>
</tr>
</tbody>
</table>

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   | (13) Benzoyl peroxide 2.5 w/w (Antibacterial for acne) | |
   | (14) Calamin Lotion (Anti septic) | |
   | (15) Xylometazoline hydrochloride 0.05% w/v (Nasal decongestant) | |
   | (16) Bisacodyl tablets 5mg (Laxative) | |

[Note: The principal rules were published in the Gazette of India vide notification number E.28.10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. ……(E), dated ……]

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.