From The Desk of Editorial Team

The department of Pharmacology, Dr. RMLIMS, Lucknow, is pleased to present the special issue of our newsletter. When the entire world including our nation India is battling Covid-19 pandemic we also cannot remain unaffected thus we dedicate this entire issue to the drug related information pertaining Corona Virus.

We have tried to put together articles which have aroused serious interest like-Can the BCG vaccine a regular in our immunisation program offer some benefit against the SARS Cov-2? Also an effort has been made to tabulate the drugs which have been touted to have some beneficial effect and also bring in the trial related information in our section heading Trial Information. It took arduous effort to bring them together with the amount of ever changing scenario and lack of authentic evidences, still we have tried to put together and tabulate them. It may be possible by the time this newsletter reaches you some new therapies may have come or some old drugs again repurposed to be used thus excuse us for such anomaly as with every second ticking we have new information. To tackle the influx of new information we have given the list of important links which give important updates regarding the current epidemic and strategies to withhold the spread.

Our article on Precision Medicine is also of great importance in present times as it may hold the key to therapeutics of future and may be a great tool for tackling pandemics like Covid-19 in future. As we all know Covid 19 has presented us with a very challenging scenario but it is also an amazing opportunity to unlearn, relearn, and test our capabilities and value systems. In these unprecedented times, we extend our gratitude to our Covid Warriors for their remarkable efforts.

The pandemic has pushed us into maintaining good hand hygiene, use of mask, proper sanitation, social distancing, but the challenge is also to remain connected via the internet and isolate COVID-19 thus we are sharing our newsletter in soft copy through your email.

Last but not the least as our honourable PM has said - ‘Today, the nation’s goal, mission and resolve are one, and this is to be victorious in this battle against the corona virus pandemic.’

With the same hope and resolution Stay Safe and Hope we soon emerge victorious against this unseen enemy of mankind.
Most countries of the world are affected by COVID-19 but there seems striking differences in mortality and morbidity among them. A study by Aaron Miller et al has shown epidemiological evidence indicating that the differences in morbidity and mortality produced by COVID-19 across countries might be partially explained by a country’s BCG vaccination policy.

BCG is a live attenuated strain derived from an isolate of Mycobacterium bovis, used in newborns as a vaccine for Tuberculosis (TB), in many countries having a universal BCG vaccination policy. Thus, BCG vaccination has been shown to produce positive “heterologous” or non-specific immune effects leading to improved response against other non-mycobacterial pathogens. BCG vaccinated mice infected with the vaccinia virus were protected by increased IFN-Y production from CD4+ cells. This is due to metabolic and epigenetic changes leading to promotion of genetic regions encoding for pro-inflammatory cytokines. BCG vaccination significantly increases the secretion of pro-inflammatory cytokines, specifically IL-1B, which has been shown to play a vital role in antiviral immunity.

BCG vaccination has been shown to produce broad protection against viral infections and sepsis, raising the possibility that the protective effect of BCG might be not directly related to actions on COVID-19 but on associated co-occurring infections or sepsis. However, BCG vaccination was correlated with a reduction in the number of COVID-19 reported infections in a country suggesting that BCG might confer some protection specifically against COVID-19. The broad use of the BCG vaccine across a population could reduce the number of carriers, and combined with other measures could act to slow down or stop the spread of COVID-19.

Italy, where the COVID 19 mortality is very high, never implemented universal BCG vaccination. On the other hand, Japan had one of the early cases of COVID-19 but it has maintained a low mortality rate, have been implementing BCG vaccination since 1947. Iran had also been heavily hit by COVID-19 and it started its universal BCG vaccination policy only in 1984. The earlier a country established BCG vaccination policy, the stronger the reduction in their number of deaths per million inhabitants.

The correlation between the beginning of universal BCG vaccination and the protection against COVID-19 suggests that BCG might confer long-lasting protection against the current strain of Corona virus. However, randomized controlled trials using BCG are required to determine how fast an immune response develops that protects against COVID-19.

BCG vaccination policies and the differences in the morbidity and mortality associated with COVID-19 infections all over the world. However, further studies are needed to substantiate this correlation.

References:
1. Aaron Miller, Mac Josh Reandelar, Kimberly Fasciglione, Violeta Roumenova, Yan Li, Gonzalo H Otazu. Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: an epidemiological study doi: https://doi.org/10.1101/2020.03.24.20042937
Precision medicine (PM), also known as personalised medicine is the tailoring of medical treatment to the individual characteristics of each patient. It provides a genomic blueprint to determine each person’s unique disease susceptibility, define preventive measures and enable targeted therapies to promote wellness.

Based on comprehensive genomic and diagnostic characterisation, different subtypes of patients within a given condition can be identified, and treatment can be tailored to the underlying cause, as illustrated in the given figure.

The four ‘P’s of Precision Medicine

- **Prediction and prevention** of disease
  Using genomic technologies and other diagnostics we will be able to identify people most at risk of disease even before the onset of their symptoms. Earlier detection will open up the prospect of new treatment options and support people to make informed lifestyle choices. This will create the potential to reduce the growing burden of disease, particularly for long term condition such as cardiovascular diseases, cancer, chronic respiratory diseases and diabetes.

- **More precise** diagnoses
  Currently a diagnosis is made based on tests and investigations of a patient’s symptoms. But whilst two patients might share the same symptoms, the cause of them could be different.

- **Targeted and personalised** interventions
  Personalised medicine offers the opportunity to move away from ‘trial-and-error’ prescribing to optimal therapy in the first round.

- **A more participatory role** for patients
  The ability for a clinician to discuss with their patients information about individual genomic characteristics, lifestyle and environmental factors, and interpret personal data from wearable technology will drive a new type of conversation. They can consider lifestyle changes, and when treatments might not be necessary. It might also lead patients to consider preventative measures when there is high likelihood of developing a disease.
Benefits of Precision Medicine

Precision Medicine (PM) has the potential to offer improved medication selection and targeted therapy, reduce adverse effects, increase patient compliance, shift the goal of medicine from reaction to prevention, improve cost effectiveness, and increase patient confidence post-marketing by approving novel therapeutic strategies and altering the perception of medicine in the healthcare system.

We can strengthen our ability to design appropriate health and care for our local populations through a more sophisticated understanding of the impact of age, gender and ethnicity or lifestyle factors that influence the onset of disease.

Strategy

For the development and rapid adoption of PM it is vital that pharmaceutical companies should show willingness to work collaboratively with academic research teams. Identification of more stringent biomarkers and are necessary to form a proactive approach to PM.

One example is the recent development of liquid biopsies, which can be used to detect DNA circulating in the blood. This type of biopsy is non-invasive, much lower risk than traditional biopsy and has been used to detect disease extremely early. One of the first uses of liquid biopsy was a test for Down syndrome in pregnant mother.

Future of Precision Medicine

Human genome research is the foundation for the future of personalized medicine, and has the ability to eventually customize medical treatments to individual patients through the incorporation of genetics, molecular profiles and clinical characteristics in treatment determination. With the use of risk algorithms, molecular diagnostics, and targeted therapies, the field of personalized medicine is striving to translate research into clinical practice.

Role of Precision Medicine in COVID-19 pandemic?

Presentations of COVID-19 have ranged from asymptomatic/mild symptoms to severe illness and mortality. While 81% of patients have a mild clinical course, 14% have developed severe illness requiring hospitalization and oxygen therapy, and 5% require ICU admission. Complications of COVID-19 includes pneumonia, pulmonary oedema, ARDS, multiple organ failure, septic shock requiring hospitalization and death.

COVID-19 pneumonia, despite falling under the definition of ARDS, is a specific disease, whose distinctive features are severe hypoxemia often associated with near normal respiratory system compliance. These severely hypoxic patients despite sharing a single etiology (SARS-CoV-2) may present quite differently from one another: normally breathing (“silent” hypoxemia) or remarkably dyspnoic; quite responsive to nitric oxide or not; deeply hypocapnic or normo/ hypercapnic; and either responsive to prone position or not. Therefore, the same disease actually presents itself with impressive non-uniformity. Primarily there are two phenotypes Type L and Type H and the respiratory treatment offered to Type L and Type H patients must be different. However, since the effective treatment regime is yet to be developed and vaccine development is under way, the adoption of PM in treatment of COVID-19 may yield better utilization of treatment though it requires more medical research throughout the world.

The PM will help in optimizing drug therapy and dosage as per requirement of each patient depending on his/her genetic constitution thus increasing efficacy & safety. With this objective in mind researchers are underway for increased development of novel therapies based on PM in future.

References:
The global pandemic of novel corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) began in Wuhan, China, in December 2019, and has since spread worldwide. The pandemic poses many challenges to the healthcare system particularly in infection control and disease treatment.

Thus, there is an urgent need for an effective treatment to treat symptomatic patients but also to decrease the duration of virus carriage in order to limit the transmission in the community.

There are no specific therapies approved by the regulatory authorities for severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). Several agents are being used under clinical trial and compassionate use protocols based on in vitro activity (against SARS-CoV-2 or related viruses) and on limited clinical experience. Efficacy has not been established for any drug therapy however ICMR and many global agencies including FDA has suggested use of Hydroxychloroquine for prophylaxis in Health care professionals and known suspects of Covid-19.

*SARS-CoV-2 is found in faecal material but no known cases of faecal transmission are yet identified. *Case fatality rate is the ratio of deaths to the total number of people diagnosed

**Potential Treatment**

Isolation remains the mainstay of containing COVID-19. Other than supportive treatment with oxygen therapy, anti-viral medications are being tested for their effectiveness against COVID-19. Current experimental treatment may include combinations of lopinavir and ritonavir, Remidesivir, Ribavirin, Interferon-1beta, Hydroxychloroquine, Azithromycin and Teicoplanin. Effective treatment regime is yet to be established and vaccine development is under way.

Potential Drugs/treatment potentials which are being used /repurposed for Covid 19 have been tabulated on page 6 and 7 and a diagrammatic representation has been given on page 8 along with the list of disinfectants found to be effective against SARS CoV-2.

With no established treatment in line various preventive measures to avoid exposure to the virus should be followed like proper hand washing with soap and water for at least 20 seconds or by use of hand sanitizers, avoid touching one’s face, avoiding close contact with people who are sick and maintaining a distance of at least 6 feet, covering the face while coughing and sneezing with bent elbow or tissue, use of mask in public, social distancing i.e keeping a distance of at least one metre in public places, avoiding mass gatherings and undue outdoor activities.

The Centres for Disease Control and Prevention (CDC) and ICMR currently recommends that discharge from hospital/isolation requires negative rRT PCR results from at least 2 consecutive sets of nasopharyngeal and throat swabs collected at least 24 hours apart from a patient with COVID-19.
<table>
<thead>
<tr>
<th>SI No.</th>
<th>DRUGS</th>
<th>MECHANISM OF ACTION</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chloroquine</td>
<td>Increases pH of endosomes and affects the glycosylation process of ACE 2 receptor and spike protein thus inhibiting the virus/cell fusion.</td>
<td>Anti malarial drug</td>
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<td>Repurposed to use in COVID-19 for treatment but evidence of efficacy is lacking, further study is needed.</td>
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<td>2</td>
<td>Hydroxychloroquine (HCQ)</td>
<td>A less toxic derivative of Chloroquine with similar mechanism of action. It has additional immunomodulatory effects through inhibition of cytokine production, autophagy, and lysosomal activity in host cells.</td>
<td>Used in malaria and rheumatoid arthritis.</td>
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<td>Recommended as prophylactic agent by ICMR for HCPs and Suspected Contacts Used in combination with Azithromycin for COVID-19</td>
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<tr>
<td>3</td>
<td>Lopinavir and Ritonavir</td>
<td>Bind well to the SARS-CoV 3C-like protease (SARS-CoV 3CL\textsuperscript{PRO}), inhibiting cleavage of the viral poly proteins and release of non structural proteins, thus inhibiting viral replication and maturation</td>
<td>Current data suggest a limited role for Lopinavir/Ritonavir in COVID-19 treatment.</td>
</tr>
<tr>
<td>4</td>
<td>Umifenovir</td>
<td>S protein/ACE2, membrane fusion inhibitor</td>
<td>Currently approved in China for treatment and prophylaxis of Influenza.</td>
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<tr>
<td></td>
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<td>There are ongoing RCTs in China for further evaluating this agent as there is limited clinical experience with Umifenovir for COVID-19</td>
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<tr>
<td>5</td>
<td>Favipiravir</td>
<td>Inhibit viral RNA dependent RNA polymerase</td>
<td>Approved in Japan and China for influenza is under investigation for use in COVID-19</td>
</tr>
<tr>
<td>6</td>
<td>Ribavirin</td>
<td>Synthetic guanosine nucleoside inhibits viral RNA-dependent RNA polymerase</td>
<td>Its activity against other nCoVs makes it a candidate for COVID 19 treatment.</td>
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<tr>
<td></td>
<td></td>
<td>Though in vitro activity against SARS CoV was limited and required high concentration to inhibit viral replication, thus necessitating high-dose and combination therapy.</td>
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<tr>
<td>7</td>
<td>Remdesivir</td>
<td>Prodrug, active form is adenosine nucleotide triphosphate analogue and gets incorporated into viral RNA and causes premature chain termination.</td>
<td>Broad-spectrum antiviral investigational drug yet to be approved thus issued an Emergency Use Authorization (EUA) in the US, for patients with severe COVID-19.</td>
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<td>SI No.</td>
<td>DRUGS</td>
<td>MECHANISM OF ACTION</td>
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<tr>
<td>8</td>
<td>Interferon-1b</td>
<td>Binds to specific cell surface receptors and affect viral replication at multiple steps. Also modulate both innate and adaptive immunity.</td>
<td>Currently being tried as a part of combination therapy in SARS-CoV-2</td>
</tr>
<tr>
<td>9</td>
<td>Tocilizumab</td>
<td>IL-6 blocking antibody that target IL-6 receptors</td>
<td>It has been under study in severe Covid-19 cases to curb cytokine storm, with early reports of success but requires further studies.</td>
</tr>
<tr>
<td>10</td>
<td>Azithromycin</td>
<td>Macrolide antibiotic but has some antiviral activity with exact mechanism not elucidated.</td>
<td>Used in combination with HCQ for COVID-19</td>
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<tr>
<td></td>
<td></td>
<td>Benefits need to be established with RCT prior to widespread adoption of these treatments.</td>
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<tr>
<td>11</td>
<td>Convalescent plasma therapy</td>
<td>A classic adaptive immunotherapy where we use the plasma of the recovered patients from the disease for the treatment of the disease in active cases. Reduction of pulmonary lesions on chest CT examinations seen.</td>
<td>CP therapy was successfully used in the treatment of SARS, MERS, and 2009 H1N1 pandemic with satisfactory efficacy and safety. Trials are going on and at the initial stage positive results have been found in some hospitals in India as well. (KGMU Lucknow and MAX Hospital New Delhi)</td>
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<tr>
<td>13</td>
<td>Teicoplanin</td>
<td>Glycopeptide antibiotic Acts on an early stage of the viral life cycle by inhibiting the low pH cleavage of the viral spike protein by cathepsin L in the late endosomes, thereby preventing the release of genomic viral RNA and continuation of the virus replication cycle.</td>
<td>A potential alternative for treatment of Covid-19; requires further investigation.</td>
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</tbody>
</table>
Figure 1: Diagrammatic representation of various site and mechanism of action of the potential drug candidates against SARS CoV-2

Effective Disinfectants Against novel Coronavirus (SARS CoV-2)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Concentration</th>
<th>Contact time required</th>
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<tbody>
<tr>
<td>Sodium hypochlorite</td>
<td>0.1%*</td>
<td>1 min</td>
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<tr>
<td>Ethanol</td>
<td>62-71%</td>
<td>1 min</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>0.5%</td>
<td>1 min</td>
</tr>
<tr>
<td>Povidone iodoine</td>
<td>0.23% - 7.5%</td>
<td>1 min</td>
</tr>
</tbody>
</table>

References:
4. JM Sanders, ML Monague, TZ Jadkowski, JB Cutrell et al; Pharmacologic treatments for coronavirus disease 2019 (COVID-19), JAMA, April 13, 2020
Trial Hopes:

- While USA has started its own vaccine trial and almost six companies are claiming that they will be ready with vaccines by September-October, here in India we have found success in a trial of MIP vaccine (also known as MW) which has been used against Leprosy and licensed for squamous cell lung carcinoma discovered by an Indian Scientist Dr Gurusharan Pran Talwar, has successfully completed the initial safety trial at PGI Chandigarh.
- Now the researchers aim to go in next stage to establish its effectiveness in treatment of COVID-19.
- MIP boosts immune response lowers inflammation and prevents the auto-immune reaction which is also seen in serious Covid-19.

- Various Cells based approaches, primarily using mesenchymal stromal cells (MSCs), have demonstrated possible efficacy in patients with ARDS, but whether these therapies are effective for treating Coronavirus-induced ARDS is unknown.
- According to the WHO ICTRP and the NIH clinicaltrials.gov databases, 27 clinical investigations of MSC-based cell therapy approaches have begun in China since the onset of the COVID-19 outbreak, as well as a growing number of academic and industry trials elsewhere.
- There may be a potential role for MSCs and other cell-based therapies in treatment of COVID-19, this need to be investigated in a rationally designed, controlled approach if safety and efficacy are to be demonstrated accurately.

References:

Important Links

1. Get the latest public health information from CDC: https://www.coronavirus.gov
2. Get the latest research from NIH: https://www.nih.gov/coronavirus
3. Various updates and guidelines from Government of India https://www.mohfw.gov.in/
4. For various training resource material https://www.mohfw.gov.in/pdf/BASEDOCforRESOURCESrev06042020.pdf
5. For COVID data portal and ICMR Guidelines https://www.icmr.gov.in/
6. For information pertaining COVID research in India https://www.csir.res.in/
7. For BMJ free access Corona hub https://www.bmj.com/coronavirus
# SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

(For Drugs Used in Prophylaxis/Treatment of COVID-19)

For VOLUNTARY reporting of ADRs by Healthcare Professionals

MINISTRY OF HEALTH & FAMILY WELFARE, GOVERNMENT OF INDIA

NDIAN PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

PvPI Helpline (Toll Free): 1800-180-3024/9:00 AM to 5:30 PM, Monday-Friday

## A. PATIENT/SUBJECT INFORMATION

<table>
<thead>
<tr>
<th>Patient/Subject Category</th>
<th>Subject Initials</th>
<th>2. Age/Date of Birth</th>
<th>4. Gender: Male □ Female □ Transgender □</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Lab confirmed COVID-19 case □</td>
<td>Reg. No. /IPD No. /OPD No. /CR No. :</td>
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<td>b. Asymptomatic healthcare worker involved in the care of suspected or confirmed COVID-19 cases □</td>
<td>AMC Report No. :</td>
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<tr>
<td>c. Asymptomatic household contacts of laboratory confirmed cases □</td>
<td>Worldwide Unique No. : To be generated by PvPI</td>
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<tr>
<td>d. Others (Please specify)</td>
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3. Weight (in Kg)

5. If female - pregnant Yes □ No □

6. Lactating Yes □ No □

## B. SUSPECTED ADVERSE REACTION

<table>
<thead>
<tr>
<th>S.No</th>
<th>Reaction</th>
<th>Start Date</th>
<th>End Date</th>
<th>Outcome*</th>
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*Outcome may be indicated as (✓) one of the following
  (a) Recovered
  (b) Not recovered
  (c) Recovered with sequelae
  (d) Recovering
  (e) Fatal
  (f) Unknown

7. Describe Event(s)/Reaction(s) with treatment details, if any in chronological order

8. Seriousness of the reaction: No □ if Yes □ (please tick appropriate box)
   - Death (dd/mm/yyyy)
   - Life threatening
   - Hospitalization/Prolongation of hospitalization
   - Other Medically important events

## 10. Any other tests performed:

1. Chest X-Ray Yes □ No □
2. ECG Findings If any Yes □ No □
3. Biochemical Examination such as Serum Electrolytes (Na, K, Mg, Ca etc) Yes □ No □
4. Ophthalmology Exam Findings, if any
5. Radiological examination
6. Other Relevant Information, if any

## 11. Recent Travel Information:

- Recent History of International Travel:
  - Yes □ No □
  - Country Visited:
  - Date of Return to India:
    - Interstate Travel/Domestic Travel

## 12. Relevant medical/medication history:

- Allergy/Hypersensitivity Reaction
- Chronic Alcoholism
- Smoking
- Obesity
- Renal Dysfunction
- Hepatic Dysfunction
- Diabetes
- Epilepsy/Seizures
- Bronchial Asthma
- Cardiovascular Disease
- Chronic Lung Disease
- Immunodeficiency Disorder
- Immunosuppressant Drug
- Anaemia
- Neurological disorder
- G-6-PD Deficiency
- Dermatological Findings If any
- Others

## 13. Drug Interaction: Mention name of any interacting (with Suspected Drug) drug taken:
### C. SUSPECTED MEDICINE(S)*

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Drug Name (Brand/Generic)</th>
<th>Manufacturer MAH* (if known)</th>
<th>Batch No./Lot No.</th>
<th>Exp. Date (if known)</th>
<th>Dosage Form</th>
<th>Dose used</th>
<th>Route of Admin.</th>
<th>Frequency (Once a day, twice a day etc.)</th>
<th>Therapy dates</th>
<th>Indication</th>
<th>Causality Assessment (Prefer WHO-UMC Scale)</th>
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### Reaction abated on (please tick)

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<thead>
<tr>
<th>Drug withdrawal</th>
<th>Dose reduction</th>
<th>Without modification of dose</th>
<th>Any other</th>
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</table>

### Reaction if reappeared after drug reintroduction

<table>
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<tr>
<th>Yes</th>
<th>No</th>
<th>Effect unknown</th>
<th>Dose (if reintroduced)</th>
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</table>

### 14. Concomitant medication including drug used for co-morbidities, and complementary medicines with therapy dates (Exclude those used to treat reaction)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name (Brand/Generic)</th>
<th>Dose used</th>
<th>Route used</th>
<th>Frequency (Once a day, twice a day etc.)</th>
<th>Therapy dates</th>
<th>Indication</th>
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<td>i.</td>
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### D. REPORTER DETAILS

15. Name of the Healthcare Professional with Address: __________________________________________________________

    Pin: __________________________________________ E-mail: __________________________________________ Tel. No. (with STD code): __________ Occupation: __________________________

    Signature: __________________________________________

16. Date of this report (dd/mm/yyyy): __________________________

    Sign. and Name of Receiver: __________________________________________

Confidentiality: The patient’s identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submission of an ADR report does not have any legal implication on the reporter.

*Use separate page for more information, *MAH* - Marketing Authorization Holder

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**For Adverse Drug Reaction Reporting Tools**

- E-mail: pypi@incindia.net or pypi.incindia@gmail.com
- PuPI Helpline (Toll Free): 1800 180 3024 (9:00 AM to 5:30 PM, Monday-Friday)
- ADR Mobile App: “ADR PuPI”
**New Drug Approvals February-March 2020**

<table>
<thead>
<tr>
<th>Sl No</th>
<th>Drug Name</th>
<th>Mechanism of action</th>
<th>Indication</th>
<th>Date of Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ozanimod</td>
<td>Specific and potent small molecule modulator of the sphingosine 1-phosphate receptor 1 (S1PR1) and receptor 5 (S1PR5)</td>
<td>To Treat Relapsing form of Multiple Sclerosis</td>
<td>25/03/2020</td>
</tr>
<tr>
<td>2</td>
<td>Osilodrostat</td>
<td>Binds to and inhibits the activity of CYP11B1, the enzyme that catalyzes the final step of cortisol synthesis from the precursor 11-deoxycortisol, and CYP11B2, the enzyme that catalyzes aldosterone synthesis from corticosterone and 11-deoxycorticosterone in the adrenal gland. The inhibition of CYP11B1 prevents the production of excess cortisol, thereby decreasing and normalizing the levels of cortisol</td>
<td>To treat adults with Cushing’s disease who either cannot undergo pituitary gland surgery or have undergone the surgery but still have the disease</td>
<td>6/03/2020</td>
</tr>
<tr>
<td>3</td>
<td>Isatuximab</td>
<td>Is an IgG1-derived monoclonal antibody targeted against CD38 proteins. Its activity against CD38 results in a number of downstream effects, including direct apoptosis of the affected cell and activation of immune which result in potent anti-tumour activity. Also inhibits CD38 ectoenzymatic activity, preventing the immunosuppressive effects of its downstream products. Also exert its effects via downstream promotion of lysosome-dependent cell death, upregulation of reactive oxygen species, and restoration of antitumor immune effector cell functions</td>
<td>To treat multiple myeloma</td>
<td>2/03/2020</td>
</tr>
<tr>
<td>4</td>
<td>Rimegepant</td>
<td>Reversibly blocks the CGRP receptor and inhibits the biological activity of CGRP neuropeptide</td>
<td>Treatment of Migraine</td>
<td>27/02/2020</td>
</tr>
<tr>
<td>5</td>
<td>Amisulpride</td>
<td>Binds selectively to dopamine D(2) and D(3) receptors in the limbic system and has 5-HT 7 antagonistic effect</td>
<td>Nausea and vomiting</td>
<td>26/02/2020</td>
</tr>
<tr>
<td>6</td>
<td>Eptinezumab-jjmr</td>
<td>Humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor. The relationship between the pharmacodynamic activity and the mechanism(s) by which eptinezumab-jjmr exerts its clinical effects is unknown.</td>
<td>For the preventive treatment of migraine in adults</td>
<td>21/02/2020</td>
</tr>
<tr>
<td>7</td>
<td>Bempedoic acid</td>
<td>Reduces cholesterol synthesis through inhibition of adenosine triphosphate citrate lyase, an enzyme upstream from 3-hydroxy-3-methylglutaryl-coenzyme A</td>
<td>To treat adults with heterozygous familial hypercholesterolemia</td>
<td>21/02/2020</td>
</tr>
</tbody>
</table>

1. Taylor Meadows, Kristen R et al. “Ozanimod (RPC1063), a selective S1PR1 and S1PR5 modulator, reduces chronic inflammation and alleviates kidney pathology in murine systemic lupus erythematosus.” PloS one vol. 13,4 e0193236. 2 Apr. 2018
3. https://www.drugbank.ca/drugs/DB14811
5. https://www.drugbank.ca/drugs/DB06288