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S&A PHARMA NEWSLETTER

EDITORIAL

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Founding Partner

We are pleased to present this Vol. II Issue XI of *S&A – Pharma Newsletter*. Through this Newsletter, we aim to share new or pertinent regulatory information on pharmaceutical sector within India as well as from foreign jurisdictions, based on information collated through research and appraisal of applicable statutory provisions.

Communicable diseases cause a huge burden on people's life and communities worldwide and can be particularly distressing for people living with it in poverty and for those socially excluded and marginalized. Despite availability of new drugs and therapies from pharmaceuticals companies, the diseases are causing millions of deaths each year worldwide. While poverty drives much disparity in access to health services worldwide, challenges extend far beyond economic barriers for regulatory authorities. People are often denied services because of their race, ethnicity, social class, age, sex, gender identity, migrant status, disability and religion.

Therefore, in the present issue, we start with a discussion on the Government's Patient Support Systems for TB Elimination in India, which analyses data collected from the sixteen states and further suggests implementation of PSS country wide. Going forward, this edition addresses the union cabinet's "Allied and Healthcare Professions Bill, 2018" which lays down the regulation and standardization of education and services by allied and healthcare professionals. The issue then covers the monthly updates of National Pharmaceutical Pricing Authority, an executive body under DPCO, 2013 which regulates drug prices and availability of the medicines in the country.

From the international arena, we talk about recent global survey reports concerning various health issues and the progress on improving health. First, we discuss the international medical humanitarian organisation 'MSF' report, where the organization criticized pharmaceutical companies for their delays in developing HIV drug formulations for children; followed by a note on the "World Malaria Report 2018", which shows a stalling in malaria cases reduction after several years of decline globally. The newsletter then has a review on approvals granted in EMA's Committee for Medicinal Products for Human Use meeting in November 2018.

We wrap up this newsletter with write-up on United States Food and Drug Administration approval to 1) Vitrakvi (larotrectinib) for the treatment of adult and pediatric patients whose cancers have a specific genetic feature (biomarker); and 2) Gamifant (emapalumab-lzsg) for the treatment of pediatric (newborn and above) and adult patients with primary hemophagocytic lymphohistiocytosis (HLH).

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Trust you enjoy reading this issue as well. Please feel free to send your valuable inputs / comments at newsletter@singhassociates.in

Thank you.

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Patient support systems encouraging TB patients to adhere to treatment

Tuberculosis (TB) is an infectious disease caused by bacteria (Mycobacterium tuberculosis), an air borne disease that most often affects the lungs of infected persons; and spread to healthy person when infected patients cough, sneeze or spit. Although TB is curable and preventable, it remains one of the top 10 causes of death worldwide.

Globally, 10 million people are estimated to have developed TB disease in 2017. The severity of national epidemics varies widely among countries. India alone is home to a quarter of the global TB burden, with 28 lakh active infected patients and 4,23,000 TB related deaths annually, where only 14 lakh patients have been captured by the system or notified to the government. Most of these incidences can be prevented through early diagnosis and adequate treatment[1].

TB is five times more common among economically weaker populations, whose physical, economic, and social marginalization causes conditions conducive for the disease to thrive and act as barrier to treatment completion. The debilitating battle against TB often forces patients out of employment.

To address these socio-economic determinants and consequences of the disease, the National Strategic Plan 2017-25 (NSP), shaped by WHO's End TB Strategy and the Sustainable Development Goals (SDGs) agenda framework has introduced new strategies for TB programming in India. In addition to advancing existing programme components (case detection, diagnostics, drugs), the NSP introduced Patient Support Systems (PSS), which envisage to support patients during the treatment period with the provision of incentives, nutrition support as well as creating linkages to other social welfare programmes.

Ongoing Patient Support Systems (PSS) in country

According to "State Initiatives on Patient Support Systems for TB Elimination in India[2]", sixteen states namely Arunachal Pradesh, Assam, Bihar, Chhattisgarh, Delhi, Goa, Gujarat, Himachal Pradesh, Jharkhand, Kerala, Maharashtra, Meghalaya, Madhya Pradesh, Punjab, Tamil Nadu, and Telangana were found to have already implemented some form of PSS like:

(i) **Nutrition support**: Fourteen out of the 16 documented states provide supplementary nutrition in the form of dry ration monthly to TB patients. Nutrition support across the 14 states was predominantly targeted at drug-resistant (DR) TB patients and patients from low income groups (in Jharkhand, Kerala Madhya Pradesh, Meghalaya, Telangana and Tamil Nadu). Chhattisgarh has been a pioneer in introducing nutrition support for all TB patients across the state. This offers a window of opportunity to counsel patients on the importance of nutrition uptake, measure weights and assess treatment adherence. Further, it allows for follow-up with patients to monitor and ensure treatment completion.

(ii) **Links with other social welfare schemes:** Support under existing social welfare schemes targets socially and economically weaker populations with TB. For instance, Chhattisgarh has been attempting to reduce high treatment costs by providing special Multi-drug Resistant (MDR) TB packages (INR 50,000/family/annum) under Rashtriya Swasthya Bima Yojana (RSBY) and Mukhyamantri Swasthya Bima Yojana (MSBY). On the other hand, Gujarat (INR 500/patient/month), Jharkhand (INR 10,000/ Patient), Kerala (INR 1000/month/patient) and Tamil Nadu (INR 1000/month/patient) link patients to state based welfare schemes that provide regular monetary support.

1 http://www.who.int/news-room/detail/18-09-2018-who-calls-for-urgent-action-to-end-tb-

2 https://tbcindia.gov.in/showfile.php?lid=3352

(iii) **Economic assistance in-kind**: Recognizing the financial difficulties of TB affected families some states are providing economic assistance in the form of in-kind support like- Kerala (housing support), Maharashtra (Travel support), Tamil Nadu (dry rations), and Telangana (Economic Development Assistance).

(iv) **Psycho-social support:** Psycho-social factors include stigma, social discrimination, and low awareness, as well as treatment interrupters and naysayers in the community who hinder treatment-seeking behaviour and treatment completion. To address this, community-based groups are created to undertake mobilization activities to tackle negative psycho-social implications of TB. The groups typically comprise of PRI members, AWWs, ASHAs, and TB Health Visitors among others. For instance - -in community mobilization and sensitization activities - Chhattisgarh, Assam and Telangana employ cured TB patients as "Axshya Saathis", encouraging them to share their experiences and challenges with other TB patients.

Conclusion

A number of states implementing several forms of PSS are targeting towards economically weaker patients or patients with DR-TB. With, strengthened patient support systems across the country all TB patients, who need most support can be targeted with adequate socioeconomic assistance.

Moreover, monitoring and evaluation mechanism should be put in place to track progress and understand the success of PSS, as only few states have a mature monitoring and evaluation system in place to track outcomes and impact.

Cabinet approves the Allied and Healthcare Professions Bill, 2018

On November 22, 2018, the Union Cabinet, chaired by Prime Minister, has approved the Allied and Healthcare Professions Bill, 2018[3], for regulation and standardization of education and services by allied and healthcare professionals. The Bill provides for setting up of an Allied and Healthcare Council of India and corresponding State Allied and Healthcare Councils which will play the role of bench-markers and facilitators for professions of Allied and Healthcare.

Allied and Healthcare Professionals (A&HPs) constitute an important element of the human resource health network. Skilled and efficient Allied and Healthcare Professionals (A&HPs) can reduce the cost of care and dramatically improve the accessibility to quality driven healthcare services. Therefore, it is estimated that the Allied and Healthcare Professions Bill, 2018, will directly benefit around 8-9 lakh existing Allied and Healthcare related professionals in the country and several other graduating professionals joining workforce annually and contributing to the health system. Since this Bill is directed to strengthen the healthcare delivery system at large, it may be said that the entire population of the country and the health sector as a whole will be benefited by this Bill.

The Bill provides for setting up of:

- **Central Allied and Healthcare Councils**: The Central Council will comprise 47 members, of which 14 members shall be ex-officio representing diverse and related roles and functions and remaining 33 shall be non-ex-officio members who mainly represent the 15 professional categories.
- **State Allied and Healthcare Councils**: The State Councils are also envisioned to mirror the Central Council, comprising 7 ex-officio and 21 non-ex officio members and the Chairperson to be elected from amongst the non-ex officio members.
- **Professional Advisory Bodies:** The advisory body will be constituted from 15 major professional categories including 53 professions in Allied and Healthcare streams. Professional Advisory Bodies under Central and State Councils will examine issues independently and provide recommendations relating to specific recognized categories.

The Bill defines the roles of the Central and State Councils that:

- The State Council will undertake recognition of allied and healthcare institutions.
- The Bill also empowers the State Governments to make rules framing policies and standards.
- Regulation of professional conduct and to check malpractices respectively.
- Creation and maintenance of live Registers, provisions for common entry and exit examinations, etc.

Expected expenditure and implementation of the bill

Total cost implication is expected to be Rupees 95 crores for the first four years. About four-fifths of the ` total budget (i.e. Rupees 75 crores) is being earmarked for the States while the remaining fund will support the Central Council operations for four years and also to establish the Central and State Registers. An interim council will be

3 http://pib.nic.in/PressReleseDetail.aspx?PRID=1553424

constituted within 6 months of passing of the Act holding charge for a period of two years until the establishment of the Central Council.

The Council at the Centre level and those at States level are to be established as a body corporate with a provision to receive funds from various sources. Councils will also be supported by Central and State Governments respectively through grant-in-aid as needed. However, if the State Government expresses inability, the Central Government may release some grant for initial years to the State Council.

Note - The Bill empowers the Central Governments to make rules and direct Council to make regulations and to add or amend the schedule. The Bill will also have an overriding effect on any other existing law for any of the covered professions.

NPPA updates for the month of November 2018

The National Pharmaceutical Pricing Authority (NPPA), is an executive body under the Drugs (Prices Control) Order (DPCO), 2013, under the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India. NPPA regulates drug prices and availability of the medicines in the country by fixing/revising the prices of controlled bulk drugs and formulations. The NPPA's key announcements/notices of November 2018 are apprised and described below:

1 NPPA has fixed/revised ceiling prices/retail prices of 68 formulations:

On November 06, 2018, NPPA fixed ceiling prices/retail prices of 68 formulations under DPCO, 2013[4]. The formulations with revised price included drugs used in treating conditions like Pain, Infections, Hypertension, Diabetes and Cancer etc.

a. NPPA fixed ceiling prices of 3 scheduled formulation under para 31 of Drugs (Prices Control) Order, 2013

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
1.	Dimercaprol	Injection 50 mg/ml	1 ml
2.	Phytomenadione (Vitamin K1)	Tablet 10mg	1 tablet
3.	Paracetamol	Oral Liquid 100 mg/ml (pediatric)	1 ml

b. NPPA revised ceiling prices of 2 scheduled formulation under para 31 of Drugs (Prices Control) Order, 2013

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
4.	Nitrous oxide	Inhalation	Cubic meter
5.	Oxygen	Inhalation (Medicinal gas)	Cubic meter

c. NPPA revised retail price of 07 scheduled formulations of Schedule-I under Drugs (Prices Control) Order, 2013 (Review)

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
6.	Ramipril + Amlodipine Tablet	Each uncoated tablet contains: Ramipril IP 5mg, Amlodipine Besylate IP eq. to Amlodipine 5mg	1 tablet
7.	Ferrous Ascorbate + Folic Acid + Cyanocobalamin + Zinc Sulphate Monohydrate tablet (AutrinXT)	Each film coated tablet contains: Ferrous Ascorbate eq. to Elemental Iron 100mg, Folic Acid IP 1.5mg, Cyanocobalamin IP 15 mcg, Zinc Sulphate Monohydrate IP eq. to Elemental Zinc 22.5mg	1 tablet
8.	Amlodipine + Valsartan Tablet (Valembic 80 AM)	Each film coated tablet contains: Amlodipine Besylate eq. to Amlodipine USP 5mg, Valsartan USP 80mg	1 tablet
9.	Amlodipine + Valsartan Tablet (Valembic 160 AM)	Each film coated tablet contains: Amlodipine Besylate eq. to Amlodipine USP 5mg, Valsartan USP 160mg	1 tablet
10.	Olmesartan + Amlodipine + Chlorthalidone Tablet (Triolmezest CH 20)	Each film coated tablet contains: Olmesartan IP 20mg Amlodipine Besylate IP eq. to Amlodipine 5mg Chlorthalidone IP – 12.5 mg	1 tablet

4 http://www.nppaindia.nic.in/wh-new-2018/wh-new-12-2018.html

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
11.	Olmesartan + Amlodipine + Chlorthalidone Tablet (Triolmezest CH 40)	Each film coated tablet contains: Olmesartan IP 40mg Amlodipine Besylate IP eq. to Amlodipine 5mg Chlorthalidone IP – 12.5mg	1 tablet
12.	Rosuvastatin + Clopidogrel Tablet (ROSUVAS CV 10)	Each film coated tablet contains: Rosuvastatin Calcium IP eq. to Rosuvastatin 10mg, Clopidogrel Bisulfate IP eq. to Clopidogrel 75mg	tablet

d. NPPA revised Ceiling price of 01 scheduled formulation of Schedule-I under Drugs (Prices Control) Order, 2013(Review)

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
13	Anti-Tetanus Immunoglobulin	250IU	Each Pack

e. NPPA fixed retail prices of 55 formulations under (Prices Control) Order, 2013

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
14	Teneligliptin Hydrobromide + Metformin HCL (SR) Tablet	Each uncoated bilayer tablet contains: Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin 20 mg Metformin Hydrochloride IP 1000 mg (SR)	1 Tablet
15.	Metformin HCL + Glimepiride Tablet (Semi Amaryl M)	Each uncoated bilayer tablet contains: Metformin Hydrochloride IP (in prolonged release form) 500 mg Glimepiride IP 0.5 mg	1 Tablet
16.	Telmisartan + Cilnidipine + Chlorthalidone tablet	Each film coated tablet contains: Telmisartan IP 40 mg Chlorthalidone IP 6.25 mg Cilnidipine IP 10 mg	1 Tablet
17.	Clarithromycin for Oral Suspension	Each 5ml (after reconstitution) contains: Clarithromycin IP 250mg, Titanium Dioxide IP (-).	1 ml
18.	Telmisartan + Amlodipine + Chlorthalidone Tablet (Telmelife 3D)	Each film coated tablet contains: Telmisartan IP 40 mg Amlodipine Besylate IP eq. to Amlodipine 5 mg Chlorthalidone IP 12.5 mg	1 Tablet
19.	Atorvastatin + Clopidogrel Capsule	Each hard gelatin capsule contains: Atorvastatin Calcium IP eq. to Atorvastatin (As film coated tablet) 20 mg	1 capsule
20.	Amoxycillin + Potassium Clavulante tablet (Clanoxy DT)	Each uncoated dispersible tablet contains: Amoxycillin Trihydrate eq. to Amoxycillin 200mg Potassium Clavulante Diluted IP eq. to Clavulanic Acid 28.5mg	1 Tablet
21	Tramadol + Paracetamol Tablet (Trson-P)	Each film coated tablet contains: Tramadol Hydrochloride IP 37.5 mg Paracetamol IP 325 mg	1 Tablet
22.	Voglibose + Metformin Tablet (Voglyson-M 0.3)	Each uncoated bilayered tablet contains: Voglibose IP 0.3 mg Metformin Hydrochloride IP 500 mg (as sustained release form)	1 Tablet
23.	Rosuvastatin + Aspirin + Clopidogrel Capsules	Each hard gelatin capsules contains: Rosuvastatin Calcium IP eq. to Rosuvastatin 10 mg (as pellets) Aspirin IP 75 mg (as enteric coated pellets) Clopidogrel Bisulphate IP eq. to Clopidogrel 75 mg (as pellets)	1 Capsule
24.	Mycophenolate Mofetil Oral Suspension IP	Each 5 ml of reconstituted suspension contains: Mycophenolate Mofetil IP 1 g, (1 bottle with 110gm powder for oral suspension containing 35gm Mycophenolate Mofetil)	Each Pack
25.	Bisacodyl Suppository	Each Suppository contains: Bisacodyl IP 10 mg	1 Suppository
26.	Telmisartan + Chlorthalidone Tablet (Telmelife CH 40)	Each film coated tablet contains: Telmisartan IP 40 mg Chlorthalidone IP 12.5 mg	Tablet
27.	Cilnidipine + Telmisartan Tablet	Each film coated tablet contains: Telmisartan IP 80 mg Cilnidipine 10 mg	1 Tablet
28.	Divalproex Tablet (Diwok OD 750 mg)	Each film coated extended release tablet contains:	1 Tablet

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
29	Clotrimazole + Beclomethasone Dipropionate Cream	Cream contains: Clotrimazole IP 1.00% w/w Beclomethasone Dipropionate IP 0.025% w/w	1 gm
30.	Telmisartan + Chlorthalidone Tablet (Cresar CT)	Each uncoated bilayered tablet contains: Telmisartan IP 40 mg Chlorthalidone IP 6.25 mg	1 tablet
31	Baclofen Oral Solution	Each 5 ml contains: Baclofen IP 5 mg	1 ML
32.	Glimepiride + Metformin Hydrochoride Tablet	Each uncoated bilayered tablet contains: Metformin Hydrochoride IP (as prolonged release) 500 mg Glimepiride IP 3 mg	1 tablet
33.	Glimepiride + Metformin Hydrochoride Tablet	Each uncoated bilayered tablet contains: Metformin Hydrochoride IP (as prolonged release) 500 mg Glimepiride IP 4 mg	1 tablet
34.	Glimepiride + Metformin Hydrochoride Tablet	Each uncoated bilayered tablet contains: Metformin Hydrochoride IP (as prolonged release) 1000mg Glimepiride IP 4 mg	1 tablet
35.	Metformin HCL + Gliclazide + Pioglitazone Tablets	Each uncoated bilayered tablet contains: Metformin Hydrochoride IP (sustained release) 500 mg Gliclazide IP (sustained release) 30 mg Pioglitazone HCL eq. to Pioglitazone 15 mg	1 Tablet
36.	Metformin HCL + Gliclazide + Pioglitazone Tablets	Each uncoated bilayered tablet contains: Metformin Hydrochoride IP (sustained release) 500 mg Gliclazide IP (sustained release) 60 mg Pioglitazone HCL eq. to Pioglitazone 15 mg	1 Tablet
37.	Chlorthalidone + Telmisartan Tablet (Telsar CH 40/6.25)	Each film coated tablet contains: Chlorthalidone IP 6.25 mg Telmisartan IP 40 mg	1 Tablet
38.	Chlorthalidone + Telmisartan Tablet (Telsar CH 40/12.5)	Each film coated tablet contains: Chlorthalidone IP 12.5mg Telmisartan IP 40 mg	1 Tablet
39.	Chlorthalidone + Telmisartan Tablet (Telsar CH 80/12.5)	Each film coated tablet contains: Chlorthalidone IP 12.5mg Telmisartan IP 80 mg	1 Tablet
40.	Divalproex Tablet (Diwok OD 250 mg)	Each film coated extended release tablet contains: Divalproex Sodium IP eq. to Valproic Acid 250 mg	1 Tablet
41.	Voglibose + Metformin tablet	Each uncoated tablet contains: Voglibose IP 0.2 mg Metformin HCL IP 500 mg	1 Tablet
42.	Amoxycillin + Potassium Clavulnate Dry Syrup (Blumox-CA Forte)	Each combipack containing: a) Amoxycillin and Potassium Clavulanate Oral Suspension IP Each 5 ml suspension containing Amoxycillin Trihydrate IP eq. to Amoxycillin 400 mg Potassium Clavulnate diluted IP eq. to Clavulanic Acid 57 mg b) 1 vial sterile water for injection IP Each vial containing Sterile water for injection IP 30 ml	1 ml
43.	Rosuvastatin + Aspirin + Clopidogrel Capsule	Each hard gelatin capsule contains: Rosuvastatin Calcium IP eq. to Rosuvastatin 20 mg (as pellets) Aspirin IP 75 mg (as enteric coated pellets) Clopidogrel Bisulphate IP eq. to Clopidogrel 75 mg (as pellets)	1 Capsule
44.	Rosuvastatin + Aspirin + Clopidogrel Capsule	Each hard gelatin capsule contains: Rosuvastatin Calcium IP eq. to Rosuvastatin 10 mg (as pellets) Aspirin IP 75 mg (as enteric coated pellets) Clopidogrel Bisulphate IP eq. to Clopidogrel 75 mg (as pellets)	1 Capsule
45.	Diclofenac + Virgin Linseed Oil + Methyl Salicylate + Menthol + Capsaicin Gel (Diclofam Hot)	Gel containing Diclofenac Diethylamine BP 1.16% w/w (eq. to Diclofenac Sodium 1% w/w) Virgin linseed Oil BP 3% w/w (containing predominantly Alpha Linolenic Acid) Methyl Salicylate IP 10% w/w Menthol IP 5% Capsaicin USP 0.0255w/w, Benzyl Alcohol IP 1%w/w	1 gm
46.	Clotrimazole + Lignocaine Ear Drops (Triben)	Ear drops contains: Clotrimazole IP 1.0% w/v Lignocaine Hydrochloride IP 2.0% w/v	1 ml
47.	Timolol + Brinzolamide Eye Drops	Each ml contains Brinzolamide IP 1.0 w/v Timolol Maleate IP eq. to Timolol 0.5% w/v, Benzalkonium Chloride IP 0.01% w/v (as preservative)	5ML

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
48.	Diclofenac + Methyl + Menthol GEL (Volini Maxx Gel)	Contains: Diclofenac Diethylamine BP 2.32% w/w (eq. to Diclofenac Sodium 2% w/w), Methyl Salcylate IP 10% w/w & Menthol IP 5% w/w	Each Pack (20 gram)
49.	Diclofenac + Methyl + Menthol GEL (Volini Maxx Gel)	Contains: Diclofenac Diethylamine BP 2.32% w/w (eq. to Diclofenac Sodium 2% w/w), Methyl Salcylate IP 10% w/w & Menthol IP 5% w/w	Each Pack (30 gram)
50.	Olmesartan + Amlodipine + Chlorthalidone Tablet (TRIOLSAR 20)	Each film coated tablet contains: Olmesartan Medoxomil 20mg, Chlorthalidone IP 6.25mg, Amlodipine Besylate IP eq. to Amlodipine 5mg tablets	1 Tablet
51.	Olmesartan + Amlodipine + Chlorthalidone Tablet (TRIOLSAR 40)	Each film coated tablet contains: Olmesartan Medoxomil 40mg, Chlorthalidone IP 6.25mg, Amlodipine Besylate IP eq. to Amlodipine 5mg tablets	1 Tablet
52.	Losartan + Chlorthalidone + Amlodipine Tablet (TRILOSAR 6.25)	Each film coated tablet contains: Losartan Potassium IP 50mg, Chlorthalidone IP 6.25mg, Amlodipine Besylate IP eq. to Amlodipine 5mg tablets	1 Tablet
53.	Losartan + Chlorthalidone + Amlodipine Tablet (TRILOSAR 12.50)	Each film coated tablet contains: Losartan Potassium IP 50mg, Chlorthalidone IP 12.50mg, Amlodipine Besylate IP eq. to Amlodipine 5mg tablets	1 Tablet
54.	Darunavir + Ritonavir tablet	Each film coated tablet contains: Darunavir Ethanolate eq. to Darunavir 600mg and Ritonavir IP 100mg tablet	1 Tablet
55.	Telmisartan + Amlodipine + Chlorthalidone Tablet (Tazloc AC 12.5)	Each uncoated bilayered tablet contains: Telmisartan IP 40 mg Amlodipine Besylate IP eq. to Amlodipine 5 mg Chlorthalidone IP 12.5 mg	1 Tablet
56.	Darunavir + Ritonavir tablet (Durart – R 450)	Each film coated tablet Contains: Darunavir 400mg & Ritonavir 50mg Tablets	1 Tablet
57.	Diclofenac + Methyl + Menthol Salicylate + Menthol + Turpentine Oil Gel (Diclotal MR Gel)	Each film coated tablet contains: Lamivudine IP 300mg, Tenofovir Disoproxil Fumarate IP 300mg eq. to Tenofovir Disoproxil 245mg, Dolugetravir Sodium eq. to Dolutegravir 50mg.	1 Tablet
58.	Lamivudine + Tenofovir + Dolugetravir tablet	Each film coated tablet contains: Darunavir Ethanolate eq. to Darunavir 800mg, Ritonavir 100mg Tablet	1 Tablet
59.	Darunavir + Ritonavir tablet (Danavir R)	Each film coated tablet contains: Darunavir Ethanolate eq. to Darunavir 800mg, Ritonavir 100mg Tablet	1 Tablet
60.	Lamivudine + Tenofovir + Dolugetravir tablet (ACRIPTEGA)	Each uncoated tablet contains: Lamivudine IP 300mg, Tenofovir Disoproxil Fumarate IP 300mg, Dolugetravir Sodium eq. to Dolutegravir 50mg.	1 Tablet
61.	Daclatasvir + Sofosbuvir tablet (HEPCINAT PLUS)	Each film coated tablet contains: Daclatasvir Dihydrochloride eq. to Daclatasvir 60mg, Sofosbuvir 400mg	1 Tablet
62.	Daclatasvir + Sofosbuvir tablet	Each film coated tablet contains: Daclatasvir Dihydrochloride eq. to Daclatasvir 60mg, Sofosbuvir 400mg	1 Tablet
63.	Daclatasvir + Sofosbuvir tablet (MYHEP DVIR)	Each film coated tablet contains: Daclatasvir Dihydrochloride eq. to Daclatasvir 60mg, Sofosbuvir 400mg	1 Tablet
64.	Diclofenac + Methyl + Menthol GEL (Volini Maxx Gel)	Contains: Diclofenac Diethylamine BP 2.32% w/w (eq. to Diclofenac Sodium 2% w/w), Methyl Salicylate IP 10% w/w & Menthol IP 5% w/w	Each Pack (15 gram)
65.	Diclofenac + Methyl + Menthol GEL (Volini Maxx Gel)	Contains: Diclofenac Diethylamine BP 2.32% w/w (eq. to Diclofenac Sodium 2% w/w), Methyl Salicylate IP 10% w/w & Menthol IP 5% w/w	Each Pack (10 gram)
66.	Ceftriaxone 1 gm plus Tazobactum 125 mg injection	Each injection vial contains: Ceftriaxone Sodium IP eq. Ceftriaxone 1 gm Tazobactum Sodium eq. Tazobactum 125 mg	1 vial
67.	Cefpodoxime + Potassium Dry Syrup (Cefoprox CV)	Each 5 ml of the reconstituted suspension contains: Cefpodoxime Proxetil IP eq. to Cefpodoxime 50 mg Potassium Clavulanate Diluted IP eq. to Clavulanic Acid 31.25 mg	1ml

Sl. No.	Name of the Scheduled Formulation	Dosage form & Strength	Unit
68.	Cefpodoxime + Potassium Dry Syrup (Cefoprox CV)	Each 5 ml of the reconstituted suspension contains: Cefpodoxime Proxetil IP eq. to Cefpodoxime 100 mg Potassium Clavulanate Diluted IP eq. to Clavulanic Acid 62.5mg	1ml

2. NPPA fixed/revised ceiling/retail prices of 01 formulations: On November 13, 2018 NPPA National Pharmaceutical Pricing Authority (NPPA) In implementation of directions given in line with the review orders issued by the Department of Pharmaceuticals (DOP) under para 31 of Drugs (Prices Control) Order, 2013 has revised/fixed the ceiling price of Tetanus Toxoid Injection, 0.5ml and 5ml each pack[5].

5 http://www.nppaindia.nic.in/ceiling/press13November18/Formulation(1).pdf

MSF criticized pharmaceutical companies for delay in formulating HIV medicines for children

The international medical humanitarian organization, *Doctors without Borders/Médecins Sans Frontières* (MSF) criticized pharmaceutical companies for their delays and failure to develop appropriate formulations of HIV medicines for children. As WHO recommends that all children diagnosed with HIV should immediately start antiretroviral therapy.[6]. But without optimal paediatric HIV drug formulations, countries will continue to struggle to implement this recommendation

WHO recommendation[7]:

The increasing levels of pretreatment antiretroviral (ARV) drug resistance documented in low and middle-income countries prompted WHO to issue guidelines recommending that countries with pretreatment resistance to efavirenz or nevirapine at or above 10% should urgently consider revising their first-line regimens.

Population	First line drug	Second line drug	Third line drug
Children	Two NRTIs + DTG/RAL	Two NRTIs + (ATV/r or LPV/r)	DRV/r + DTG + 1-2 NRTIs (if possible, consider optimization using genotyping)
	Two NRTIs + LPV/r	Two NRTIs + DTG	
	Two NRTIs + NNRTI	Two NRTIs + DTG	

Nucleoside reverse-transcriptase inhibitors (NRTIs), dolutegravir (DTG), raltegravir (RAL), lopinavir/ ritonavir (LPV/r), non-nucleoside reverse-transcriptase inhibitor (NNRTI), atazanavir/ritonavir (ATV/r), Darunavir/ritonavir (DRV/r).

Note –

- ATV/r can be used as an alternative to LPV/r among children older than three months, but the limited availability of suitable formulations for children younger than six years, the lack of a fixed-dose formulation and the need for separate administration of a ritonavir booster should be considered when choosing this regimen.
- This applies to children for whom approved DTG dosing is available.
- RAL should remain the preferred second-line regimen for the children for whom approved DTG dosing is not available. and may be recommended as a preferred first-line regimen for neonates (conditional recommendation)
- ATV/r or LPV/r should remain the preferred second-line treatment for the children for whom approved DTG dosing is not available.
- Children younger than three years should not use DRV/r.

Paediatric HIV remains a neglected disease, and the small market for paediatric HIV medicines means they have never been a priority for either multi-national pharmaceutical corporations or generic manufacturers. Delays have plagued both the development and introduction of newer paediatric drug formulations, and scale-up of existing formulations. For example:

6 https://www.msfindia.in/hivaids-pharmaceutical-corporations-failing-children-hiv

7 http://apps.who.int/iris/bitstream/handle/10665/273632/WHO-CDS-HIV-18.18-eng.pdf

- DTG approved for children older than six years is still not available for children because pharmaceutical corporation ViiV Healthcare is yet to finalize necessary studies and register a dispersible tablet formulation for younger children.
- RAL has now been approved for use from birth, providing additional options for neonates and children living with HIV. A paediatric granule formulation of RAL, already exists, but pharmaceutical corporation Merck has been slow to register it in developing countries.
- The LPV/r paediatric formulation currently supplied by generics manufacturers Mylan and Cipla, has also been plagued with problems of its slow supply and higher price compared to the harsh-tasting lopinavir/ritonavir syrup, which supposed to be replaced by their products.

Note –These are new WHO interim guideline / recommendations regarding preferred first-line regimens for children initiating ART, which now include DTG and RAL. WHO also recommends active toxicity surveillance of emerging toxicity issues of DTG and other new ARV drugs.

WHO launches country-led response to put stalled malaria control efforts back on track

India, the only country out of 11 highest burden countries worldwide, has recorded a substantial decline in malaria cases in 2017

On November 19, 2018, World Health Organization (WHO) released the World Malaria Report 2018[8] which provides a comprehensive update on global and regional malaria data and trends. The latest report, tracks investments in malaria programmes and research as well as progress across all intervention areas - prevention, diagnosis, treatment and surveillance.

Highlights of the World Malaria Report 2018

According to the new World Malaria Report 2018, the reductions in malaria cases have stalled globally after several years of decline. For the second consecutive year, the annual report produced by WHO reveals a plateauing in numbers of people affected by malaria.

Malaria Cases: In 2017, there were an estimated 219 million cases of malaria, compared to 217 million the year before. But in the years prior, the number of people contracting malaria globally had been steadily falling, from 239 million in 2010 to 214 million in 2015.

The incidence rate of malaria declined globally between 2010 and 2017, from 72 to 59 cases per 1000 population at risk. India with fifteen countries in sub-Saharan Africa carried almost 80% of the global malaria burden. Five countries accounting for nearly half of all malaria cases worldwide include Nigeria (25%), Democratic Republic of the Congo (11%), Mozambique (5%), India (4%) and Uganda (4%).

The 10 highest burden countries in Africa reported increase in cases of malaria in 2017 compared to 2016. Of these, Nigeria, Madagascar and the Democratic Republic of the Congo had the highest estimated increases, all greater than half a million cases. In contrast, India reported 3 million fewer cases in the same period, a 24% decrease compared with 2016.

Malaria deaths: In 2017, there were an estimated 4,35,000 deaths from malaria globally, compared to 4,51,000 estimated malaria deaths in 2016, and 6,07,000 in 2010. The WHO African Region accounted for 93% of all malaria deaths in 2017. All WHO regions except the WHO Region of the Americas recorded reductions in mortality in 2017 compared with 2010. The largest declines occurred in the WHO regions of South-East Asia (54%), Africa (40%) and the Eastern Mediterranean (10%).

Malaria-related anaemia: This year's report includes a section on malaria-related anaemia, a condition that, if left untreated, can result in death, especially among vulnerable populations such as pregnant women and children aged under 5 years. Data from household surveys conducted in 16 high-burden African countries between 2015 and 2017 show that, the prevalence of any anaemia was 18% higher in children who tested positive for malaria compared to children who tested negative for malaria.

Positive findings in Malaria Report 2018

Despite a levelling off in progress since 2015, the global malaria response is in a much better position for some countries that carry a high burden of malaria, such as India, Rwanda, Ethiopia and Pakistan.

8 http://www.who.int/malaria/publications/world-malaria-report-2018/report/en/

For example - India, a country that accounted for 4% of global malaria cases in 2017 is making significant progress in bringing down its malaria burden. As reflected in this year's World Malaria Report, the country registered a 24% reduction in cases over 2016, largely due to substantial declines of the disease in the high burden state like Odisha, home to approximately 40% of all malaria cases in the country.

Success factors include rejuvenated political commitment, strengthened technical leadership, which focused on prioritizing the right mix of vector control measures, and increased levels of domestic funding to back efforts. A notable aspect of Odisha's approach is its network of Accredited Social Health Activists, or ASHAs, who serve as front-line workers to deliver essential malaria services across the state, particularly in rural and remote areas.

The report also reveals that, in a subset of countries that are nearing elimination, the pace of progress is quickening. For example, 46 countries reported fewer than 10,000 indigenous malaria cases in 2017, up from 37 countries in 2010.

WHO's country-led response "High burden to high impact"

WHO and partners have launched a new country-led response "High burden to high impact" to get the reduction in malaria deaths and disease back on track, to scale up prevention and treatment, and increased investment, to protect vulnerable people from the deadly disease.

According to this, the approach will be driven by the 11 countries that carry the highest burden of the disease. Key elements of the new approach include:

- Political will to reduce the toll of malaria;
- Strategic information to drive impact;
- Better guidance, policies and strategies; and
- A coordinated national malaria response.

Note – The current report also highlights that the immediate barriers to achieving the fast-approaching Global Technical Strategy milestones for 2020 and 2025 are malaria's continued rise in countries with the highest burden of the disease and inadequate international and domestic funding. At the same time, the continued emergence of parasite resistance to antimalarial medicines and mosquito resistance to insecticides pose threats to progress.

European Medicines Agency (EMA): Recommends approval of four medicines in its November meeting

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) recommended four medicines for approval, including a medicine for use in countries outside the European Union, at its November 2018 meeting[9].

A The four medicines recommended for approval are:

1. **Erleada -** for the treatment of non-metastatic castration resistant prostate cancer

On November 15, 2018, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorization for the medicinal product Erleada, intended for the treatment of non-metastatic castration resistant prostate cancer.

Erleada will be available as 60-mg tablets. The active substance of Erleada is apalutamide, a selective androgen receptor inhibitor that binds directly to the ligand binding domain of the androgen receptor. The benefits with Erleada are its ability to delay metastatic disease.

The applicant for Erleada is Janssen-Cilag International N.V[10].

2. **Macimorelin Aeterna Zentaris -** for the diagnosis of growth hormone deficiency in adults

On November 15, 2018, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorization for the medicinal product Macimorelin Aeterna Zentaris intended for the diagnosis of growth hormone deficiency in adults.

Macimorelin Aeterna Zentaris will be available as 60 mg granules for oral solution. The active substance of Macimorelin Aeterna Zentaris is macimorelin, a peptide mimetic with growth hormone secretagogue activity similar to ghrelin (ATC code: V04CD06). Macimorelin stimulates growth hormone release by activating growth hormone secretagogue receptors present in the pituitary and hypothalamus.

The applicant for Macimorelin is Aeterna Zentaris GmbH[11].

3. **Silodosin Recordati -** for the treatment of the signs and symptoms of benign prostatic hyperplasia

On November 15, 2018, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorization for the medicinal product Silodosin Recordati, intended for the treatment of the signs and symptoms of benign prostatic hyperplasia.

Silodosin Recordati will be available as 4-mg and 8-mg capsules. The active substance of Silodosin Recordati is silodosin, a α1A-adrenoreceptor antagonist (ATC code: G04CA04) that decreases the bladder outlet resistance and improves storage (irritative) and voiding (obstructive) lower urinary tract symptoms. Silodosin Recordati is a generic of Urorec which has been authorized in the EU since January 29, 2010.

The applicant for Silodosin is Recordati Ireland Ltd[12].

9 https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-12-15-november-2018

10 https://www.ema.europa.eu/documents/smop-initial/chmp-summary-positive-opinion-erleada_en.pdf

11 https://www.ema.europa.eu/documents/smop-initial/chmp-summary-positive-opinion-macimorelin-aeterna-zentaris_en.pdf

12 https://www.ema.europa.eu/documents/smop-initial/chmp-summary-positive-opinion-silodosin-recordati_en.pdf

4. **Fexinidazole Winthrop -** for the treatment of human African trypanosomiasis (HAT)

On November 15, 2018, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, in accordance with Article 58 of Regulation (EC) No 726/20041 for the medicinal product Fexinidazole Winthrop, intended for the treatment of human African trypanosomiasis (HAT) due to Trypanosoma brucei gambiense in adults and children ≥ 6 years old and weighing ≥ 20 kg.

Fexinidazole Winthrop will be available as 600-mg tablets. The active substance of Fexinidazole Winthrop is fexinidazole, a nitro-imidazole derivative that generates reactive amines that exert indirect toxic and mutagenic effects on the trypanosomes. Fexinidazole Winthrop has been shown to be effective at curing the disease (measured as the number of patients having no evidence of trypanosomes in any body fluid, not requiring rescue medication and having a cerebrospinal fluid white blood cell count ≤20 cells/µL).

Fexinidazole Winthrop has been developed by DNDi and Sanofi-Aventis Groupe and intended exclusively for markets outside the European Union[13].

B CHMP recommendations on extensions of therapeutic indication

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended a change to the terms of the marketing authorization for seven drugs on extensions of therapeutic indication as described in table (*New indication are marked in bold, and removed indication are marked in strikethrough*)

Sl.no.	Name of medicine	Full Indication	Marketing-authorisation holder
1	Kisqali (ribociclib)	Kisqali ~~in combination with an aromatase inhibitor~~ is indicated for the treatment of ~~postmenopausal~~ women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine based therapy or in women who have received prior endocrine therapy. In pre or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone releasing hormone (LHRH) agonist.	Novartis Europharm Limited
2	Mabthera (rituximab)	MabThera is indicated in adults for the following indications: *Non-Hodgkin's lymphoma (NHL)* MabThera is indicated for the treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy. MabThera maintenance therapy is indicated for the treatment of follicular lymphoma patients responding to induction therapy. MabThera monotherapy is indicated for treatment of patients with stage III-IV follicular lymphoma who are chemo-resistant or are in their second or subsequent relapse after chemotherapy. MabThera is indicated for the treatment of patients with CD20 positive diffuse large B cell non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy. Chronic lymphocytic leukaemia (CLL) MabThera in combination with chemotherapy is indicated for the treatment of patients with previously untreated and relapsed/refractory CLL. Only limited data are available on efficacy and safety for patients previously treated with monoclonal antibodies including MabThera or patients refractory to previous MabThera plus chemotherapy. Rheumatoid arthritis MabThera in combination with methotrexate is indicated for the treatment of adult patients with severe active rheumatoid arthritis who have had an inadequate response or intolerance to other disease modifying anti rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies. MabThera has been shown to reduce the rate of progression of joint damage as measured by X ray and to improve physical function, when given in combination with methotrexate. Granulomatosis with polyangiitis and microscopic polyangiitis MabThera, in combination with glucocorticoids, is indicated ~~for the induction of remission in~~ **treatment of** adult patients with severe, active granulomatosis with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA).	Roche Registration GmbH

13 https://www.ema.europa.eu/documents/smop-initial/chmp-summary-opinion-fexinidazole-winthrop_en.pdf

Sl.no.	Name of medicine	Full Indication	Marketing-authorisation holder
3	Orkambi (lumacaftor / ivacaftor)	Orkambi granules are indicated for the treatment of cystic fibrosis (CF) in children aged 2 years and older who are homozygous for the **F508del** mutation in the CFTR gene.	Vertex Pharmaceuticals (Europe) Ltd
4	Ravicti (glycerol phenylbutyrate)	Ravicti is indicated for use as adjunctive therapy for chronic management of ~~adult and paediatric~~ patients ~~≥ 2 months of age~~ with urea cycle disorders (UCDs) including deficiencies of carbamoylmphosphate synthetase I (CPS), ornithine carbamoyltransferase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase I (ARG) and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements).	Horizon Pharma Ireland Limited
5	Blincyto (blinatumomab)	Blincyto is indicated as monotherapy for the treatment of adults with Philadelphia chromosome negative CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL). **Blincyto is indicated as monotherapy for the treatment of adults with Philadelphia chromosome negative CD19 positive B-precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%.** Blincyto is indicated as monotherapy for the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation.	Amgen Europe B.V.
6	Opdivo (nivolumab)	*Melanoma* Opdivo as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults. *Adjuvant treatment of melanoma* Opdivo as monotherapy is indicated for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection. Non-Small Cell Lung Cancer (NSCLC) Opdivo as monotherapy is indicated for the treatment of locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults. Renal Cell Carcinoma (RCC) Opdivo as monotherapy is indicated for the treatment of advanced renal cell carcinoma after prior therapy in adults. **Opdivo in combination with ipilimumab is indicated for the first-line treatment of adult patients with intermediate/poor-risk advanced renal cell carcinoma.** Classical Hodgkin Lymphoma (cHL) Opdivo as monotherapy is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin. Squamous Cell Cancer of the Head and Neck (SCCHN) Opdivo as monotherapy is indicated for the treatment of recurrent or metastatic squamous cell cancer of the head and neck in adults progressing on or after platinum-based therapy. Urothelial Carcinoma Opdivo as monotherapy is indicated for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy. urothelial carcinoma in adults after failure of prior platinum-containing therapy	Bristol-Myers Squibb Pharma EEIG
7	Yervoy (ipilimumab)	*Melanoma* Yervoy as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults, and adolescents 12 years of age and older. Yervoy in combination with nivolumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults. Renal Cell Carcinoma (RCC) Yervoy in combination with nivolumab is indicated for the first-line treatment of adult patients with intermediate/poor-risk advanced renal cell carcinoma.	Bristol-Myers Squibb Pharma EEIG

Note - The CHMP's assessments are based on a comprehensive scientific evaluation of data. They determine whether the medicine meets the necessary quality, safety and efficacy requirements and that it has a positive risk-benefit balance. The CHMP carries out a scientific assessment of the application and gives a recommendation on whether the medicine should be marketed or not. Once granted by the European Commission, the centralized marketing authorization is valid in all EU Member States as well as in the European Economic Area (EEA) countries Iceland, Liechtenstein and Norway.

FDA approval to Larotrectinib is the first treatment to receive a tumor-agnostic indication

On November 26, 2018, the U.S. Food and Drug Administration granted accelerated approval to Vitrakvi (larotrectinib), a treatment for adult and pediatric patients whose cancers have a specific genetic feature (biomarker)[14, 15]. The approval is for the treatment of adult and pediatric patients[16] with solid tumors with a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation that are either metastatic or where surgical resection will likely result in severe morbidity and have no satisfactory alternative treatments or have progressed following treatment.

This is the second time the agency has approved a cancer treatment based on a common biomarker across different types of tumors rather than the location in the body where the tumor originated. The approval marks a new paradigm in the development of cancer drugs that are "tissue agnostic."

Larotrectinib demonstrated a 75 percent overall response rate across different types of solid tumors. These responses were durable, with 73 percent of responses lasting at least six months, and 39 percent lasting a year or more at the time results were analyzed. Examples of tumor types with an NTRK fusion that responded to larotrectinib include soft tissue sarcoma, salivary gland cancer, infantile fibrosarcoma, thyroid cancer and lung cancer.

The FDA granted Priority Review, Breakthrough Therapy designation and Orphan Drug designation to Vitrakvi. The approval of Vitrakvi is granted to Loxo Oncology.

About Vitrakvi (larotrectinib)

Larotrectinib, is a CNS active TRK inhibitor designed to inhibit these proteins. TRK fusions can be found in many types of solid tumors and affect both children and adults. In the clinical trials that were the basis for this approval, larotrectinib showed clinical benefit across numerous unique tumor types, including lung, thyroid, melanoma, GIST, colon, soft tissue sarcoma, salivary gland and infantile fibrosarcoma.

About NTRK gene fusion

NTRK genes, which encode for TRK proteins, can become fused to other genes abnormally, that result in constitutively-activated chimeric TRK fusion proteins, which act as an oncogenic driver, promoting cell proliferation and survival in tumor cell lines. NTRK fusions are rare but occur in cancers arising in many sites of the body. Prior to this approval, there had been no treatment for cancers that frequently express this mutation, like mammary analogue secretory carcinoma, cellular or mixed congenital mesoblastic nephroma and infantile fibrosarcoma.

Note- Larotrectinib has been developed by Bayer and Loxo Oncology, Inc.; Bayer submitted a Marketing Authorization Application in the European Union in August 2018 and additional filings in other countries are underway. Larotrectinib will be available in the U.S. market in oral capsules as well as a liquid formulation for adults and children.

14 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm626710.htm

15 https://media.bayer.com/baynews/baynews.nsf/id/US-FDA-approves-Larotrectinib-first-TRK-inhibitor-patients-advanced-solid-tumors-harboring-a-TRK?Open&parent=news-overview-category-search-en&ccm=020

USFDA approval to Gamifant: The first and only treatment for a rare and life-threatening type of immune disease

On November 20, 2018, the U.S. Food and Drug Administration approved Gamifant (emapalumab-lzsg) for the treatment of pediatric (newborn and above) and adult patients with primary hemophagocytic lymphohistiocytosis (HLH) who have refractory, recurrent or progressive disease or intolerance to conventional HLH therapy[17,18]. This is the first FDA approval for a drug specifically for HLH.

The approval is based on data from pivotal phase 2/3 study which enrolled patients with primary HLH. The efficacy of Gamifant was studied in a clinical trial of 27 pediatric patients with suspected or confirmed primary HLH with either refractory, recurrent or progressive disease during conventional HLH therapy or who were intolerant of conventional HLH therapy. The median age of the patients in the trial was 1 year old. The study showed that 63 percent of patients experienced a response and 70 percent were able to proceed to stem cell transplant.

The FDA granted Priority Review, Breakthrough Therapy designation and also Orphan Drug designation to Gamifant earlier. The FDA approval of Gamifant is granted to Novimmune SA.

About HLH

HLH is a condition in which the body's immune cells do not work properly. The cells become overactive releasing molecules, which leads to inflammation. The immune cells start to damage the body's own organs, including the liver, brain and bone marrow. It can be inherited, which is known as primary or "familial" HLH. It can also have non-inherited causes. People with primary HLH usually develop symptoms within the first months or years of life. Symptoms may include fever, enlarged liver or spleen and decreased number of blood cells.

About Gamifant (emapalumab)

Emapalumab is a monoclonal antibody (mAb) that binds and neutralises interferon gamma (IFNy). In the US, Gamifant is indicated for paediatric (newborn and older) and adult primary haemophagocytic lymphohistiocytosis (HLH) patients with refractory, recurrent or progressive disease, or intolerance to standard-of-care HLH therapy. Gamifant is the first and only medicine approved in the US for primary HLH, an ultra-rare syndrome of hyperinflammation that usually occurs within the first year of life and can rapidly become fatal unless diagnosed and treated. Gamifant is indicated to be administered through intravenous (IV) infusion over one hour twice per week until haematopoietic stem cell transplant (HSCT).

Note - Gamifant is developed and submitted for approval to the USFDA by Nonimmune, and now Sobi will commercialise the Gamifant globally.

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16 https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm626263.htm

17 https://www.novimmune.com/en/swiss-biopharmaceutical-company/news/2018/fda-approves-gamifantreg-emapalumab-first-and-only-treatment-primary-haemophagocytic-lymphohistiocytosis-hlh.html

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