Drug Development Process and Novel Drugs Approved by FDA for 2017-18

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Abstract: Delivering authentic healthcare Innovation worldwide is a demanding and complex task. The global discovery and approval of new drugs, medical devices and biologics will revolutionize the availability of health care products worldwide. The mission of pharmaceutical research companies is to discover and develop new drugs with safe and effective treatment to patients. Drug development is a science-driven process that at its base involves exploiting biological processes to trigger a therapeutic benefit. The process of discovering and developing a new molecular entity on average requires approximately 13.5-15 years. The developer must reveal efficacy and safety for a novel new drug to become commercially available. A drug in human subjects is governed by rules that fall under the responsibility of overseeing the US Food and Drug Administration. The average cost for the research and development of each successful drug is estimated at $ 800 million to $ 1 billion. The discovery process includes the first steps of the investigation, which are designed to identify a drug in the research and perform initial tests in the laboratory. In this article, we focused on the drug discovery, development process and list of new drugs approved by U.S. Food and Drug Administration (FDA) in 2017.

Keywords: Drug discovery, drug development, health care products, FDA approved drugs, pharmaceutical research companies.

1. INTRODUCTION

Discovery and innovation of new drug is a lengthy and risky process that came with expensive and complexity with time [1]. A drug is a chemical compound that acts on the structure and function of the body by its chemical nature and is specific for use in diagnosis, cure, improvement and treatment of the disease [2]. The International Committee on Harmonization (ICH) and the subsequent implementation of its outcome will take time before the approvals of worldwide registrations for new pharmaceutical products can occur simultaneously. The global discovery and approval of new drugs, devices, and biologics will revolutionize the availability of health care products worldwide. Pharmaceutical research companies are energetic to find the new approaches to decrease the cost and time for the innovation and approval of new drugs [3]. The process of discovering and developing a new molecular entity on average requires approximately 13.5 years. A promising candidate drug to become commercially available, the developer must demonstrate efficacy and safety [4]. The FDA has the primary fate for the regulation and supervision of pharmaceutical industries and its products. FDA must rely that novel new medical treatments must reach the public quickly [5]. The primary responsibility for the regulation of review and approval of new drug in the United States is with Center for Drug Evaluation and Research (CDER) within FDA [6]. New models for R&D in the pharmaceutical industry have changed an interest in the productivity to bring innovative products to market [7]. In turn, the scientific, technical and regulatory challenges associated with drug development create complex-
ity as companies often focus their research and development when science is difficult and the risks of failure are higher [8]. The mission of pharmaceutical research companies is to take the path of understanding a disease to bring a new safe and effective treatment for patients [9]. Each phase of the life cycle is very complex and requires the experience of many professionals. The goal of adopting a life-cycle approach is to maximize return on investment while maintaining the health and safety of the population [1].

2. SUCCESS RATE AND TIME REQUIRED FOR DEVELOPING A NEW DRUG

From the 1000 compounds released from the company only 30 get an outcome for the clinical trials and from that, only a single drug gets approval to enter the market [1]. Compounds usually do not pass the initial development process due to toxicity, tolerance, lack of efficacy, or lack of bioavailability of the drug in humans. To introduce a new drug, pharmaceutical industries desire to begin with thousands of compounds in its discovery. This complete step may take about 10-15 years to develop a new drug. Drug development includes about 6.5 years of discovery, non-clinical testing, and toxicity studies; 1.5 years is required in Phase-I trials to determine safety in a healthy person; then 2 years in Phase-II trials with a few hundred patients to access the drug’s effectiveness and ill effects. The expansion process continues with 3.5 years in Phase-III trials involving thousands of patients including data of research centers to confirm evaluation of long-term effects, then it takes 1.5 years for regulatory review, where all data are presented. Even after the drug is approved, it may undergo further Phase-IV testing so more safety and efficacy data can be collected [1]. Time required for developing a new drug is shown in Fig. (1).

3. OVERVIEW OF DRUG DISCOVERY AND DEVELOPMENT PROCESS

3.1. Discovery

Drug discovery is a multifaceted process that requires teamwork in multiple scientific disciplines. For most pharmaceutical companies, the discovery process begins with the identification of an unsatisfied medical need or marketing opportunity and then defines a strategy for targeted intervention [1]. Scientists are beginning to understand the internal functioning of human disease at the molecular level [9]. Biopharmaceutical companies conduct basic research independently and in collaboration with researchers and others throughout the biomedical research ecosystem [8]. Drug discovery includes identification and validation of goals. The production and synthesis of a large number of compounds within each series and all compounds are processed through a series of high productivity screening assays (HTS). Furthermore, biomarkers can be used as genotype or phenotype, plasma concentration, target occupation, target activation, physiological measures and pathological process [1].

3.2. Target Identification

The identification of the objective involves the study of the mechanism and points of intervention for the disease or condition of interest. The strategies and approaches cover the range of technologies available to study the expression of the disease. Understanding the similarity of disease patterns in animals and humans is essential to generate trust in the translation of animal outcomes in human diseases [1].

3.3. Target Validation

The objective validation is the confirmation that the objectives of interest play a role in the disease [1]. Validation of objectives is essential to help scientists avoid research paths that seem promising but ultimately lead to dead ends [9]. The translation between humans and animals is an important feature to generate confidence in the development of screening tests for the identification of lead molecules [1].

3.4. Lead Generation and Optimization

Lead generation uses key objective attributes to define chemical properties and attributes related to affinity, power and selectivity to select large chemical libraries for the desired activity. Lead optimization is working within or between chemical series to identify lead molecules that have physico-chemical and biological characteristics that indicate a greater likelihood of success in the
drug development process [1]. The main research compounds that survive the initial exam are "optimized" or modified to make them more effective and safe [8]. This is often a long process that considers the power and selectivity in the target, the efficacy models, the characteristics of ADME (absorption, tissue distribution, metabolism, excretion) and information on transporters, pharmacokinetics, solubility, pharmaceutical properties, ability to formulation, toxicity and safety. Biologists test the effects of analogs on biological systems while chemists take this information to make further changes [9].

3.5. Quantitative Structure–Activity Relationships (QSAR)

QSARs can increase the fraction of truly active compounds passing through the system. Toxicology and pathology can also help in identifying target distribution to anticipate off-target organ effects [1]. Flowchart for drug discovery and development is illustrated in Fig. (2).

4. PRECLINICAL DRUG DEVELOPMENT

To check the safety status of a given drug through the examination of toxic effects with
respect to target organ as well as dose dependence is the primary responsibility of preclinical studies [1]. Steps of preclinical development for a new drug is shown in Fig. (3).

5. CLINICAL DRUG DEVELOPMENT

5.1. Investigational New Drug Application

The aim of Investigational New Drug (IND) application is to give information about the tests which are to be applied on humans [13]. FDA and institutional review board (IRB) reviewed the tested drug used for human’s studies [14]. An IRB is an independent ethics committee which ensures the ongoing clinical trials are in suitable way [15].

The document contains information into three broad areas of research:

1. Animal pharmacology, safety, and toxicology study.
2. Chemistry, Manufacturing, and Controls (CMC).

3. Clinical trial protocols.

There are two IND categories:
- Commercial.
- Research [16].

Types of IND applications:
- Investigator IND.
- Emergency use investigational new drug (EIND).
- Treatment IND.

5.2. Clinical Trials

Clinical studies provide a framework for assessing the benefits and harms of interventions and contributing to the evidence base that informs clinical decision-making [17]. Clinical trials are divided into three phases known as I,II & III and to check the efficacy and safety of given tested drug. These clinical trials are important to generate rapid liberation of new and effective drug to patients.

Post-approval surveillance studies are generally called Phase IV studies [5]. Global clinical trials are important because they facilitate more rapid delivery of new, more effective drugs to patients [18]. Clinical researchers who initiate a pharmaceutical study invoke a set of specific regulatory requirements [19].

5.3. Good Clinical Practice

GCP provides the guidelines that specify the standards through government that can be used for the clinical trials. These are the standards that specify the rules of clinical trials including design, performance, completion, recording and analysis [20].

5.3.1. ICH GCP Guidelines

The ethical principles that arrived from the Helsinki declaration conducted the clinical trials which are consistent with regulatory rules. Expected benefits justify the proceedings of the trials. The rights and safety of the test subject are the important consideration at the same time. Proposed clinical trials are supported with clinical and non-clinical information. They should be described in the detailed protocol. The same protocol is reviewed by independent ethics...
committee (IEC). All decisions are made on behalf of the responsible qualified doctors. The person involved in the production of an essay must be educated and trained. The information of the clinical trials must be recorded and managed in a way that allows proper verification for further use and privacy should be applied to such records. Manufacturing of research products occurs in accordance with good manufacturing practices (GMP). Systematic procedures that rely on the quality of test are done [21].

5.3.2. Phase-0 Clinical Trials

The pharmacokinetic and pharmacodynamics characteristics of the drug are determined during phase-0 studies which are applied on small group of patients [5].

5.3.3. Phase-I Clinical Trials

Phase I studies are applied on the small number of healthy individuals which evaluate the safety of the drug. The main purpose of the phase I trials is to check the safe dosing and side effects with its toxicity [8].

5.3.3.1. Major Steps in Clinical Trials Phases

Major steps in the clinical trials phase and review for INDs proceeds up by first file INDs to FDA to start clinical trials. As the application got submitted, clinical trials proceeded if there is no objection from FDA and if suggestions made by FDA reviewer then a consultation with reviewer occurs. Sometimes mandatory changes are required then trials can’t be preceded until the changes are made. After that Phase-I trial goes on with small study to determine the adverse effects of toxicity and safety of drug which is followed by a report submitted to FDA. Then phase-II trials get run through. In these trials moderate size study of patient is determined and check efficacy and less common side effects of the same drug. Then report till the completion of clinical study is submitted to the FDA so that discussion between the sponsor and FDA occurs that how further proceedings will be going on for phase-III. In phase-III clinical trials large prospective studies of clinical efficacy followed by the pre-NDA meeting in which sponsors meet with FDA. Then NDA get submitted followed by discussion for marketing approval of drug with FDA. After successful submission of NDA, FDA review team assigned the new drug for marketed in the country [5].

5.3.4. Phase II Clinical Trials

The phase II clinical trials are begun with the completion of phase I trials. The domination of healthy patients is higher in phase I rather than in phase II trials to check whether the candidate drug has potency to save the lives of examined patients. Depending upon the nature of the indications, phase II studies require at least 100-300 patients with 2 years of time under investigation. Major aim of phase II of clinical development is the preparation of doses that are used in phase III studies. Classifications of doses are prepared which includes one dose of potentially low action, other two of intermediate and fourth one of high potential activity [16]. The major milestones of the overall clinical development program are that of meeting with the appropriate regulatory agency [22]. The main objective of the phase II is to specify the good or positive sign in the patient population. So many times in phase II trial, patient may exposed first time treatment to the candidate drug. All patients are needed to be monitored to find out any possible safety measure because such patient is used for longer duration of course [16]. The disease and condition which is to be examined demonstrate the design of clinical trials.

5.3.5. Phase-III Clinical Trials

The drug efficacy as well as monitoring the secondary effects by applying on large number of people approx. (1000 to 3000) by collecting the drug information data that allow the treatment through new medication [23]. Launching a new drug requires 90% cost of the total investment associated to phase III trials. This process normally processed in many clinical sites which may takes 2.5 years to 5 years. It depends upon the nature of the disease and the frequency of patients. The fate of phase III trials is to demonstrate the effectiveness of drug to the targeted disease or condition. The outcomes must be choosing carefully as it is critical task of the trial design and in well defined way [16]. Continuous studies are required during phase III of clinical drug development [24].

6. NEW DRUG APPLICATION (NDA)

When the drug successfully overcomes all three stages of clinical trials, then submission of new drug application including animal data to FDA is required of data analysis, pharmacokinetics of the
drug and its labeling and production data. A group of scientists from the Center for Drug Assessment and Research (CDRH) examined preclinical clinical reports and risk-benefit analysis of the same drug [25]. (NDA) signifies the regulation of new drug in US. The NDA provides information on all data on animals and humans and how the drug behaves in the organism with its production [26]. The NDA application serves as a vehicle through which the drug sponsor proposes that the FDA approve the sales and marketing of a new pharmaceutical product in the United States [27]. The group of medical experts, chemists, statisticians, microbiologists, pharmacologists and other FDA experts mainly assesses that the drug is safe and effective for its proposed use [28].

6.1. Goals of the NDA

The main perspective of goals of NDA is that drug should be safe with effectiveness with the perfect labeling and the method applied for manufacturing the drug should maintain the drug quality adequately [29].

6.2. General Data Requirements for Innovative Drug Approved in the U.S

The general data required for the approval of new drug in U.S includes clinical and non-clinical data such as complete summary of investigation with manufacturing data. It also includes non-clinical pharmacological and toxicological status. Which is followed by human pharmacokinetics and bioavailability clinical microbiology and safety update report is also required for the same purpose [30, 31].

6.3. Electronic Common Technical Document (eCTD)

The ordinary format for submission of application amendments and supplements to FDA’s centre called Center for Drug Evaluation and Research (CDER) and center for Biologics Evaluation and Research (CBER) is refer to (eCTD).

6.4. eCTD Guidance

The implementation of submission of requirements to new drug application (NDA), certain Biologics License Application (BLAs) and to (IND) as well as to center for Drug evaluation and Research (CDER) proceeds through the (eCTD) guidance under section 745(a.) [32].

6.5. Files Submit Electronically Under This Guidance

A. Types of Submission

As per the eCTD guidance Investigational new drug application (INDs), New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), Biologics License Applications (BLAs) can be submitted electronically in the US FDA [32].

B. Timetable for Implementation of Electronic Submission Requirements

The application of NDAs, ANDAs and BLAs get electronically effective for submission from May 5, 2017 and the application of INDs become electronically active for the same from 5 May, 2018.

C. Pre-Submission Considerations

D. The eCTD Specifications

6.6. FDA Organization Chart

FDA is an agency under the Department of Health and Human Services which including nine Centers and Office. Named as - Office of Operation, Office of Policy, Planning, Legislation, and Analysis followed by Center for Biologics Evaluation and Research, FDA's Office of Medical Products and Tobacco. It also includes Office of Regulatory Affairs (ORA, National Center for Toxicological Research Office of Global Regulatory Operations and Policy (OGROP) Center for Devices and Radiological Health Organization, Center for Drug Evaluation and Research and Center for Tobacco Products [33].

7. PHASE IV CLINICAL TRIALS

Phase IV trials are performed when the drug has a product license and is available for regular prescription [34]. During phase IV trials we mainly examined the adverse effects over huge population [35]. Phase IV trial includes certain objectives which include specification of new directions for use, extension of safety profile, collecting new information about the clinical investi-
nigation [36]. Section 505(o) of the federal food, drug and cosmetics act of 2007 (FDAAA) includes the basic requirements of the PMC trials [37].

Post-approval trials might be designed to analyze the drug with other patient populations [38]. Good surveillance practice establishes standards for post-marketing safety management linked to the collection and evaluation of appropriate use information on the establishment of suitable safety measure [39]. Effectiveness is the actual test of a drug when it is used in a huge population [40]. The patient population in a phase IV clinical trial normally much larger and more varied than phase III study [16].

The most common objectives of the FDA’s post-marketing surveillance includes the collection, evaluation and reporting of drug safety data which provide the financial risk to the manufacturers and also rely on government agencies to approve the drug with its evidences for existence [41].

Harmful effects found in Phase IV trials can result in which drug may not been sold longer or limited to certain uses [42].

A well executed clinical study may provide the facts needed to change clinical practice and create guidelines for patient management with improvement in patient care are the possible keys in drug development [43]. In recent times, the importance of conducting medical research on a global platform cannot be exaggerated [44].

8. LIST OF DRUGS APPROVED BY FDA IN 2017

FDA approved 34 therapeutic classes of drugs till today. Despite them, 22 categories of drugs had been approved in 2017. In this calendar year more than 80 Novel drugs got approval from different therapeutic classes by FDA till 10th of November. As we know that the patients caused by oncogenes are increasing day by day therefore higher no. of drugs i.e. 15 drugs had been approved for oncology class and least no. goes to cardiology and nephrology class. By seeing this data we can determine the patients towards various diseases. As higher no. of drugs had been approved in August (19) followed by (11) in both March and April. Only 3 drugs had been approved in January. Novartis is the only company which had approved more than 5 new drugs this year followed by Genentech and Pfizer.

This database contain general introduction about several specific approved drugs and as follows: The drugs designed for Oncology are numerous in no. which precisely shows that Oncology is very severe issue to think and increasing day by day. FDA approved 15 new drugs this year for the same therapeutic class of drugs. Many pharmaceuticals came across this year for the approval of their manufactured drugs for the Oncology like Novartis, Lexicon, Eli lilly, Tesaro and kite pharmaceuticals. Then the more no. of drugs had been approved for the diseases related to blood and its components as the infections in blood through various pathways and factors are increasing day by day. So, 9 drugs for hematology had been approved this year in which again famous pharmaceuticals like Bayer, Novartis, Pfizer and kite pharmaceuticals had taken their grant towards it. With this many pharmaceuticals came forward towards the drugs for infectious diseases as the infections of various organs and location of body are increasing with alert due to increase in pollution and many other factors which support the infections. Therefore in support to infectious diseases therapeutic class of drug 7 new drugs had been approved this year for the relevantly treatment of individual diseases with their specific drugs like Baxdela, Benznidazole and Solosec. Novartis give their best and approved highest no. of drugs in this year in the area of Hematology, Gynaecology and Oncology with 2 drugs each in the month of March, April and August. As the change in environment with the weather and climatic response now a day’s people are getting attraction towards the skin diseases which are severe too. To get rid of these diseases FDA approved 6 drugs in respect to Dermatology therapeutic class for example: Bavencio and Siliq from moderate to severe treatment like psoriasis and Markel cell carcinoma. To Investigate and diagnose, some pharmaceuticals like Biomarin, Janssen and Gilead’s came forward this year with their innovation in the area of Neurology, Immunology and Musculoskeletal disorders with approval of 6-7 drugs in each category. Some therapeutic classes remains least in the approval of new drugs towards them this year like Nephrology, Cardiology, Urology, Ophthalmology, Vaccines and Endocrinology.
Table 1. List of drugs Approved by FDA in 2017.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Drug Name</th>
<th>Company Name</th>
<th>Approval Status</th>
<th>Drug Therapeutic Area</th>
<th>M.O.A</th>
<th>Specific Treatment</th>
<th>Side Effects</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Rhofade (oxymetazoline hydrochloride)</td>
<td>Allergan</td>
<td>January 2017</td>
<td>Dermatology</td>
<td>alpha1A adrenoceptor agonist</td>
<td>Facial erythema associated with rosacea</td>
<td>Application site pruritus, application site erythema</td>
<td>[45]</td>
</tr>
<tr>
<td>2.</td>
<td>Trulance (plecanatide)</td>
<td>Synergy Pharmaceuticals</td>
<td>January 2017</td>
<td>Gastroenterology, Family Medicine</td>
<td>guanylate cyclase-C agonist</td>
<td>Chronic idiopathic constipation</td>
<td>Diarrhea</td>
<td>[46]</td>
</tr>
<tr>
<td>3.</td>
<td>Siliq (brodalumab)</td>
<td>Valeant Pharmaceuticals</td>
<td>February 2017</td>
<td>Dermatology</td>
<td>interleukin-17 receptor A (IL-17RA) antagonist.</td>
<td>Plaque psoriasis</td>
<td>Influenza, neutropenia, tinea infections</td>
<td>[47]</td>
</tr>
<tr>
<td>4.</td>
<td>Emflaza (deflazacort)</td>
<td>Marathon Pharmaceuticals</td>
<td>February 2017</td>
<td>Musculoskeletal, Pediatrics/Neonatology</td>
<td>corticosteroid which exerts anti-inflammatory and immunosuppressive effects</td>
<td>Duchenne muscular dystrophy</td>
<td>Pollakiuria, hirsutism, central obesity</td>
<td>[48]</td>
</tr>
<tr>
<td>7.</td>
<td>Xermelo (telotristat ethyl)</td>
<td>Lexicon Pharmaceuticals</td>
<td>February 2017</td>
<td>Gastroenterology, Oncology</td>
<td>tryptophan hydroxylase inhibitor</td>
<td>Carcinoid syndrome diarrhea</td>
<td>Peripheral edema, pyrexia, flatulence</td>
<td>[51]</td>
</tr>
<tr>
<td>8.</td>
<td>Kisqali (ribociclib)</td>
<td>Novartis</td>
<td>March 2017</td>
<td>Obstetrics/Gynecology, Oncology</td>
<td>kinase inhibitor</td>
<td>Breast cancer</td>
<td>Leucopenia, alopecia</td>
<td>[52]</td>
</tr>
<tr>
<td>S. No.</td>
<td>Drug Name</td>
<td>Company Name</td>
<td>Approval Status</td>
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<td>M.O.A</td>
<td>Specific Treatment</td>
<td>Side Effects</td>
<td>Refs.</td>
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<td>9.</td>
<td>Symproic (naldemedine)</td>
<td>Shionogi</td>
<td>March 2017</td>
<td>Gastroenterology</td>
<td>opioid antagonist</td>
<td>Opioid-induced constipation</td>
<td>abdominal pain, diarrhea</td>
<td>[53]</td>
</tr>
<tr>
<td>10.</td>
<td>Bavencio (Avelumab)</td>
<td>EMD Serono/Pfizer</td>
<td>March 2017</td>
<td>Dermatology and Oncology</td>
<td>programmed death ligand-1 (PD-L1) blocking antibody</td>
<td>Merkel cell carcinoma</td>
<td>Fatigue, musculoskeletal pain, diarrhea</td>
<td>[54]</td>
</tr>
<tr>
<td>11.</td>
<td>Xadago (safinamide)</td>
<td>Newron Pharmaceuticals</td>
<td>March 2017</td>
<td>Neurology</td>
<td>monoamine oxidase type B (MAO-B) inhibitor</td>
<td>Parkinson's disease</td>
<td>Dyskinesia, nausea</td>
<td>[55]</td>
</tr>
<tr>
<td>12.</td>
<td>Ocrevus (ocrelizumab)</td>
<td>Genentech</td>
<td>March 2017</td>
<td>Immunology, Musculoskeletal</td>
<td>CD20-directed cytolytic antibody</td>
<td>Multiple sclerosis</td>
<td>Upper respiratory tract infections, infusion reaction</td>
<td>[56]</td>
</tr>
<tr>
<td>13.</td>
<td>Zejula (niraparib)</td>
<td>Tesaro</td>
<td>March 2017</td>
<td>Obstetrics/Gynecology (Women’s Health), Oncology</td>
<td>poly(ADP-ribose) polymerase (PARP) inhibitor</td>
<td>Recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer</td>
<td>Neutropenia, leukopenia, palpitations</td>
<td>[57]</td>
</tr>
<tr>
<td>14.</td>
<td>Dupixent (Dupilumab)</td>
<td>Regeneron Pharmaceuticals</td>
<td>March 2017</td>
<td>Dermatology</td>
<td>interleukin-4 receptor alpha antagonist</td>
<td>Atopic dermatitis</td>
<td>Conjunctivitis, Blepharitis</td>
<td>[58]</td>
</tr>
<tr>
<td>15.</td>
<td>Rydapt (midostaurin)</td>
<td>Novartis</td>
<td>April 2017</td>
<td>Hematology, Oncology</td>
<td>multi kinase inhibitor</td>
<td>FLT3 positive acute myeloid leukemia and mastocytosis</td>
<td>Petechiae, musculoskeletal pain, epistaxis</td>
<td>[59]</td>
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<tr>
<td>16.</td>
<td>Ingrezza (valbenzine)</td>
<td>Neurocrine Biosciences</td>
<td>April 2017</td>
<td>Neurology</td>
<td>vesicular monoamine transporter 2 (VMAT2) inhibitor</td>
<td>Tardive dyskinesia</td>
<td>Somnolence</td>
<td>[60]</td>
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<tr>
<td>17.</td>
<td>Austedo (deutetrabenazine)</td>
<td>Teva Pharmaceuticals</td>
<td>April 2017</td>
<td>Neurology</td>
<td>vesicular monoamine transporter 2 (VMAT2) inhibitor</td>
<td>chorea associated with Huntington’s disease and tardive dyskinesia</td>
<td>Somnolence, diarrhea</td>
<td>[61]</td>
</tr>
</tbody>
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Table 1. contd…
<table>
<thead>
<tr>
<th>S. No.</th>
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<th>Specific Treatment</th>
<th>Side Effects</th>
<th>Refs.</th>
</tr>
</thead>
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<tr>
<td>19.</td>
<td>Tymlos (abaloparatide)</td>
<td>Radius Health</td>
<td>April 2017</td>
<td>Musculoskeletal, Obstetrics/Gynecology /Women’s Health</td>
<td>human parathyroid hormone related peptide [PTHrP(1-34)] analog</td>
<td>Postmenopausal women with osteoporosis at high risk for fracture</td>
<td>Hypercalcemia, dizziness</td>
<td>[63]</td>
</tr>
<tr>
<td>20.</td>
<td>Brineura (cerliponase alfa)</td>
<td>BioMarin</td>
<td>April 2017</td>
<td>Musculoskeletal, Neurology/Pediatrics/Neonatology</td>
<td>hydrolytic lysosomal N-terminal tripeptidyl peptidase</td>
<td>Late infantile neuronal ceroid lipofuscinosis type 2</td>
<td>Pyrexia, ECG abnormalities</td>
<td>[64]</td>
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<tr>
<td>21.</td>
<td>Kevzara (sarihumab)</td>
<td>Sanofi</td>
<td>May 2017</td>
<td>Musculoskeletal, Rheumatology</td>
<td>interleukin-6 (IL-6) receptor antagonist</td>
<td>Active rheumatoid arthritis</td>
<td>Neutropenia</td>
<td>[65]</td>
</tr>
<tr>
<td>22.</td>
<td>Imfinzi (durvalumab)</td>
<td>AstraZeneca</td>
<td>May 2017</td>
<td>Oncology, Urology</td>
<td>programmed death-ligand 1 (PD-L1) blocking antibody</td>
<td>Advanced or metastatic urothelial carcinoma</td>
<td>musculoskeletal pain, Constipation, decreased appetite</td>
<td>[66]</td>
</tr>
<tr>
<td>23.</td>
<td>Radicava (edaravone)</td>
<td>Mitsubishi Tanabe Pharma</td>
<td>May 2017</td>
<td>Neurology</td>
<td>free radical scavenger</td>
<td>Amyotrophic lateral sclerosis</td>
<td>Contusion, gait disturbance</td>
<td>[67]</td>
</tr>
<tr>
<td>24.</td>
<td>Zerviate (cetirizine ophthalmic solution 0.24%)</td>
<td>NicOx</td>
<td>May 2017</td>
<td>Immunology, Ophthalmology</td>
<td>second generation antihistamine (H1 receptor antagonist)</td>
<td>Ocular itching associated with allergic conjunctivitis</td>
<td>Ocular hypereemia, instillation site pain</td>
<td>[68]</td>
</tr>
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<td>25.</td>
<td>Bevyxxa (Betrixaban)</td>
<td>Portola Pharmaceuticals</td>
<td>June 2107</td>
<td>Cardiology/Vascular Diseases</td>
<td>factor Xa (FXa) inhibitor</td>
<td>Prophylaxis of venous thromboembolism</td>
<td>Bleeding</td>
<td>[69]</td>
</tr>
<tr>
<td>26.</td>
<td>Rebinyn</td>
<td>Novo Nordisk</td>
<td>June 2107</td>
<td>Hematology, Pediatrics/Neonatology</td>
<td>proprietary glycopegylated recombinant factor IX in hemophilia B</td>
<td>Hemophilia B</td>
<td>Itching</td>
<td>[70]</td>
</tr>
</tbody>
</table>

Table 1. contd…
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Drug Name</th>
<th>Company Name</th>
<th>Approval Status</th>
<th>Drug Therapeutic Area</th>
<th>M.O.A</th>
<th>Specific Treatment</th>
<th>Side Effects</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.</td>
<td>Baxdela (Delafloxacin)</td>
<td>Melinta Therapeutics</td>
<td>June 2017</td>
<td>Dermatology, Infections and Infectious Diseases</td>
<td>fluoroquinolone antibacterial</td>
<td>Acute bacterial skin and skin structure infections</td>
<td>Transaminase elevations, Vomiting</td>
<td>[71]</td>
</tr>
<tr>
<td>28.</td>
<td>Haegard</td>
<td>CSL Behring</td>
<td>June 2017</td>
<td>Immunology, Genetic Disease</td>
<td>plasma-derived concentrate of C1 Esterase Inhibitor (Human)</td>
<td>Routine prophylaxis to prevent Hereditary Angioedema attacks</td>
<td>Hypersensitivity, nasopharyngitis</td>
<td>[72]</td>
</tr>
<tr>
<td>29.</td>
<td>Tremfya (guselkumab)</td>
<td>Janssen Biotech</td>
<td>July 2017</td>
<td>Dermatology and Immunology</td>
<td>interleukin-23 Cytokine blocker</td>
<td>Moderate-to-severe plaque psoriasis</td>
<td>Upper respiratory infections, arthralgia</td>
<td>[73]</td>
</tr>
<tr>
<td>30.</td>
<td>Nerlynx (neratinib)</td>
<td>Puma Biotech</td>
<td>July 2017</td>
<td>Oncology</td>
<td>kinase inhibitor that irreversibly binds to Epidermal Growth Factor Receptor (EGFR)</td>
<td>HER2 breast cancer</td>
<td>Stomatitis, decreased appetite, muscle spasms, dyspepsia</td>
<td>[74]</td>
</tr>
<tr>
<td>31.</td>
<td>Vosevi (sofosbuvir, velpatasvir, and voxilaprevir)</td>
<td>Gilead</td>
<td>July 2017</td>
<td>Immunology, Hepatology (Liver, Pancreatic, Gall Bladder)</td>
<td>hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, HCV NS5A inhibitor, HCV NS3/4A protease inhibitor</td>
<td>Hepatitis C</td>
<td>Fatigue, diarrhea</td>
<td>[75]</td>
</tr>
<tr>
<td>32.</td>
<td>Endari (L-glutamine oral powder)</td>
<td>Emmaus Life Sciences</td>
<td>July 2017</td>
<td>Hematology</td>
<td>reduces oxidant damage to red blood cells by improving the redox potential of nicotinamide adenine dinucleotide (NAD)</td>
<td>Sickle cell disease</td>
<td>Constipation, nausea</td>
<td>[76]</td>
</tr>
</tbody>
</table>

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<table>
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<tr>
<th>S. No.</th>
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<th>Specific Treatment</th>
<th>Side Effects</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.</td>
<td>IDHIFA (enasidenib)</td>
<td>Celgene</td>
<td>August 2107</td>
<td>Hematology, Oncology</td>
<td>Inhibit isocitrate dehydrogenase 2 (IDH2) enzyme</td>
<td>Relapsed or refractory acute myeloid leukemia with IDH2 mutation</td>
<td>Increased levels of bilirubin, decreased appetite</td>
<td>[77]</td>
</tr>
<tr>
<td>34.</td>
<td>Kymriah (tisagenlecleucel)</td>
<td>Novartis</td>
<td>August 2017</td>
<td>Hematology, Oncology</td>
<td>CD19-directed genetically modified autologous T cell immunotherapy</td>
<td>Refractory B-cell precursor acute lymphoblastic leukemia</td>
<td>Cytokine release syndrome, hypogammaglobulinemia</td>
<td>[78]</td>
</tr>
<tr>
<td>35.</td>
<td>Vyxeos (daunorubicin and cytarabine)</td>
<td>Jazz Pharma</td>
<td>August 2107</td>
<td>Hematology, Oncology</td>
<td>Anthracycline topoisomerase inhibitor, nucleoside metabolic inhibitor</td>
<td>Newly-diagnosed therapy-related AML or AML with myelodysplasia-related changes</td>
<td>Febrile neutropenia, Rash, edema</td>
<td>[79]</td>
</tr>
<tr>
<td>36.</td>
<td>Besponsa (inotuzumab ozogamicin)</td>
<td>Pfizer</td>
<td>August 2017</td>
<td>Hematology, Oncology</td>
<td>CD22-directed antibody-drug conjugate (ADC)</td>
<td>Refractory B-cell precursor acute lymphoblastic leukemia</td>
<td>Thrombocytopenia, neutropenia</td>
<td>[80]</td>
</tr>
<tr>
<td>37.</td>
<td>Benznidazole</td>
<td>Chemo Group</td>
<td>August 2017</td>
<td>Infections and Infectious Diseases</td>
<td>Nitroimidazole antimicrobial</td>
<td>Chagas disease</td>
<td>Urticaria, pruritus</td>
<td>[81]</td>
</tr>
<tr>
<td>38.</td>
<td>Vabomere (meropenem and vaborbactam)</td>
<td>The Medicines Company</td>
<td>August 2017</td>
<td>Infections and Infectious Diseases, Urology</td>
<td>Penem antibacterial, beta-lactamase inhibitor</td>
<td>Complicated urinary tract infections</td>
<td>Phlebitis, infusion site reactions, diarrhea</td>
<td>[82]</td>
</tr>
<tr>
<td>40.</td>
<td>Duzallo (lesinurad and allopurinol)</td>
<td>Ardea Biosciences</td>
<td>August 2017</td>
<td>Musculoskeletal, Rheumatology, Internal Medicine</td>
<td>Uric acid reabsorption inhibitor, xanthine oxidase inhibitor</td>
<td>Hyperuricemia associated with gout</td>
<td>Blood creatinine increase, gastroesophageal reflux disease</td>
<td>[84]</td>
</tr>
</tbody>
</table>

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<th>S. No.</th>
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<th>Specific Treatment</th>
<th>Side Effects</th>
<th>Refs.</th>
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</thead>
<tbody>
<tr>
<td>41.</td>
<td>Mavyret (glecaprevir and pibrentasvir)</td>
<td>AbbVie</td>
<td>August 2017</td>
<td>Hepatology (Liver, Pancreatic, Gall Bladder, Infections)</td>
<td>hepatitis C virus (HCV) NS3/4A protease inhibitor, HCV NS5A inhibitor</td>
<td>Chronic HCV genotype 1, 2, 3, 4, 5 or 6</td>
<td>Headache, fatigue</td>
<td>[85]</td>
</tr>
<tr>
<td>42.</td>
<td>Actemra (tocilizumab)</td>
<td>Genentech</td>
<td>September 2017</td>
<td>Immunology, Pharmacology/Toxicology</td>
<td>humanized anti IL-6 receptor monoclonal antibody</td>
<td>CAR T-cell induced Cytokine Release Syndrome</td>
<td>Upper respiratory tract infections, nasopharyngitis</td>
<td>[86]</td>
</tr>
<tr>
<td>43.</td>
<td>Verzenio (abemaciclib)</td>
<td>Eli Lilly</td>
<td>September 2017</td>
<td>Obstetrics/Gynecology (Women’s Health), Oncology</td>
<td>kinase inhibitor</td>
<td>HR+, HER2-breast cancer</td>
<td>Diarrhea, neutropenia and leukopenia</td>
<td>[87]</td>
</tr>
<tr>
<td>44.</td>
<td>Solosec (secnidazole)</td>
<td>Symbionix Therapeutics</td>
<td>September 2017</td>
<td>Obstetrics/Gynecology (Women’s Health), Infections and Infectious Diseases</td>
<td>nitromidazole antimicrobial</td>
<td>Bacterial vaginosis</td>
<td>Vulvo-vaginal candidiasis, vulvovaginal pruritis</td>
<td>[88]</td>
</tr>
<tr>
<td>45.</td>
<td>Aliqopa (copanlisib)</td>
<td>Bayer</td>
<td>September 2017</td>
<td>Hemaology, Oncology</td>
<td>kinase inhibitor</td>
<td>Follicular lymphoma</td>
<td>Hyperglycemia, diarrhea</td>
<td>[89]</td>
</tr>
<tr>
<td>46.</td>
<td>Shingrix</td>
<td>GlaxoSmith-Kline</td>
<td>October 2017</td>
<td>Infections and Infectious Diseases, Vaccines</td>
<td>Recombinant adjuvanted vaccine against the virus that causes shingles</td>
<td>Herpes zoster (shingles)</td>
<td>Pain, redness, swelling</td>
<td>[90]</td>
</tr>
<tr>
<td>47.</td>
<td>Zilretta</td>
<td>Flexion Therapeutics</td>
<td>October 2017</td>
<td>Musculoskeletal, Rheumatology</td>
<td>extended-release injectable suspension of triamcinolone acetonide, a short-acting corticosteroid</td>
<td>Osteoarthritis knee pain</td>
<td>Sinusitis, cough, contusions</td>
<td>[91]</td>
</tr>
</tbody>
</table>

Table 1. contd…
in— which only 1 or 2 drugs had been approved from each class.

The above table (Table 1) intended for drug database of 2017 contains the complete information including drug name, name of company, therapeutic class of drug, mode of action, side effects, approval status and indication of use with their general information [94].

9. DRUGS APPROVED BY FDA IN 2018

FDA approved only one therapeutic class (Oncology) of drug in January 2018. Lutathera (lutetium Lu 177 dotatate) drug is approved by company Advanced Accelerator Applications. It is specifically indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) including foregut, midgut, and hindgut neuroendocrine tumors in adults. Lutathera is supplied as an injection for intravenous administration. Therapeutic areas covered by lutathera are gastroenterology and Oncology [95].

CONCLUSION

Currently, the United States is the most stringent standards for the approval of drugs in the world. The average FDA approval time for medical drug is 12 years, the estimated average cost of taking a new drug for a market is more than $1 billion. Regulatory processes are under constant study in the direction of identify means of streamlining approval processes. After approval of an IND application, the FDA allows human clinical trial phase 0, I, II, and III studies and provided safety and efficacy. For NDA, the FDA requires significant evidence of drug safety and efficacy. The FDA encourages early and regular communication to investigators and sponsors for seeking drug approval and purpose of avoiding failures application or clinical holds that may waste valuable time, effort, and finances in the process of bringing a drug to market.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES


approved-drugs/drug/100232/shingrix-zoster-vaccine-recombinant-adjuvanted-


