In 2013, there were 27 new molecular entities (NMEs) approved by the US Food and Drug Administration (FDA), of which more than 50% were specialty pharmaceuticals. However, compared with 2012, when 39 NMEs were approved, the number of new FDA-approved drugs fell by more than 30% in 2013. Of the 27 NMEs approved last year, 16 were specialty drugs and almost 33% of the approvals were for rare diseases, continuing a multiyear trend favoring specialty and orphan drugs.

Despite the decline in total NMEs approved last year, the total approved innovative medications is in line with the historical trend of the FDA, which has, on average, approved 28 NMEs annually over the past 5 years. According to experts, the decline in NMEs approved is a result of fewer drug applications submitted to the agency. The FDA received at least 32 applications for innovative medicines in 2013, down from 41 in 2012, according to a recent presentation by FDA representative John K. Jenkins, MD, Director of the Office of New Drugs at the FDA’s Center for Drug Evaluation and Research.

Among the new FDA NME approvals for 2013 were:

- 10 drugs (37%) targeting novel mechanisms of action
- 4 drugs (15%) that received accelerated approval
- 8 drugs (30%) for cancer
- 5 approvals (19%) for anti-infective drugs, including 4 antivirals
- 3 approvals for drugs designated as breakthrough therapies.

Specialty Drugs Continued to Dominate 2013 Approvals

As was the case in 2012, new drug approvals in 2013 continued the trend of growth for new specialty drugs. The Table lists the new agents approved in 2013 that are generally considered to be specialty agents.

Among the newly approved drugs last year, 16 agents may be classified as specialty agents (Table). Of those 16 specialty drugs, 50% are indicated for the treatment of various cancers, which is again a continuation of a multiyear trend. However, there were also approvals for 2 new agents for hepatitis C virus (HCV) infection, 2 new agents for pulmonary hypertension, and 1 oral agent for the treatment of multiple sclerosis (MS).

The emphasis on specialty drug development is here to stay, and it will likely remain the major focus of pharmacy innovation in 2014 and beyond.

Breakthrough Therapies Emerge in 2013

On July 9, 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) was signed. FDASIA Section 902 provided a new designation for breakthrough therapies. A breakthrough therapy is a designation given for a drug that is intended to be used alone or in combination with 1 or more other drugs for the treatment of a serious or life-threatening disease or condition. Furthermore, preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant end points, such as substantial beneficial clinical effects observed early in a drug’s clinical development.

If a drug is designated as a breakthrough therapy, the FDA is required to expedite the development and review of that drug. The classification was designed to speed up the development of promising drugs by providing companies with extra meetings and earlier communication with scientists at the FDA. In January 2013, Vertex was the first company to disclose that their therapies for cystic fibrosis had been granted this status by the FDA. Less than 1 year later, 3 therapies that were granted a breakthrough therapy designation by the FDA received approval last year. These include obinutuzumab (Gazyva; Genentech) for the treatment of previously untreated chronic lymphocytic leukemia (CLL), ibrutinib (Imbruvica; Pharmacyclics) for the treatment of mantle-cell lymphoma, and sofosbuvir (Sovaldi; Gilead Sciences) for the treatment of chronic HCV infection.

Cancer Drugs Continued to Dominate the Therapeutic Categories

For the third consecutive year, drugs for the treatment of cancer dominated the new drug approvals. The FDA approved 8 new agents for cancer (Table). Although this is a decrease from 2012, it is identical to the number of drugs for cancer that were approved in 2011.
Malignant Melanoma Therapies

The FDA approved 2 targeted oral therapies for patients with melanoma at the same time in 2013. Trametinib (Mekinist) was approved for the treatment of patients with metastatic or unresectable melanoma with the BRAF V600E or BRAF V600K mutation who have not been previously treated with BRAF inhibitor therapy. Dabrafenib (Tafinlar) was approved for the treatment of patients with unresectable or metastatic melanoma with the BRAF V600E mutation. Both drugs were approved concurrently with the FDA approval of a companion diagnostic assay for the detection of BRAF V600E and BRAF V600K mutations. Subsequently, in 2014 these drugs were approved by the FDA as the first combination therapy indicated for the treatment of patients with advanced or metastatic melanoma.

Hematologic Malignancies

Two important new agents were approved in 2013 to treat hematologic malignancies. As noted earlier, ibrutinib was approved in November 2013 for the treatment of patients with mantle-cell lymphoma. This agent inhibits the function of the Bruton’s tyrosine kinase (BTK). The BTK is a key signaling molecule of the B-cell receptor–signaling complex that plays an important role in the survival of malignant B-cells.5 Of note, the FDA subsequently approved ibrutinib for the treatment of patients with CLL in early 2014.

With its approval in November 2013, obinutuzumab became the first agent to be approved under the breakthrough therapy designation. Obinutuzumab is a humanized anti-CD20 monoclonal antibody of the immunoglobulin G1 subclass. It recognizes a specific epitope of the CD20 molecule found on B-cells.6 Obinutuzumab is specifically indicated for use in combination with chlorambucil for the treatment of patients with previously untreated CLL.

Solid-Organ Tumors

The year 2013 also had important approvals for the treatment of solid-organ tumors. Radium Ra 223 dichloride (Xofigo; Bayer HealthCare) was approved by the FDA in May 2013 for symptomatic metastatic castration-resistant prostate cancer that affects bones but not other organs (ie, with no known visceral metastatic disease). The active ingredient of this drug, radium Ra 223 dichloride, is an alpha particle–emitting radioactive therapeutic agent that mimics calcium and forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover, such as bone metastases.

Afatinib (Gilotrif) tablets were approved by the FDA in mid-2013 as a first-line oral treatment for non–small-cell lung cancer with epidermal growth factor receptor (EGFR) mutations. The FDA approved afatinib concurrently with the companion diagnostic (EGFR RGQ PCR Kit), which helps determine if a patient’s lung cancer cells express the EGFR mutations. Therefore, afatinib joins a growing group of anticancer drugs that have been launched with companion diagnostics to appropriately target this drug for the treatment of patients who are most likely to benefit from it—a growing trend in oncology therapies.

Hepatitis C Treatments in the Spotlight in 2013

In the United States, there are approximately 3.2

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Malignant Melanoma Therapies

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Brand (generic) name</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actelion</td>
<td>Opsumit (macitentan)</td>
<td>Pulmonary arterial hypertension</td>
</tr>
<tr>
<td>Bayer HealthCare</td>
<td>Xofigo (radium Ra 223 dichloride)</td>
<td>Castration-resistant prostate cancer</td>
</tr>
<tr>
<td>Bayer HealthCare</td>
<td>Adempas (riociguat)</td>
<td>Chronic thromboembolic pulmonary hypertension</td>
</tr>
<tr>
<td>Biogen Idec</td>
<td>Techdiera (dimethyl fumarate)</td>
<td>Relapsing forms of multiple sclerosis</td>
</tr>
<tr>
<td>Boehringer Ingelheim</td>
<td>Gilotrif (afatinib)</td>
<td>Non–small-cell lung cancer</td>
</tr>
<tr>
<td>Celgene</td>
<td>Pomalyst (pomalidomide)</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>Genentech</td>
<td>Kadcyla (ado-trastuzumab emtansine)</td>
<td>Metastatic breast cancer</td>
</tr>
<tr>
<td>Genentech</td>
<td>Gazyva (obinutuzumab)</td>
<td>Chronic lymphocytic leukemia</td>
</tr>
<tr>
<td>Genzyme</td>
<td>Kynamro (mipomersen sodium)</td>
<td>Homozygous familial hypercholesterolemia</td>
</tr>
<tr>
<td>Gilead Sciences</td>
<td>Sofosbuvir</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>Tafinlar (dabrafenib)</td>
<td>Unresectable or metastatic melanoma</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>Mekinist (trametinib)</td>
<td>Unresectable or metastatic melanoma</td>
</tr>
<tr>
<td>Hyperion Therapeutics</td>
<td>Ravicti (glycerol phenylbutyrate)</td>
<td>Urea cycle disorders</td>
</tr>
<tr>
<td>Janssen Biotech</td>
<td>Olysio (simprevir)</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Pharmacycics</td>
<td>Imbruvica (ibrutinib)</td>
<td>Mantle-cell lymphoma</td>
</tr>
<tr>
<td>Raptor</td>
<td>Procysbi (cysteamine bitartrate)</td>
<td>Cystinosis</td>
</tr>
</tbody>
</table>
millon persons who have chronic HCV infection, many of whom will develop chronic liver disease, cirrhosis, and liver cancer if left untreated.

The first of 2 new HCV treatments, simprevir (Olysio; Janssen Biotech) was approved in November 2013. This drug is an oral capsule that is intended to be used as part of a combination regimen for the treatment of chronic HCV infection in adults, including patients with compensated cirrhosis or other stable liver disease. Simprevir is indicated, in combination with peginterferon alfa and ribavirin, for the treatment of infections caused by HCV genotype 1, according to the drug's labeling. The addition of simprevir to the treatment regimen resulted in up to 80% of clinical trial participants with genotype 1 HCV infection becoming free of infection after completing their treatment. Genotype 1 infections are more difficult to treat than some other genotypes of HCV infection, and the results of the clinical trials were considered a significant advance.

The second agent to be approved for HCV infection was sofosbuvir (Sovaldi; Gilead Sciences). Sofosbuvir oral tablets are used as part of a regimen for the treatment of chronic HCV infection caused by viruses of genotypes 1, 2, 3, or 4. According to the FDA, sofosbuvir is the first drug that can be used without an interferon agent to treat certain types of chronic HCV infection.

These 2 new agents are just the beginning of a new era in HCV infection treatment that will ultimately result in better cure rates and all-oral treatments for the majority of patients with this type of infection.

Significant Advances in Other Therapeutic Categories

Many other important approvals or expanded indications for existing drugs occurred in 2013. Dimethyl fumarate (Tecfidera; Biogen Idec) became the third oral agent approved for adults with relapsing forms of MS. Additions to the arsenal of agents to treat pulmonary arterial hypertension (PAH) included macitentan (Opsumit; Actelion), an oral endothelin receptor antagonist, and riociguat (Adempas; Bayer HealthCare), which represents a new class of therapies for PAH. Riociguat belongs to a class of drugs called soluble guanylate cyclase stimulators that help arteries relax to increase blood flow and decrease blood pressure.

Not all significant new therapies approved in 2013 were specialty agents. It is beyond the scope of this introduction to mention all the newly released agents; significant small-molecule agents approved by the FDA in 2013 include:

- Canagliflozin (Invokana; Janssen Pharmaceuticals), the first treatment for diabetes approved in a new class of drugs known as sodium-glucose cotransporter 2 inhibitors. This new agent works by blocking the reabsorption of glucose by the kidney, increasing glucose excretion, and lowering blood glucose levels in diabetic patients who have elevated blood glucose levels.
- Levomilnacipran extended-release capsules (Fetzima; Forest Laboratories), a serotonin and norepinephrine reuptake inhibitor, received a new FDA indication for the treatment of major depressive disorders in adults.
- The combination of fluticasone furoate and vilanterol—an inhaled corticosteroid and a long-acting beta2-adrenergic agonist (Breo Ellipta; GlaxoSmithKline)—was approved as an inhaled long-term, once-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. It is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations.

Looking Forward

For the drug industry, and for all healthcare stakeholders, 2013 included the release of many new and innovative therapies. Although the approvals of new drugs did not match the 15-year high seen in 2012, there were many approvals for novel agents that offer first-in-class treatments for patients with serious diseases. As we enter 2014, the pipeline of new agents, particularly specialty agents and therapies for cancer, is robust, and we will likely see another year of significant growth for the drug industry and for patients.

Author Disclosure Statement

Dr Owens is a consultant to Allergan, Biogen Idec, Boston Scientific, CardioDx, Crescendo Bioscience, Eli Lilly, Johnson & Johnson, and Millennium Pharmaceuticals.

References