



Truven Health Analytics™ Micromedex® Solutions Clinical Content Updates

February, March and April 2016 Selected Content Updates

Selected New Drug Approvals	
FDA Approvals – New Monographs and Patient Medication Instructions	
Topic / Title	Implication
Acetylcysteine (Cetylev™)	Approved this effervescent tablet to prevent or lessen hepatic injury after an acetaminophen overdose
Antihemophilic factor VIII (recombinant) (Kovaltry®)	Approved to prevent and control bleeding episodes in patients with hemophilia A
Brivaracetam (Briviact®)	Approved as adjunctive therapy for partial-onset seizures in patients with epilepsy who are 16 years of age and older
Defibrotide sodium (Defitelio®)	Approved to treat adult and pediatric patients with hepatic VOD, also known as sinusoidal obstruction syndrome, with renal or pulmonary dysfunction following HSCT
Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey®)	Approved the smallest sized single-tablet regimen for treating HIV-1 in patients 12 years of age or older
Factor IX albumin fusion protein recombinant (Idelvion®)	Approved to prevent and manage bleeding episodes in patients with hemophilia B
Glycopyrrolate/ formoterol fumarate (Bevespi Aerosphere™)	Approved for the long-term, maintenance treatment of airflow obstruction in patients with COPD
Ibrutinib (Imbruvica®)	Approved as a first-line treatment for chronic lymphocytic leukemia

Infliximab-dyyb (Inflectra™)	Approved this biosimilar of infliximab indicated to treat Crohn disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis
Ixekizumab (Taltz®)	Approved to treat patients with moderate or severe plaque psoriasis
Melphalan (Evomela™)	Approved for use in patients with multiple myeloma, either for high-dose conditioning treatment prior to stem cell transplantation or for palliative treatment
Obiltoxaximab (Anthim®)	Approved for treatment of inhalational anthrax in combination with appropriate antibacterial drugs, as well as for anthrax prevention when other therapies cannot be used.
Oxycodone (Xtampza™ ER)	Approved to manage pain severe enough to require daily, around-the-clock, long-term opioid treatment
Reslizumab (Cinqair®)	Approved for add-on maintenance treatment of patients with severe asthma aged 18 years and older
Riboflavin 5-phosphate (Photrexa®, Photrexa® Viscous)	Approved for use with the KXL System in corneal collagen cross-linking to treat progressive keratoconus
Venetoclax (Venclexta™)	Approved to treat patients with chronic lymphocytic leukemia who have a chromosomal abnormality called 17p deletion and who have been treated with a least 1 prior therapy; this is the first treatment that targets the B-cell lymphoma 2 protein
EMA Approvals (not already approved by FDA – New Monographs)	
Topic / Title	Implication
Ferric maltol (Feraccru)	Indicated to treat iron deficiency anemia in adult patients with inflammatory bowel disease
Pitolisant (Wakix)	Indicated to treat narcolepsy with or without cataplexy in adult patients
New FDA-approved Indications – Revised Monographs and Patient Medication Instructions	
Crizotinib (Xalkori®)	Now approved to treat patients with metastatic non-small cell lung cancer with ROS1-positive tumors
Daclatasvir (Daklinza™)	Expanded to include patients with hepatitis C virus genotype 1

Fosaprepitant dimeglumine (Emend®)	Now approved to prevent delayed nausea and vomiting in patients who are receiving moderately emetogenic chemotherapy
Ledipasvir/sofosbuvir (Harvoni®)	Expanded treatment specifics and updated information to include patients who have decompensated cirrhosis (HCV genotype 1) and liver transplant recipients (HCV genotypes 1 and 4)
Obinutuzumab (Gazyva®)	Expanded the indication to include treatment-experienced patients with follicular lymphoma
Palbociclib (Ibrance®)	Tablets now approved to treat hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer in combination with fulvestrant in women with disease progression following endocrine therapy
Tofacitinib citrate (Xeljanz® XR)	Now approved as the first once-daily oral Janus kinase inhibitor rheumatoid arthritis treatment
Drug Safety Updates	
Topic / Title	Implication
Alogliptin benzoate and saxagliptin hydrochloride single agents and combinations (numerous brand names)	Based on a safety review, the US FDA announced that alogliptin and saxagliptin may increase the risk of heart failure, particularly in patients who already have heart or kidney disease. The US FDA recommends discontinuing treatment and monitoring for diabetes control in patients that develop heart failure.
Fluconazole (Diflucan®)	The US FDA is evaluating the results of a Danish clinical trial which demonstrates a possible association between the use of oral fluconazole for yeast infections and an increased risk of miscarriages. The FDA will provide final conclusions and recommendations after reviewing these trial data.
Idelalisib (Zydelig®)	The US FDA announced that clinical trials of idelalisib in combination with other cancer drugs were halted due to an increased rate of adverse events including death. The FDA will provide updates, as needed, after reviewing these findings.

Metformin hydrochloride single agent and combination (numerous brand names)	The US FDA is calling on metformin product manufacturers to update the product information with the recommendations for use in patients with renal impairment based on clinical trial findings.
Other Significant Updates – Drug	
Topic / Title	Implication
Niacin ER/lovastatin (Advicor®) Niacin ER/simvastatin (Simcor®)	The US FDA announced a decision to remove approval on the cholesterol medications Using data from several clinical trials, the US FDA has concluded that the benefits of these medications do not outweigh the risks.
Other Significant Updates – New Topic – Disease	
Topic / Title	Implication
Zika Virus	<p>There was a new disease topic written for Zika Virus which includes the following guidelines:</p> <ul style="list-style-type: none"> • CDC Health Advisory updates: <ul style="list-style-type: none"> ○ Interim Guidelines for Pregnant Women During a Zika Virus Outbreak — United States, 2016 ○ Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016 ○ Interim Guidelines for Health Care Providers Caring for Infants and Children with Possible Zika Virus Infection — United States, February 2016 ○ Interim Guidelines for Prevention of Sexual Transmission of Zika Virus – United States, 2016 • FDA issues recommendations to reduce the risk for Zika virus blood transmission in the United States; CDC Health Advisory • Revision to CDC’s Zika Travel Notices: Minimal Likelihood for Mosquito-Borne Zika Virus Transmission at Elevations Above 2,000 Meters; • Congenital Microcephaly Case Definitions
Other Significant Updates – Updated Topics – Disease	
Topic / Title	Implication
Diabetes Mellitus	Diabetes Mellitus was updated with the following guidelines:

	<ul style="list-style-type: none"> Standards of Medical Care in Diabetes-2016 AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY – CLINICAL PRACTICE GUIDELINES FOR DEVELOPING A DIABETES MELLITUS COMPREHENSIVE CARE PLAN – 2015 New Guidelines for Abnormal Glucose Screening CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY ON THE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM – 2016 EXECUTIVE SUMMARY
Heart Failure	Heart Failure was updated with the following guideline: <ul style="list-style-type: none"> Transitional Care Interventions to Prevent Readmissions for People With Heart Failure
Typhoid Vaccine	Typhoid vaccine was updated with the following guideline: <ul style="list-style-type: none"> Updated Recommendations for the Use of Typhoid Vaccine — Advisory Committee on Immunization Practices, United States, 2015
Other Significant Updates – CareNotes	
Topic / Title	Implication
79 New CareNotes and 200+ Updated CareNotes	New and updated patient instructions cover a variety of topics including: <ul style="list-style-type: none"> Adverse effects and allergies Diabetes conditions and health concerns Infectious diseases and vaccines Pre- and post-mastectomy biopsy and breast reconstruction topics Pregnancy and well-children visits Stroke
Other Significant Updates – Toxicology Content	
Cariprazine (Vraylar™)	
<ul style="list-style-type: none"> A partial agonist of serotonin 5-HT-1A activity and dopamine D2 receptors, and an antagonist of serotonin 5-HT-2A activity Indicated to treat schizophrenia and acute mania or mixed episodes associated with bipolar I disorder 	

- An inadvertent overdose ingestion of 48 mg/day produced orthostasis and sedation. In general, overdose effects are anticipated to be an extension of adverse effects
- Common adverse effects are extrapyramidal symptoms, akathisia dyspepsia, vomiting, somnolence and restlessness.
- Mainstay of treatment is good supportive care, including airway management for patients with severe CNS sedation.

Idarucizumab (Praxbind®)

- A humanized monoclonal antibody fragment indicated for reversal of the anticoagulant effects of dabigatran for life-threatening or uncontrolled bleeding or when an emergency procedure or surgery is required.
- Effects are anticipated to be an exaggeration of adverse effects following therapeutic doses
- Common effects have included headache, hypokalemia, delirium, constipation, pyrexia, and pneumonia have been reported. Hypersensitivity reactions can develop. Intravenous products contain sorbitol which may cause serious adverse reactions, including fatalities, with parenteral administration.
- Treatment is supportive. In patients with acute allergic reaction, oxygen therapy, bronchodilators, diphenhydramine, corticosteroids, vasopressors and epinephrine may be required.

Osimertinib (Tagrisso®)

- An epidermal growth factor receptor (EGFR) kinase inhibitor used to treat patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer whose disease has progressed during or following EGFR TKI therapy
- Presently, there are no reports of overdose.
- Common adverse reactions include diarrhea, rash, dry skin and nail toxicity; QTc prolongation and neutropenia were the most common adverse events that led to dose reduction or interruption of therapy. Serious events have included pneumonia, pulmonary embolus and cardiomyopathy.

Treatment is supportive. Monitor respiratory and cardiac function following a significant exposure in patients at risk to develop cardiomyopathy, interstitial lung disease and/or pneumonitis.

Zika Virus

- Zika is an arbovirus of the flavivirus genus
- Primarily transmitted through bite of an infected *Aedes* species (eg, *Aedes aegypti*) mosquito; other modes of transmission have included perinatal, in utero, and potentially blood transfusions, and sexual transmissions;

- First confirmed cases of Zika virus infection were reported in Brazil. As of January 2016, outbreaks have occurred in numerous countries and is anticipated to continue to spread to other countries including regions of the US.
- The incubation period is likely a few days to a week.
- Only 1 in 5 people infected with the Zika virus will become symptomatic; severe disease requiring hospitalization is uncommon and clinical illness is usually mild; symptoms usually include fever, maculopapular rash, arthralgia, myalgia, headache or conjunctivitis
- In infants, microencephaly has been reported in some infants born to pregnant women exposed to the Zika virus.
- Currently there is no specific antiviral therapy. Treatment is primarily preventive (ie, avoid mosquito bites, use of insect repellents, protective clothing) and supportive care as indicated.
- Abstinence or the consistent use of condoms can reduce risk of transmission in at-risk individuals

1st Quarter 2016 Selected NeoFax and Pediatrics Content Updates

New Monographs and Calculators	Pegfilgrastim
Revised Monographs	Acetaminophen, acetylcysteine, acyclovir, alprostadil, amikacin, aminophylline, amiodarone, amphotericin B, amphotericin B lipid complex, amphotericin B liposome, ampicillin, anidulafungin, asfotase alfa, azithromycin, aztreonam, bosentan, bumetanide, buprenorphine, caffeine citrate, calcium chloride 10%, calcium gluconate 10%, captopril, caspofungin, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, chlorothiazide, cimetidine, clindamycin, clonidine, colistin, darbepoetin alfa, dexamethasone, didanosine, digoxin, dobutamine, dopamine, DT/Td vaccine, DTaP vaccine, emtricitabine, enalapril maleate, epinephrine (adrenaline), epoetin alfa, erythromycin, famotidine, fat emulsion, fentanyl, fluconazole, fosphenytoin, furosemide, ganciclovir, gentamicin, glucagon, haemophilus B (Hib) conjugate vaccine, heparin, hepatitis B vaccine (recombinant), Hib conjugate/hepatitis B combination vaccine, hyaluronidase, hydrochlorothiazide, hydrocortisone, ibuprofen, ibuprofen lysine, immune globulin (human), indomethacin, infuvite® pediatric, insulin, iron dextran, isoproterenol, lamivudine, levetiracetam, lidocaine - antiarrhythmic, lidocaine - CNS, linezolid, lopinavir/ritonavir, lorazepam, magnesium sulfate, meropenem, methadone, metoclopramide, metronidazole, micafungin, midazolam, milrinone, morphine, mupirocin, nafcillin, naloxone, netilmicin, nevirapine, nifedipine, nitric oxide, nystatin, octreotide, omeprazole, oxacillin, pancuronium, penicillin G, pentobarbital, phenobarbital, phenytoin, piperacillin, piperacillin/tazobactam, pneumococcal 13-valent conjugate vaccine (PCV13), poliovirus vaccine enhanced-inactivated, pyridoxine, ranitidine, remifentanyl, rotavirus vaccine (Rotarix®), rotavirus vaccine

	(Rotateq®), sildenafil, sodium bicarbonate, spironolactone, sucrose, ticarcillin/clavulanate, tobramycin, vaccination schedule ACIP- 2016, vancomycin, vecuronium, vitamin a, vitamin k1, zidovudine.
Dose Changes	Acetylcysteine, amphotericin B lipid complex, amphotericin B liposome, ampicillin, clonidine, lorazepam, phenobarbital.
Pediatrics	
New Monographs and Calculators	Brivaracetam, defibrotide, emtricitabine/rilpivirine/tenofovir alafenamide, emtricitabine/rilpivirine/tenofovir disoproxil, factor X human, filgrastim-sndz, isradipine, pegfilgrastim, sebelipase alfa.
Revised Monographs	Abacavir, abacavir/lamivudine, acetaminophen, acetaminophen/codeine, acetylcysteine, acyclovir, adalimumab, alprostadil, amikacin, aminophylline, amiodarone, amlodipine, amoxicillin, amoxicillin/clavulanate, amphotericin B, amphotericin B lipid complex, amphotericin B liposome, ampicillin, ampicillin/sulbactam, anidulafungin, aprepitant, aripiprazole, asfotase alfa, atazanavir, atenolol, azelastine, azelastine/fluticasone, azithromycin, aztreonam, bosentan, budesonide, bumetanide, buprenorphine, c1 esterase inhibitor, human, calcium chloride 10%, calcium gluconate 10%, candesartan, captopril, caspofungin, ceftazidime, cefazolin, cefdinir, cefepime, cefixime, cefotaxime, cefotetan, cefoxitin, cefpodoxime, cefprozil, ceftazidime, ceftibuten, ceftriaxone, cefuroxime, cephalixin, cetirizine, chloramphenicol, chlorothiazide, cimetidine, clarithromycin, clindamycin, clobazam, clonazepam, clonidine, colistin, darbepoetin alfa, darunavir, dexamethasone, dexmethylphenidate, diazepam, didanosine, digoxin, diltiazem, dobutamine, dolutegravir, dopamine, DT/Td vaccine, DTaP vaccine, eculizumab, efavirenz, elvitegravir/cobicistat/emtricitabine/tenofovir, emtricitabine, enalapril maleate, epinephrine (adrenaline), epoetin alfa, epoprostenol, ertapenem, erythromycin, etravirine, factor VIII (recombinant), fc fusion protein, famotidine, fentanyl, fexofenadine, fluconazole, fosamprenavir, fosphenytoin, furosemide, ganciclovir, gentamicin, glucagon, haemophilus B (Hib) conjugate vaccine, heparin, hepatitis A vaccine, hepatitis B vaccine (recombinant), Hib conjugate/hepatitis B combination vaccine, human papillomavirus (HPV) vaccine, hyaluronidase, hydrochlorothiazide, hydrocodone/acetaminophen, hydrocodone/ibuprofen, hydrocortisone, hydromorphone, hydroxyzine, hypertonic saline, ibuprofen, iloprost, immune globulin (human), indomethacin, influenza virus vaccine, infuvite® pediatric, insulin, iron dextran, itraconazole, lamivudine, levetiracetam, lidocaine - antiarrhythmic, lidocaine - CNS, linezolid, lopinavir/ritonavir, loratadine, lorazepam, losartan, magnesium sulfate, measles, mumps, rubella (MMR) virus vaccine, live, meningococcal vaccine, group B, meningococcal vaccine; group a, c, y, and w-135, meningococcal/Hib conjugate combination vaccine, meropenem, metformin, methadone, methotrexate, methylphenidate,

	<p>methylprednisolone, metoclopramide, metronidazole, micafungin, midazolam, milrinone, morphine, mupirocin, nafcillin, naloxone, nevirapine, nifedipine, nifedipine, nitric oxide, nystatin, octreotide, olanzapine, omeprazole, ondansetron, oxacillin, oxycodone, oxycodone/acetaminophen, oxycodone/ibuprofen, palonosetron, pancuronium, penicillin G, pentobarbital, phenobarbital, phenytoin, piperacillin, piperacillin/tazobactam, pneumococcal 13-valent conjugate vaccine (PCV13), pneumococcal polysaccharide vaccine (PPSV23), poliovirus vaccine enhanced-inactivated, prednisolone, prednisone, propofol, pyridoxine, quetiapine, raltegravir, ranitidine, remifentanyl, rilpivirine, risperidone, ritonavir, rotavirus vaccine (Rotarix®), rotavirus vaccine (Rotateq®), sildenafil, sodium bicarbonate, spironolactone, sucrose, tacrolimus, Tdap vaccine, tenofovir disoproxil fumarate, ticarcillin/clavulanate, tobramycin, tramadol, trimethoprim/sulfamethoxazole, vaccination schedule ACIP- 2016, valproic acid and derivatives, vancomycin, varicella virus vaccine, live, vecuronium, vitamin a, vitamin k1, voriconazole, warfarin, zidovudine.</p>
Dose Changes	Ampicillin, clobazam, clonidine, diazepam, fluconazole, itraconazole, pentobarbital, phenobarbital, tacrolimus.
Enteral Formula New	Enfamil® Enfacare® Powder in Breast Milk