Pharmacy News

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Special Points of Interest:

- Contraception and Pregnancy in Abdominal Transplant
- Management of Post Intensive Care Syndrome (PICS)
- Vaccine Hesitancy: A Global Health Issue
- Welcome to our New Pharmacist

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P&T Update

Formulary Additions

- **Andexanet alfa (Andexxa®)** – Formulary addition was approved
- **Hepatitis B vaccine (Heplisav-B)** - Formulary addition was approved
  Restrict to outpatient use only
- **Naltrexone (Revia®)** – Formulary addition approved
  Restrict to detox certified prescribers and psychiatry department only
- **Polidocanol (Asclera®)** – Formulary addition approved
- **Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (Genvoya®)** – Formulary addition approved

Formulary Restriction Modification

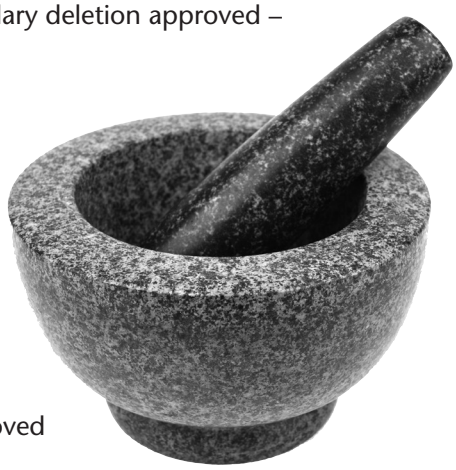
- **Ticagrelor (Brilinta®)** – Modification approved to include prescribing by neurointerventionalist in addition to the cardiologist
- **Formulary Reinstatement**
- **Phentolamine** – Formulary addition approved

Formulary Extensions

- **IV acetaminophen (Ofirmev®)** – Formulary extension approved for use in neonates for the treatment of Patent Ductus Arteriosus (PDA) up to 7 days
- **Intrauteral devices (IUD)** – Formulary extension approved
  Restrict for outpatient use only

Formulary Deletions

- **Promethazine 50 mg/mL injection** – Formulary deletion approved – Alternative strengths remain available.
- **Theophylline 100 mg, 200 mg tablets** – Formulary deletion approved. Alternative strengths remain available.
- **Acetaminophen 80 mg chewable tablets** – Formulary deletion approved. Alternative strengths remain available.
- **Morhuate sodium** – Formulary deletion approved
- **Potassium iodide** – Formulary deletion approved
- **Trichophyton skin test** – Formulary deletion approved



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P&T Updates
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- **Temazepam 30 mg** – Formulary deletion approved. Alternative strengths remain available.
- **Candida albicans skin test** - Formulary deletion approved

Policies & Procedures/Floorstocks
Naloxone guideline for use in emergency department
Dosing guidance provided for both bolus and infusion doses – approved

- **Fecal Microbiota Transplantation (FMT) policy** – approved with restrictions provided
- **UH antibiogram** – including unit specific antibiograms – approved

Miscellaneous

- **Levonoregestrel** - Request from OBGYN, all samples have to be approved
  Sample medications approved
- **Alaris Drug Library revision** – Approved

Contraception and Pregnancy in Abdominal Transplant

Fertility is usually impaired in women who have end-stage renal and liver disease. Nearly three quarters of women listed for liver transplant (LT) have secondary amenorrhea, with cessation of menstrual cycles in the setting of progressive liver disease.[1] The cause of impaired fertility is largely attributed to dysregulation in the hypothalamic–pituitary–ovarian axis, which resolves following transplant. The majority of women resume regular menstrual cycles within 1 year post-transplant and more importantly, ovulation may resume as early as within the first postoperative months, highlighting the importance of reproductive counseling in the initial post-transplant period.

The fact that contraception use is not prioritized was highlighted in a US study of liver and kidney transplant female recipients of child bearing age in which only half of women used any form of contraception, and 44% were unaware that pregnancy was possible after transplant.[2] In another study of liver and kidney recipients, nearly half were using no contraception, and about 40% of women were relying upon high failure methods such as condoms, rhythm, or withdrawal.[3] Hence, it is extremely important that providers, including pharmacists, assess reproductive intentions and provide contraceptive or preconception counseling as appropriate.

Recommendations to guide contraceptive use in solid organ transplant recipients have been issued in the Medical Eligibility Criteria Guidelines by the Centers for Disease Control and Prevention (CDC).[4] These recommendations are categorized from 1 to 4, varying from low risk to unacceptable risk.[4] The recommendations are separately provided for uncomplicated and complicated graft function (Table 1). Complicated graft conditions include those who display acute deterioration in kidney or liver function associated with specific pathologic changes in the graft. As chronic rejection is less well defined, typical characteristics are identified via biopsy including fibrosis in the kidney or obliterative vasculopathy and loss of bile ducts in the hepatic graft.

Table 1. CDC Recommendations for contraception use after transplant

	Copper IUD	Hormonal IUD	CHC	POP	DMPA	Implant
Graft Condition:						
Uncomplicated	**2**	**2**	**2**	**2**	**2**	**2**
Complicated	**3**	**3**	**4**	**2**	**2**	**2**

**Defined by the Centers for Disease Control as acute or chronic rejection or graft failure*

1 = No restriction 2 = Benefits outweigh theoretical/proven risks
3 = Risks may outweigh benefits 4 = Unacceptable risk

Centers for Disease Control recommendations for contraception use after solid organ transplant.[4] CHC, combined hormonal contraception; DMPA, depot medroxyprogesterone acetate; IUD, intrauterine device; POP, progestin-only pill

All hormonal methods are considered safe in women with stable, uncomplicated graft function. Progestin-only agents are the only contraceptives that have a favorable safety grade 2 for complicated graft function; however, it is important to note that these recommendations did not incorporate additional larger studies also demonstrating favorable safety data of intrauterine devices (IUDs).[5,6]

The primary contraceptive option that is affected by severity of graft dysfunction is combined hormonal contraception (CHC) as they may worsen hypertension and predispose to thrombosis. Thus, it is important for practitioners to offer and counsel patient on risks and benefits of these agents and provide recommendations based on each woman's medical history.

Immunosuppressive therapy During Pregnancy

It is recommended to defer pregnancy for at least 1 year after transplant due to the complexity of medications, comorbidities and risks of infection soon after transplant.[7] Successful outcomes are dependent on time post-transplant to ensure stability of graft function while patients are on the lowest amount of immunosuppression, leading to a lower risk of infectious complications. Of note, the prevalence of hypertension and gestational diabetes remains higher in kidney and liver transplant recipients compared to the general population; due in part to side effects of immunosuppression. Thus, along with an increased risk of pre-eclampsia, pregnancy in the setting of solid organ transplant is considered high risk. However, when cared for by coordinated specialists, ~75% of kidney and liver transplant recipients will have successful outcomes, similar to that of the general population.[8-10]

Contraception and Pregnancy in Abdominal Transplant
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As the impact of pregnancy on rejection and graft loss remains controversial, optimizing immunosuppression in every transplant patient is imperative. Calcineurin inhibitors (CNIs) such as cyclosporine and tacrolimus remain the cornerstone of immunosuppression and are generally considered safe during pregnancy. The incidence of birth defects in women using CNIs are similar to the general population. However, the pharmacokinetics of tacrolimus are affected during pregnancy as this medication is highly protein bound and concentrated within red blood cells.[11] Due to the increased total body water during pregnancy, plasma tacrolimus concentrations decline requiring up to a 20-25% increase in dose to maintain therapeutic levels. The effect on free tacrolimus is less understood, thus patients should be monitored for tacrolimus toxicity when adjusting toward a goal trough concentration.[10, 11]

Mycophenolic acid (MPA) products such as mycophenolate mofetil (Cellcept®) and enteric-coated MPA (Myfortic®) are contraindicated during pregnancy due to the known risks to the developing fetus. Birth defects include microtia, oral-facial, esophageal, cardiac and renal abnormalities. Spontaneous abortions were found to occur in approximately 45% of women using MPA after conception.[8, 10] Due to these deleterious effects, women of child-bearing age should use two forms of contraception or an IUD while taking MPA. Providers should discuss family planning and discontinue this agent at least 6 weeks prior to conceiving. Temporary replacement of MPA include azathioprine and/or prednisone if tacrolimus monotherapy is not safe or efficacious. Of note, MPA is part of the Risk Evaluation and Mitigation Strategy (REMS) program. Patients and providers must be educated regarding contraception, family planning and fetal risks. The program also collects pregnancy outcome data on patients who have conceived while taking MPA.[12]

Azathioprine is an alternative antimetabolite agent that was previously used for maintenance immunosuppression until the introduction of MPA. This medication is generally considered safe during pregnancy and can serve as an adjunctive agent in combination with CNIs.[13] The recommended dose is 1-1.5 mg/kg/day. Patients' CBC should be routinely monitored until on a stable dose as higher doses increase risk of hematologic adverse effects. Prednisone is also a safe option for pregnant patients with no higher risk of fetal abnormalities identified when studied in non-transplant patients.[14]

The existing data on use of mTOR inhibitors, sirolimus and everolimus, during pregnancy is scarce. Animal studies reported decreased fetal weights, delayed ossification and increased fetal mortality however this has not been reported in human cases. There is not enough information to recommend these agents during pregnancy.[10] Of note, a common side effect of mTOR inhibitors is delayed would healing, which may impact women undergoing cesarean section.

In conclusion, while close follow up is necessary, a majority of pregnant transplant recipients can have successful outcomes while maintaining their graft function. Immunosuppression regimens may require modifications to ensure patients maintain stable grafts while minimizing any potential risks to the fetus.

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Management of Post Intensive Care Syndrome (PICS)

Post Intensive Care Syndrome (PICS) refers to a combination of cognitive, psychological, and physical signs and symptoms that are newly recognized or get worsened after recovering from a critical illness.[1] The true prevalence of PICS is unknown due to limited awareness, but studies have shown that up to 30% of family or caregivers ICU survivors experience stress, anxiety, depression, and complicated grief.[1] The common symptoms most of the survivors report are depression, sleep disturbances, decreased mobility, memory loss, reduced concentration, body weakness, and fatigue.[3]

A study on the long term cognitive impairment after critical illness published in the New England Journal of Medicine showed that patients discharged from ICU after surviving critical illness such as sepsis continued to have cognitive (mental) problems a year after discharge.[2] PICS is more commonly seen in patients who were placed on mechanical ventilation, patients who were on sedation, and patients who had a prolonged stay in the ICU. Studies have shown that the longer a patient stays on mechanical ventilation or sedation in the ICU, the higher the risk of developing Post Intensive Care Syndrome.[2]

Post Intensive Care Syndrome can be prevented and managed by performing a psychological evaluation of all patients being admitted into the ICU.[1] All patients should be evaluated for PICS after staying in the ICU and those having signs and symptoms of it should be carefully managed by a multidisciplinary team. This team should include a critical care physician, a neuro-psychiatrist, a physiotherapist, and a respiratory therapist. These patients would benefit from the use of both pharmacological and non-pharmacological interventions. An example of a preventative measure includes the ABCDE bundle which consists of awakening (using light or minimal sedation), breathing (spontaneous breathing trials), coordination of care and communication among various disciplines, delirium monitoring, assessment, and management, and early ambulation in the ICU. The treatment of the ICU syndrome includes the elimination or correction of causative factors, the appropriate administration of sedatives (anxiolytic and antipsychotic agents), reduction or elimination of sources of environmental stress, and frequent patient and family communication. Overall, the management of Post Intensive Care Syndrome improves patients' quality of life and overall wellness.

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Vaccine Hesitancy: A Global Health Issue

There is an ongoing global struggle to promote vaccines and increase immunization rates. The factors affecting vaccination acceptance and perception is an area of active research. Articles about public trust, confidence or hesitancy in vaccines were seen to have more than doubled between 2007 and 2012.[1] In 2014, The World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) published a report on Vaccine Hesitancy. They defined Vaccine Hesitancy as the "delay in acceptance or refusal of vaccines despite availability of vaccination services".[2] The report details that Vaccine Hesitancy is complex and context specific varying across time, place and vaccines. Currently, The World Health Organization lists Vaccine Hesitancy as one of the ten threats to global health in 2019.

In the United States, healthcare services are generally available. Despite high national vaccine coverage, there are clusters of patients with suboptimal immunization rates where vulnerable members of the community are at risk. The Centers for Disease Control and Prevention (CDC) monitors vaccination coverage and exemption rates for Kindergarteners in the United States. For the 2017-2018 school year, they found that the national median kindergarten vaccination coverage was close to 95% for MMR, DTaP, and varicella vaccine.[3] While the number of states with coverage ≥95% has increased over the past year, the percentage ranged widely, between 80% to 99%.[3] Further understanding of vaccine hesitancy may benefit policy changes and improve coverage in states where children are not being vaccinated.

The Strategic Advisory Group of Experts (SAGE) on Immunization group describes Vaccine Hesitancy with the "3Cs" Model: complacency, convenience and confidence.[2] Complacency describes when there is low perceived risk for vaccine-preventable diseases and therefore considers vaccines as unnecessary. Convenience is determined by accessibility, affordability, and appeal of vaccine services. Convenience can also be affected by cultural context as a patient's social environment can affect the comfort of their decision. Confidence relates to the trust in vaccine safety and effectiveness, in the reliability in healthcare services and providers, and in the motivation of policy makers who impose requirements for vaccination. The degree to which these factors impact vaccine hesitancy is not well understood.

Globally studies of vaccine acceptance demonstrate the complexity of vaccine hesitancy. A systematic review of vaccine hesitancy was done for studies published from 2007 to 2012. They found that studies from China, Lebanon, Israel, Bangladesh and USA all identified higher

education as a potential barrier to vaccine acceptance.[2] However, studies from Greece, The Netherlands, Nigeria and Pakistan identified it as a promoter of vaccine acceptance.[2] Because vaccine hesitancy is multifactorial, predictors of vaccine acceptance is under ongoing investigation. There are cases of clear shifts towards vaccine acceptance. As an example, Israel vaccine acceptance rates rose when local rabbis in the orthodox Jewish community began accepting polio vaccine when it was previously shunned.[2] On the other hand, poor communication can lead to worsening vaccine hesitancy. In 1999, the US reduced the amount of thimerosol in some vaccines.[2] Because the reasoning behind this change was poorly communicated, the change lead to decreased public confidence in vaccines.

In conclusion, vaccine hesitancy is a global health threat that is influenced by many factors that are not well understood or controlled. Vaccine acceptance is difficult to predict as the same factors have different impacts depending on the geographic location and cultural context. Improvements in community support and communication with patients are necessary to reduce vaccine hesitancy. Strategies aimed to change vaccine education or policies should be done with care as poor communication or perceptions can result in worsening vaccine hesitancy.

HCP Resources	Resources to Share with Parents
"Talking to parents about vaccines" "Understanding vaccines and vaccine safety" "Immunization schedules" "Creating a culture of immunization within your practice"	"If you choose not to vaccinate" "Vaccine-preventable disease fact sheets" "Childhood immunization schedule" "Combination Vaccines" "Easy-to-read Schedules", Etc.

Key Message[5]	Target Audience
You make decisions that impact your child's future every day. Vaccines are the most effective way to protect your child from life-threatening illnesses. It's your choice—get the facts. - This message acknowledges the parents' decision to vaccinate their child, and supports the safety of vaccines by showing that not vaccinating puts a child at even greater risk.	Parents
States, cities and towns with lower vaccination rates have higher rates of life-threatening diseases. Even if your child is vaccinated, this still puts them at some level of risk. - As parents who vaccinated their children learned more about community immunity, there appeared to be great potential for activating them as advocates for vaccines. They were eager to know the immunization rates in their daycare, school, and community, and the risks to their children, even if they are vaccinated.	Parents, Media, Policy Makers
We're not just doctors and public health officials. We are parents too, and we vaccinated our children, and ourselves. - Vaccine-hesitant parents do not understand the role of public health programs, and as a result, question health officials' authority and intent on the subject. Educating these parents about public health programs is critical to earning their trust and influencing them.	Parents, Media

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Vaccine Hesitancy: A Global Health Issue

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To address parent's rising concerns for vaccine safety, healthcare providers should review vaccine communication strategies and provide patient education resources on vaccine risks and benefits. The CDC collaborated with the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP) to create several informational handouts. These resources are helpful to show parents a clear map of their child's immunization schedule and discuss the related risks to choosing not to vaccine.[4] Also, Association of State and Territorial Health Officers (ASTHO) outlines a communication strategy that recommends certain key messages to be discussed.[5] ASTHO encourages providers to tell patients to visit their state health department's website, stay informed, and relate to their patient's concerns. Through consistent messaging and open discussions, healthcare providers can increase confidence in vaccine safety and help to maintain high immunization rates.

Provider Resources for Vaccine Conversations with Parents[4]: https://www.cdc.gov/vaccines/hcp/conversations/index.html

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Welcome our New Pharmacist

Dr. Ambika Ramlogan graduated with her Pharm D. from Touro College of Pharmacy in Manhattan, NY. Touro College of Pharmacy offered a 2+2 program which allowed her to have 2 full years of Advanced Practice Experience at a variety of hospitals throughout the tri-borough area. She also worked at Walgreens Pharmacy for the past 5 years in Jamaica, NY. She is excited to be a part of the University Hospital and she looks forward to learning from and working with UH pharmacy staff. When time permits she enjoys traveling, practicing hot yoga and she loves a little retail therapy (shopping).