Specialty Networks
Powered by PPS Analytics

PRACTICAL APPROACH TO IBD
(Advanced Therapies)

9/2023

Advanced Therapies for Adults with IBD										
Name of Advanced Therapy	**Black Box Warning**	**Pearls**	**CD or UC? (easy read)**	**Standard Dosing (Adult)** (refer to package insert for dose adjustments)	**Most Common Adverse Reactions**	**Contraindications**	**Monitoring**	**Drug Levels (Trough Level for Biologic)**	**Pregnancy/Lactation**	**Other Indications**
Biologic: Anti-TNF										
Remicade (Infliximab) **Abbreviation:** IFX **Delivery method:** IV **MOA:** binds to human tumor necrosis factor alpha (TNFα), thereby interfering with endogenous TNFα activity. *Biosimilars:* *Avsola (Infliximab-axxq)* *Inflectra (Infliximab-dyyb)* *IXIFI (Infliximab-qbtx)* *Renflexis (Infliximab-abda)*	**Serious infection** **Malignancy** (including hepatosplenic T-cell lymphoma, which occurs predominantly with condominant immunomodulator therapy in young males)	Anti-TNFs are efficacious in treating fistulizing Crohn's disease. Use careful consideration in selecting an anti-TNF for patients with history of demyelinating disorders, skin cancers (especially melanoma) and lymphoma, as these are low risk, but more common. Combination therapy with an immunomodulator should be considered.	CD & UC	**CD and UC (moderate to severe)** 5 mg/kg at 0, 2, and 6 weeks, followed by 5 mg/kg every 8 weeks thereafter	Abdominal pain Nausea Anemia Increased ALT Infusion-related reaction Antibody development Positive ANA titer Headache Cough Pharyngitis Sinusitis Upper respiratory tract infection Other infections	Hypersensitivy to Infliximab, murine proteins, or any component of the formulation Doses >5 mg/kg in patients with moderate or severe heart failure (NYHA class III/IV)	Refer to IBD pathway	**CD and UC:** ≥5* *Higher levels are often needed for fistulizing disease. Draw trough level as close as possible to next scheduled dose (ideally within 1 week) after the patient has already completed induction.	Low risk Continuing therapy in pregnancy and with breastfeeding is recommended	Ankylosing spondylitis Immune checkpoint inhibitor colitis (off-label use) Plaque psoriasis, severe chronic Psoriatric arthritis Pustular psoriasis (off-label use) Rheumatoid arthritis, moderate to severe Sarcoidosis, refractory (off-label use)
Humira (Adalimumab) **Abbreviation:** ADA **Delivery method:** SUBQ **MOA:** binds to human tumor necrosis factor alpha (TNF-alpha), thereby interfering with endogenous TNFα activity. *Biosimilars:* *Abrilada (Adalimumab-afzb)* *Amjevita (Adalimumab-atto)* *Cyltezo (Adalimumab-adbm)* *Hadlima (Adalimumab-bwwd)* *Hulio (Adalimumab-fkjp)* *Hyrimoz (Adalimumab-adaz)* *Idacio (Adalimumab-fkjp)* *Yuflyma (Adalimumab-aaty)* *Yusimry (Adalimumab-aqvh)*			CD & UC	**CD and UC (moderate to severe)** 160 mg (given over 1 or 2 days), then 80 mg 2 weeks later (day 15), followed by 40 mg every other week beginning day 29	Rash Positive ANA titer Antibody development Injection-site reaction Headache Sinusitis Upper respiratory tract infection Other infections	None on U.S. manufacturer labeling		**CD and UC:** ≥7.5* *Higher levels are often needed for fistulizing disease. Draw trough level as close as possible to next scheduled dose (ideally within 1 week) after the patient has already completed induction.		Ankylosing spondylitis Hidradenitis suppurativa, moderate to severe, refractory Nonradiographic axial spondyloarthritis (off-label use) Peripheral spondyloarthritis, nonpsoriatic (off-label use) Plaque psoriasis, moderate to severe Psoriatic arthritis Rheumatoid arthritis, moderate to severe Sarcoidosis, refractory, (adjunctive agent; off-label use) Uveitis (noninfectious intermediate, posterior, and panuveitis)
Cimzia (Certolizumab pegol) **Abbreviation:** CEZ **Delivery method:** SUBQ **MOA:** binds to human tumor necrosis factor alpha (TNF-alpha), thereby interfering with endogenous TNFα activity. *No biosimilar to date*			CD	Cimzia is typically reserved for patients who have responded to Infliximab or Adalimumab but lost response or developed an intolerance. **CD (moderate to severe)** Initial dose of 400 mg, repeat dose 2 and 4 weeks after initial dose. Maintenance: 400 mg every 4 weeks.	Nausea Antibody development Upper respiratory tract infection Other infections	Hypersensitivity to Certolizumab pegol or any component of the formulation		**CD:** ≥20* *Higher levels are often needed for fistulizing disease. Draw trough level as close as possible to next scheduled dose (ideally within 1 week) after the patient has already completed induction.		Ankylosing spondylitis Axial spondyloarthritis, nonradiographic Plaque psoriasis Psoriatic arthritis Rheumatoid arthritis, moderate to severe
Simponi (Golimumab) **Abbreviation:** GOL **Delivery method:** SUBQ **MOA:** binds to human tumor necrosis factor alpha (TNF-alpha), thereby interfering with endogenous TNFα activity. *No biosimilar to date*			UC	Simponi is typically reserved for patients who have responded to Infliximab or Adalimumab but lost response or developed an intolerance. **UC (moderate to severe)** Induction: 200 mg at week 0, then 100 mg at week 2, followed by maintenance therapy of 100 mg every 4 weeks.	Positive ANA titer Antibody development Upper respiratory tract infection Other infections	Hypersensitivity to Golimumab or any component of the formulation		N/A		Ankylosing spondylitis Psoriatic arthritis Rheumatoid arthritis Axial spondyloarthritis, nonradiographic (off-label use)
Biologic: Integrin Receptor Antagonist										
Entyvio (Vedolizumab) **Abbreviation:** VDZ, Vedo **Delivery method:** IV **MOA:** binds to the α4β7 integrin and blocks the interaction between the α4β7 integrin and MAdCAM-1, which is mainly expressed on GI tract endothelial cells *No biosimilar to date*	None	More colon specific, thus less systemic immunosuppression. Not necessarily as effective as other therapies for Crohn's disease involving sites other than the colon.	CD & UC	**CD and UC (moderate to severe)** 300 mg at 0, 2, and 6 weeks and then every 8 weeks thereafter	Antibody development Headache Arthralgia Nasopharyngitis	Hypersensitivity to Vedolizumab or any component of the formulation	Refer to IBD pathway	**CD and UC:** ≥25, but ≥40 if fistulizing disease Draw trough level as close as possible to next scheduled dose (ideally within 1 week) after the patient has already completed induction.	Low risk Continuing therapy in pregnancy and with breastfeeding is recommended	Colitis, immune checkpoint inhibitor-induced (off-label use)

Specialty Networks
Powered by PPS Analytics

PRACTICAL APPROACH TO IBD
(Advanced Therapies)

Name of Advanced Therapy	Black Box Warning	Pearls	CD or UC? (easy read)	Standard Dosing (Adult) (refer to package insert for dose adjustments)	Most Common Adverse Reactions	Contraindications	Monitoring	Drug Levels (Trough Level for Biologic)	Pregnancy/Lactation	Other Indications
Biologic: Interleukin 12 and 23 Antagonist										
Stelara (Ustekinumab) **Abbreviation:** UST **Delivery method:** induction IV and maintenance SUBQ **MOA:** binds to and interferes with the proinflammatory cytokines, interleukin (IL)-12 and IL-23. Biological effects of IL-12 and IL 23 include natural killer (NK) cell activation, CD4+ T-cell differentiation and activation. Ustekinumab also interferes with the expression of monocyte chemotactic protein-1 (MCP-1), tumor necrosis factor-alpha (TNF-α), interferon-inducible protein-10 (IP-10), and interleukin-8 (IL-8). *No biosimilar to date*	None	Stelara is efficacious in treating fistulizing Crohn's disease and should be considered as a first-line therapy.	CD & UC	**CD and UC (moderate to severe)** Induction (IV): ≤55 kg: 260 mg as single dose >55 kg to 85 kg: 390 mg as single dose >85 kg: 520 mg as single dose Maintenance (SUBQ): 90 mg every 8 weeks; begin maintenance dosing 8 weeks after the IV induction dose.	Antibody development Nasopharyngitis Other infections	Hypersensitivity to Ustekinumab or any component of the formulation	Refer to IBD pathway	**CD and UC:** 3-4* *Higher levels are often needed for fistulizing disease. Draw trough level as close as possible to next scheduled dose (ideally within 1 week) after the patient has already completed induction.	Low risk Continuing therapy in pregnancy and with breastfeeding is recommended	Plaque psoriasis Psoriatic arthritis
Biologic: Interleukin 23 Antagonist										
Skyrizi (Risankizumab-rzaa) **Abbreviation:** RIZ **Delivery method:** induction IV and maintenance SUBQ **MOA:** selectively binds to the p19 subunit of interleukin (IL)-23, thereby inhibiting its interaction with the IL-23 receptor, resulting in inhibition of the release of proinflammatory cytokines and chemokines. *No biosimilar to date*	None	Skyrizi is efficacious in treating fistulizing Crohn's disease and should be considered as a first-line therapy.	CD	**CD (moderate to severe)** Induction: IV: 600 mg at weeks 0, 4, and 8. Maintenance: SUBQ: Prefilled cartridge: 180 to 360 mg at week 12 and every 8 weeks thereafter. Use the lowest effective dose.	Antibody development Upper respiratory infection Other infections	Hypersensitivity to Risankizumab or any component of the formulation	Refer to IBD pathway Monitor LFTs not just at baseline but during induction as well.	N/A	Inadequate human trial data available in pregnancy and with breastfeeding.	Plaque psoriasis, moderate to severe Psoriatic arthritis

Specialty Networks
Powered by PPS Analytics

PRACTICAL APPROACH TO IBD
(Advanced Therapies)

Name of Advanced Therapy	Black Box Warning	Pearls	CD or UC? (easy read)	Standard Dosing (Adult) (refer to package insert for dose adjustments)	Most Common Adverse Reactions	Contraindications	Monitoring	Drug Levels (Trough Level for Biologic)	Pregnancy/Lactation	Other Indications
Targeted Synthetic Small Molecules: JAK Inhibitors										
Rinvoq (Upadacitinib) **Abbreviation:** UPA **Delivery method:** PO (tablet) **MOA:** inhibits Janus kinase (JAK) enzymes, which are intracellular enzymes involved in stimulating hematopoiesis and immune cell function through a signaling pathway. JAKs activate signal transducers and activators of transcription (STATs), which regulate gene expression and intracellular activity. The inhibition of JAKs prevents the activation of STATs.	**Serious infection** **Major adverse cardiovascular events and mortality** **Malignancy** (including lymphoma) **Thrombosis**	Avoid grapefruit during therapy, as it increases exposure to the JAK inhibitor. Recommend alternative therapy in patients with: -Cardiovascular risk factors (including high blood pressure, high low-density lipoprotein (LDL) cholesterol, diabetes, smoking and secondhand smoke exposure, obesity, unhealthy diet, and physical inactivity) -Intentions to become pregnant or who are pregnant or breastfeeding -History of thrombosis or risk factors for thrombosis A pregnancy test is recommended prior to intitiating therapy for females of reproductive age.	CD & UC	JAK inhibitors for IBD are reserved for patients who have not responded to or could not tolerate at least one anti-TNF. **CD and UC (moderate to severe)** Induction: 45 mg once daily for 12 weeks for Crohn's and 8 weeks for UC Maintenance: 30 mg once daily	Acne vulgaris Upper respiratory infection	Hypersensitivity to Upadacitinib or any component of the formulation	Refer to IBD pathway Also should check a fasting lipid panel at baseline then 8-12 weeks thereafter with JAK inhibitors. Pregnancy test at baseline.	N/A	Avoid use of Upadacitinib or Tofacitinib in patients who are pregnant or are planning to become pregnant. Patients should avoid becoming pregnant for 4 weeks after their final dose of Upadacitinib or Tofacitinib. Ensure female patients of reproductive age are using an effective birth control method. Patients should not breastfeed during treatment and for 6 days following their last dose.	Ankylosing spondylitis Atopic dermatitis Nonradiographic axial spondyloarthritis Psoriatic arthritis Rheumatoid arthritis
Xeljanz (Tofacitinib) **Abbreviation:** TOF, Tofa **Delivery method:** PO (tablet) **MOA:** inhibits Janus kinase (JAK) enzymes, which are intracellular enzymes involved in stimulating hematopoiesis and immune cell function through a signaling pathway. JAKs activate signal transducers and activators of transcription (STATs), which regulate gene expression and intracellular activity. The inhibition of JAKs prevents the activation of STATs.			UC	JAK inhibitors for IBD are reserved for patients who have not responded to or could not tolerate at least one anti-TNF. **UC (moderate to severe)** IR tablet: Induction: 10 mg twice daily for at least 8 weeks; based on therapeutic response, may continue 10 mg twice daily for a maximum of 16 weeks or transition to maintenance dose. Maintenance: 5 mg twice daily; if patient experiences loss of response on 5 mg twice daily, then use 10 mg twice daily after assessing the benefits and risks and use for the shortest duration; use lowest effective dose to maintain response. ER tablet: Induction: 22 mg once daily for at least 8 weeks; based on therapeutic response, may continue 22 mg once daily for a maximum of 16 weeks or transition to maintenance dose. Maintenance: 11 mg once daily; if patient experiences loss of response on 11 mg once daily, then use 22 mg once daily after assessing the benefits and risks and use for the shortest duration; use lowest effective dose to maintain response.	Hyperlipidemia Nasopharyngitis Other infections	Hypersensitivity to Tofacitinib or any component of the formulation	Refer to IBD pathway Also should check a fasting lipid panel at baseline then 8-12 weeks thereafter with JAK inhibitors CBC at baseline then 4-8 weeks after treatment start, then every 3 months thereafter. Pregnancy test at baseline.			Ankylosing spondylitis COVID-19, hospitalized patients (alternative agent) (off-label use) Psoriasis (off-label) Psoriatic arthritis Rheumatoid arthritis

Specialty Networks
Powered by PPS Analytics

PRACTICAL APPROACH TO IBD
(Advanced Therapies)

Name of Advanced Therapy	Black Box Warning	Pearls	CD or UC? (easy read)	Standard Dosing (Adult) (refer to package insert for dose adjustments)	Most Common Adverse Reactions	Contraindications	Monitoring	Drug Levels (Trough Level for Biologic)	Pregnancy/Lactation	Other Indications
Targeted Synthetic Small Molecules: Sphingosine 1-Phosphate (S1P) Receptor Modulator										
Zeposia (Ozanimod) **Abbreviation:** N/A **Delivery method:** PO **MOA:** has a high affinity to sphingosine 1-phosphate receptors 1 and 5. Ozanimod blocks the lymphocytes' ability to emerge from lymph nodes; therefore, the amount of lymphocytes available to the CNS and intestine is decreased.	None	Warnings for hepatic impairment, cardiac arrhythmia and stroke or heart attack within the last 6 months A pregnancy test is recommended prior to intitiating therapy for females of reproductive age. Baseline testing required beyond standard workup (see "monitoring").	UC	**UC (mild to moderate)** Days 1-4: 0.23 mg once daily Days 5-7: 0.46 mg once daily Day 8 and thereafter: 0.92 mg once daily If a dose is missed during the first 2 weeks of treatment, reinitiate the titration regimen with 0.23 mg once daily. If a dose is missed after the first 2 weeks of treatment, continue with treatment as planned.	Increased liver enzymes Upper respiratory infection Other infections	Myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or class III or IV heart failure in the last 6 months; Mobitz type II second- or third-degree atrioventricular block, sick sinus syndrome, or sinoatrial block, unless the patient has a functioning pacemaker; severe untreated sleep apnea; concomitant use of a monoamine oxidase inhibitor.	Refer to IBD pathway The following baseline tests are required prior to initiating therapy: EKG, CBC and LFTs if not done in the last 6 months and ophthalmologic exam (if history of macular edema, uveitis or diabetes).	N/A	Avoid use of Ozanimod in patients who are pregnant or are planning to become pregnant. Patients should avoid becoming pregnant for 3 months after their final dose of Ozanimod. Ensure female patients of reproductive age are using an effective birth control. It is not known if ozanimod is present in breast milk. According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother.	Multiple sclerosis, relapsing
Immunomodulators										
Methotrexate **Abbreviation: MTX** **Delivery method: PO, IM or SUBQ** **MOA:** inhibits DNA synthesis, repair, and cellular replication. Methotrexate binds to and inhibits dihydrofolate reductase, inhibiting the formation of reduced folates, and thymidylate synthetase, resulting in inhibition of purine and thymidylic acid synthesis, thus interfering with DNA synthesis, repair, and cellular replication. *Brand names:* *Jylamvo* *Oxtrexup* *Rasuvo* *RediTrex* *Xatmep*	**Serious adverse reactions, including death** **See package insert**	Methotrexate is NOT typically used as monotherapy for treatment of CD, and is instead utilized as dual therapy with an anti-TNF. Combination therapy (Methotrexate and an anti-TNF) is used more favorably in young men, and is to be avoided in women of childbearing age. Interferes with the way folic acid is broken down in the body, thus supplementation with 1 mg daily is recommended. Has been linked to the occurence of photosensitive reactions, so patients should wear sunscreen and limit their sun exposure. Can cause myelosuppression.	CD (off-label use)	**CD (moderate to severe)** Start with 15 to 25 mg administered IM or SUBQ once weekly (in combination with folic acid); an initial dose of 12.5 to 15 mg/week administered orally or parenterally may be used when adding to biologic therapy. For lower initial doses, may gradually increase dose (eg, by 5 mg/week every month) if needed (maximum: 25 mg/week). If remission is sustained after 4 months, may reduce dose to 15 mg/week administered orally or parenterally. Consider discontinuing one year after initiation if it is being used as combination therapy (with an anti-TNF).	Diarrhea Nausea Vomiting Oral mucosal ulcer Hepatic cirrhosis Hepatotoxicity Increased liver enzymes Dizziness Fatigue Headache Cough	Hypersensitivity to Methotrexate or any component of the formulation Additional contraindications for patients with psoriasis, rheumatoid arthritis or polyarticular-course juvenile idiopathic arthritis: Pregnancy, alcohol use disorder, alcoholic liver disease or other chronic liver disease, immunodeficiency syndromes (overt or laboratory evidence); preexisting blood dyscrasias (eg, bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anemia).	See package insert	N/A	Methotrexate is contraindicated in patients who are pregnant or are planning to become pregnant. Patients should discontinue Methotrexate at least 3 months prior to becoming pregnant. Additionally, effective contraception is recommended for patients with partners who may become pregnant during therapy and for 3 months after the final dose of methotrexate. Ensure female patients of reproductive age are using an effective birth control method while on this medication and following discontinuation as above. Patients should not breastfeed during treatment and for 1 week following their final dose.	There are a plethora of other conditions that Methotrexate treats. Please see package insert.

Specialty Networks
Powered by PPS Analytics

PRACTICAL APPROACH TO IBD
(Advanced Therapies)

Name of Advanced Therapy	Black Box Warning	Pearls	CD or UC? (easy read)	Standard Dosing (Adult) (refer to package insert for dose adjustments)	Most Common Adverse Reactions	Contraindications	Monitoring	Drug Levels (Trough Level for Biologic)	Pregnancy/Lactation	Other Indications
Immunomodulators (Thiopurines)										
Imuran (Azathioprine) **Abbreviation:** AZA **Delivery method:** PO **MOA:** Following absorption, 6-thioguanine nucleotides (6-TGN) exert their immunosuppressive effects by inhibition of purine and protein synthesis in lymphocytes. Azathioprine is a prodrug that is quickly converted to 6-mercaptopurine via a nonenzymatic nucleophilic attack by sulfhydryl-containing compounds, such as glutathione, present in red blood cells and other tissues.	**Malignancy** (post-transplant lymphoma and hepatosplenic T-cell lymphoma*)	Thiopurines are NOT typically used as monotherapy for treatment of IBD, and are instead utilized as dual therapy with an anti-TNF. TPMT enzyme should be checked prior to initiating therapy. Use careful consideration in selecting a thiopurine in patients with a history of skin cancer. Consider avoiding thiopurines in young men.	CD & UC (both off-label use)	**CD and UC (Moderate to Severe)** Start with 50 mg once daily; titrate up to 2.5 mg/kg once daily over ≥12 weeks as indicated and tolerated. Despite lack of pharmacokinetic data to suggest optimal dosing weight, some experts favor using lean body weight given the toxicities of Azathioprine. Consider discontinuing one year after initiation if it is being used as combination therapy (with an anti-TNF). **If the patient does not have a normal TPMT level, a dose adjustment will need to be considered (vs. alternative therapy). Please refer to clinical guidelines.**	Nausea Vomiting Leukopenia Diarrhea Rash Infections	Hypersensitivity to azathioprine or any component of the formulation; patients with rheumatoid arthritis and a history of treatment with alkylating agents (eg, cyclophosphamide, chlorambucil, melphalan) may have a prohibitive risk of malignancy with azathioprine treatment	CBC at baseline then weekly for 4 weeks, then every 2 weeks for 4 weeks, then at least monthly thereafter. CMP at baseline then every 4 months. Consider checking every week for a few weeks in higher risk patients.	Thiopurine Metabolites (See your lab reference range)	Ensure female patients of reproductive age are using an effective birth control method while on this medication. Ideally, thiopurines are not started in pregnancy, but continuation of therapy can be considered for those who do become pregnant. Breastfeeding can also be considered.	Behçet syndrome (off-label use) Bullous pemphigoid (adjunctive agent) (off-label use) Dermatomyositis/polymyositis (adjunctive agent) (off-label use) Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (off-label use) Granulomatosis with polyangiitis and microscopic polyangiitis (off-label use): Hepatitis, autoimmune (adjunctive agent) (off-label use) Immune thrombocytopenia, chronic, refractory or relapsed (off-label use) Interstitial pneumonia/interstitial lung disease (adjunctive agent) (off-label use) Lupus nephritis (alternative agent) (off-label use) Myasthenia gravis, chronic immunosuppressive therapy (off-label use) Pemphigus vulgaris and pemphigus foliaceus (alternative agent) (adjunctive agent) (off-label use) Polyarteritis nodosa (off-label use) Rheumatoid arthritis (alternative agent) Sarcoidosis, pulmonary, steroid-refractory disease (alternative agent) (off-label use) Solid organ transplantation (alternative agent) Takayasu arteritis (adjunctive agent) (off-label use) Uveitis, noninfectious (alternative agent) (off-label use)
Purinethol (Mercaptopurine) **Abbreviation:** 6-MP **Delivery method:** PO **MOA:** Following absorption, 6-thioguanine nucleotides (6-TGN) exert their immunosuppressive effects by inhibition of purine and protein synthesis in lymphocytes	None, however it is still associated with post-transplant lymphoma and hepatosplenic T-cell lymphoma, as above.	The thiopuriones have been linked to the occurence of photosensitive reactions, so patients should wear sunscreen and limit their sun exposure. Thiopurines can cause myelosuppression.	CD & UC (both off-label use)	**CD and UC (Moderate to Severe)** Start at 50mg daily; maximum dose is 1.5 mg/kg based on estimated lean body weight. Consider discontinuing one year after initiation if it is being used as combination therapy (with an anti-TNF). **If the patient does not have a normal TPMT level, a dose adjustment will need to be considered (vs. alternative therapy). Please refer to clinical guidelines.**	Rash Anorexia Diarrhea Nausea Vomiting Bone marrow suppression Malaise	No contraindications listed in the US manufacturer's labeling		Thiopurine Metabolites (See your lab reference range)		Acute lymphoblastic leukemia (ALL) Acute promyelocytic leukemia, maintenance (off-label use) Hepatitis, autoimmune (off-label use) Lymphoblastic lymphoma (off-label use)
Sources	Sources: UpToDate, Epocrates, Crohn's & Colitis Foundation, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7018581/									