Figure 1. Clinical decision support tool for pharmacological management of **adult outpatients with moderate to severe luminal Crohn's disease.**

Moderate to luminal Crohn's disease defined as:

- CDAI score of 220 or higher
- High risk of adverse disease-related complications including surgery, hospitalization, and disability based on a combination of structural damage, inflammatory burden, and impact of quality of life

Adult outpatients with moderate to severe luminal Crohn's disease

Suggest using biologic agents (with or without immunomodulators) EARLY, rather than delaying their use until after failure of mesalamine and/or corticosteroids
(Conditional recommendation, low quality of evidence)

Biologic therapy

For Induction and maintenance of remission:
Recommends any of the following over no treatment:
infliximab, adalimumab, certolizumab pegol (Strong recommendation, moderate quality of evidence for ifx/ada and low quality for certolizumab pegol)
vedolizumab (Conditional recommendation, low quality of evidence for induction, moderate quality of evidence for maintenance)
ustekinumab (Strong recommendation, moderate quality of evidence)
Suggests *AGAINST* the use of natalizumab over no treatment
(Strong recommendation, moderate quality of evidence)*

Biologic-naïve patients; first-line therapy

Suggest using infliximab, adalimumab or ustekinumab rather than certolizumab pegol for induction of remission (Strong recommendation, moderate quality of evidence)
Suggest using vedolizumab rather than certolizumab pegol for induction of remission
(Conditional recommendation, low quality of evidence)

Prior failure of infliximab, particularly primary non-response

Suggest using ustekinumab for induction of remission
(Strong recommendation, moderate quality of evidence)
Suggests using vedolizumab for induction of remission
(Conditional recommendation, low quality of evidence)

Prior failure of infliximab, particularly secondary non-response

Recommends using adalimumab or ustekinumab for induction of remission
(Strong recommendation, moderate quality of evidence)
Suggests using vedolizumab for induction of remission
(Conditional recommendation, low quality of evidence)
Comment: if adalimumab was the first line drug utilized there is indirect evidence to suggest using infliximab as a second line agent

Thiopurines and Methotrexate

Corticosteroids and Mesalamine

Suggests the use of corticosteroids over no treatment for induction of remission
(Conditional recommendation, moderate quality of evidence)
Recommends AGAINST the use of corticosteroids over no treatment for maintenance of remission (Strong recommendation, moderate quality of evidence)
Recommends AGAINST use of 5-ASA or sulfasalazine for induction or maintenance of remission
(Strong recommendation, moderate quality of evidence)

In those naïve to biologics and immunomodulators, suggests use of infliximab or adalimumab in combination with thiopurine for induction and maintenance of remission over infliximab or adalimumab monotherapy (Conditional recommendation, moderate quality of evidence for infliximab and very low quality evidence for adalimumab)
Comment: Based on indirect evidence combination infliximab or adalimumab with methotrexate may be more effective than infliximab monotherapy
***No recommendation* regarding use of ustekinumab or vedolizumab in combination with a thiopurine or methotrexate over biologic drug monotherapy**
(No recommendation, knowledge gap)
In quiescent CD, *no recommendation* for withdrawal of either immunomodulator or the biologic over combination therapy of a biologic and an immunomodulator
(No recommendation, knowledge gap)

Suggest AGAINST using thiopurine monotherapy for *inducing remission* in patients with active disease (Conditional recommendation, very low quality of evidence)
Suggest using thiopurine monotherapy, rather than no treatment, for *maintaining remission* in patients with quiescent disease (Conditional recommendation, moderate quality of evidence)
Suggests using subcutaneous or intramuscular methotrexate over no treatment for inducing and maintaining remission
(Conditional recommendation, low quality of evidence)
Suggest AGAINST using oral methotrexate monotherapy for *inducing or maintaining remission*
(Conditional recommendation, low quality of evidence)

Recommends using biologic monotherapy rather than thiopurine monotherapy for inducing remission in patients with active disease
(Strong recommendation, moderate quality of evidence)

Figure 2. Clinical decision support tool for pharmacological management of **adult outpatients with fistulizing Crohn's disease.**

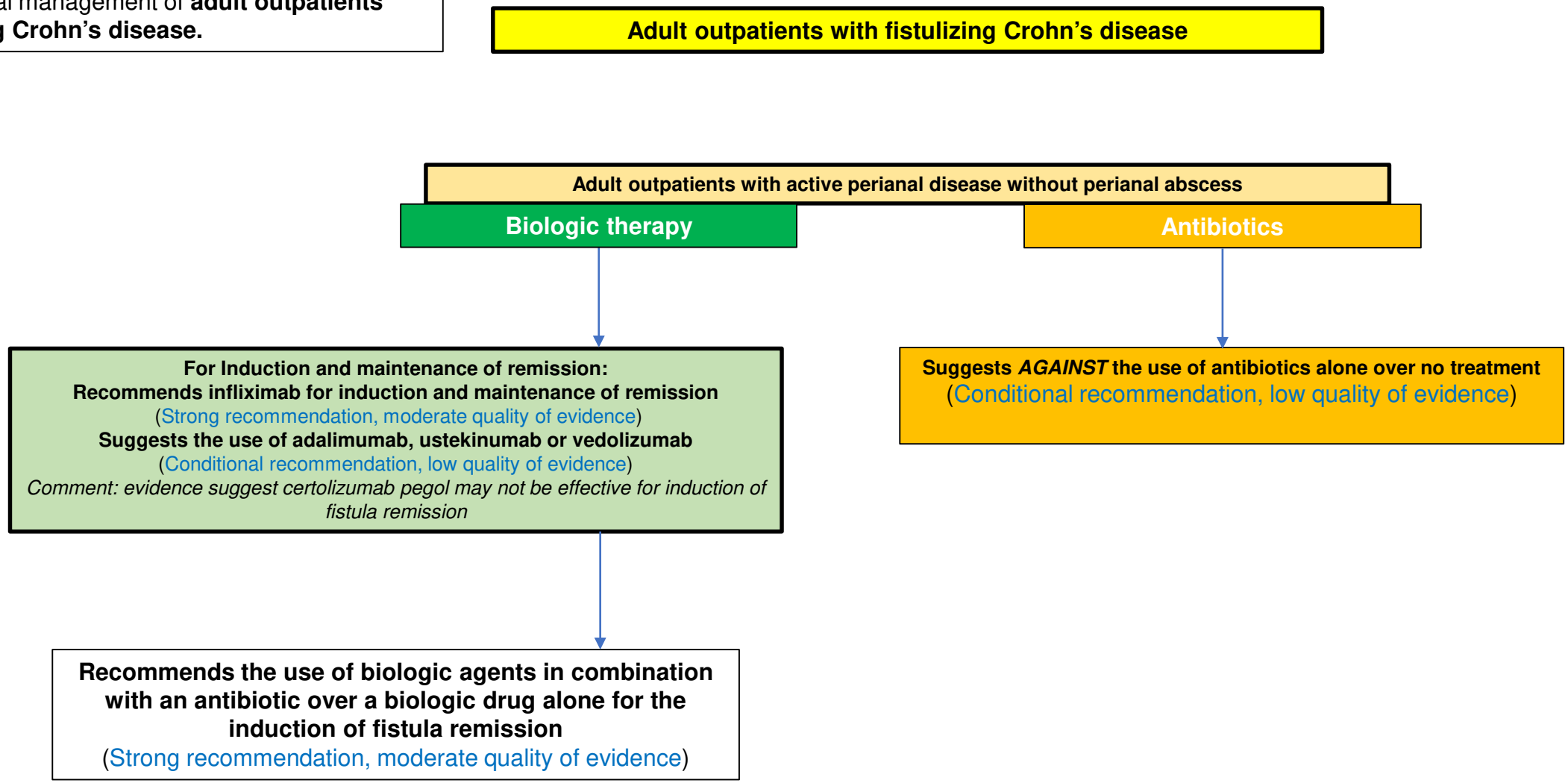

Figure 1: * Comment: Given evidence of harm in post marketing data from progressive multifocal leukoencephalopathy (PML) and the availability of other drugs, the AGA suggests against the use of natalizumab. Patients who are JC virus antibody negative who put a high value on the potential benefits and lower value on PML risk and who will adhere to ongoing monitoring for JC virus positivity, may consider using natalizumab