This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutic Subcommittee.

**Class:** Aminosalicylates (5-ASA)

**Non-formulary medication:** Delzicol (mesalamine), Apriso (mesalamine), Dipentum (olsalazine), Lialda (mesalamine), Pentasa (mesalamine), Asacol HD (mesalamine), Canasa (mesalamine rectal suppository), Rowasa (mesalamine enema), Giazo (balsalazide)

**Formulary medication:** Azulfidine (sulfasalazine), Azulfidine En-Tabs (sulfasalazine), Colazal (balsalazide)

**LOB:** Non-Medicare

**Effective Date:** May 20, 2015

**Renewal Date:** May 18, 2016

**Policy/Criteria:**

1. **Delzicol DR (mesalamine):**
   a. Confirmed diagnosis of ulcerative colitis (e.g. ulcerative proctitis, proctosigmoiditis, colitis, pancolitis) or Crohn’s disease
   b. Must be prescribed by GI specialist (new start)
   c. Failed, intolerant or contraindicated to formulary sulfasalazine or balsalazide

2. **Apriso (mesalamine), Lialda (mesalamine), Pentasa (mesalamine), Asacol HD (mesalamine):**
   a. Confirmed diagnosis of ulcerative colitis (e.g. ulcerative proctitis, proctosigmoiditis, colitis, pancolitis) or Crohn’s disease
   b. Must be prescribed by GI specialist (new start)
      i. Failed, intolerant or contraindicated to formulary sulfasalazine or balsalazide AND preferred non-formulary product Dezicol DR (mesalamine)

3. **Topical 5-ASA medications (e.g. mesalamine rectal suppository, rectal enema):**
   a. Confirmed diagnosis of ulcerative colitis (e.g. ulcerative proctitis, proctosigmoiditis, colitis, pancolitis)
   b. Prescribed by GI specialist (new start)

4. **Dipentum (osalazine):**
   a. Confirmed diagnosis of ulcerative colitis (e.g. ulcerative proctitis, proctosigmoiditis, colitis, pancolitis)
   b. Must be prescribed by GI specialist (new start)
   c. Failed, intolerant or contraindicated to formulary sulfasalazine or balsalazide AND preferred non-formulary product Dezicol DR (mesalamine)
5. Giazo (balsalazide):
   a. Confirmed diagnosis of ulcerative colitis (e.g. ulcerative proctitis, proctosigmoiditis, colitis, pancolitis) in adult male
   b. Must be prescribed by GI specialist (new start)
   c. Failed, intolerant or contraindicated to formulary sulfasalazine or balsalazide AND preferred non-formulary product Dezicol DR (mesalamine)

Clinical justification:

2010 American College of Gastroenterology, Practice Parameters Committee: Ulcerative Colitis Practice Guidelines

Recommendations for Management of Mild-Moderate Distal Colitis

- Patients with mild to moderate distal colitis may be treated with oral aminosalicylates, topical mesalamine or topical steroids (Evidence A)
- Topical mesalamine agents are superior to topical steroids or oral aminosalicylates (Evidence A)
- The combination of oral and topical aminosalicylates is more effective than either alone (Evidence A)
- In patients refractory to oral aminosalicylates or topical corticosteroids, mesalamine enemas or suppositories may still be effective (Evidence A)
- The unusual patient who is refractory to all of the above agents in maximal doses or who is systemically ill, may require treatment with oral prednisone in doses up to 40-60mg per day, or a biological may be considered.

Recommendations for Maintenance of Remission in Distal Disease

- Mesalamine suppositories are effective in the maintenance of remission in patients with proctitis, whereas mesalamine enemas are effective in patients with distal colitis when dosed even as infrequently as every third night (Evidence A)
- Sulfasalazine, mesalamine compounds and balsalazide are also effective in maintaining remission; the combination of oral and topical mesalamine is more effective than either one alone (Evidence A)
- Topical corticosteroids including budesonide, however, have not proven effective for maintaining remission in distal colitis (Evidence A).
- When all of these measures fail to maintain remission in distal disease, thiopurines (6-mercaptopurine or azathioprine) and infliximab (Evidence A), but not corticosteroids, may prove effective (Evidence B)

Recommendations for Management of Mild-Moderate Extensive Colitis: Active Disease

- Patients with mild to moderate extensive colitis should begin therapy with oral sulfasalazine in daily doses titrated up to 4-6 grams per day, or an alternate aminosalicylate in doses up to 4.8 gram per day of the active 5-aminosalicylate acid (5-ASA) moiety (Evidence A)
• Oral steroids are generally reserved for patients who are refractory to oral aminosalicylates in combination with topical therapy, or for patients whose symptoms are so troubling as to demand rapid improvement (Evidence B).
• 6-MP and azathioprine are effective for patients who do not respond to oral steroids, and continue to have moderate disease, and are not so acutely ill as to require intravenous therapy (Evidence A)
• A biological may be considered for patients who are steroid refractory or steroid dependent despite adequate doses of a thiopurine, or who are intolerant of these medications.

Recommendations for Mild-Moderate Extensive Colitis: Maintenance of Remission

• Once the acute attack is controlled, a maintenance regimen is usually required, especially in patients with extensive or relapsing disease. Sulfasalazine, olsalazine, mesalamine and balsalazide are all effective in reducing relapses (Evidence A)

2009 American College of Gastroenterology, Practice Guidelines: Management of Crohn’s Disease in Adults

Recommendations for Management of Mild-Moderate Disease

• Ileal, ileocolonic or colonic disease has commonly been treated in clinical practice with oral mesalamine 3.2-4 grams daily (grade C) or sulfasalazine for the ileocolonic or colonic disease as 3-6 grams daily (grade A) in divided doses
• New evidence suggests that this approach is minimally effective as compared with placebo (grade A), and less effective than budesonide or conventional corticosteroids (grade A)

Recommendations for Management of Moderate-Severe Disease

• Patients with moderate to severe disease are treated with prednisone 40-60mg daily until resolution of symptoms and resumption of weight gain (generally 7-28 days) (grade A)
• Azathioprine and 6-MP are effective for maintaining a steroid-induced remission (gradeA), and parenteral methotrexate at a dose of 25mg/week is effective for steroid-dependent and steroid-refractory CD (gradeB)

1. Cochrane review conducted by Feagan et al. assessed the efficacy, dose responsiveness, and safety of newer release formulation of 5-ASA compared to placebo and sulfasalazine in the maintenance of remission of Ulcerative Colitis. The authors determined that 5-ASA products were superior to placebo but inferior to sulfasalazine in maintaining remission.
2. Studies indicate remission rates appear to be similar across all mesalamine products at 35-50% with mild to moderate ulcerative colitis and maintained for 6 months at a rate of 55-75%
3. The differences in the various oral mesalamine products are not due to differences in mechanism of action, but the location of the medication is released in the gastrointestinal tract. Oral mesalamine is mostly absorbed in the small intestine and does not reach the colon. Sulfasalazine (Azulfidine), balsalazide (Colazal) and olsalazine (Dipentum) are prodrugs in which mesalamine is azo-bonded to a second moiety and released in the colon following bacterial cleavage of the bond. Asacol and Asacol HD tablets are coated with a pH-sensitive film that disintegrates at the higher pH of the terminal ileum and proximal colon, releasing the drug. Pentasa is an ethylcellulose-coated
formulation that releases mesalamine gradually throughout the gastrointestinal tract. Lialda and Apriso both delay the release of the drug until it reaches the distal ileum and colon. Mesalamine is also available as an enema (Rowasa, and others) and as a rectal suppository (Canasa).

4. Delzicol was formulated to replace Asacol for the treatment of mildly to moderately active ulcerative colitis and the maintenance of remission in adults. Delzicol has been shown to be equivalent in safety and efficacy to Asacol.

### Comparison of formulations of aminosalicylates:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulary Status</th>
<th>Usual Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azulfidine (sulfasalazine)</td>
<td>F</td>
<td>500mg QID</td>
</tr>
<tr>
<td>Azulfidine En-Tabs (sulfasalazine) 500mg DR</td>
<td>F</td>
<td>500mg QID</td>
</tr>
<tr>
<td>Colazal (balsalazide) 750mg</td>
<td>F</td>
<td>2250mg TID</td>
</tr>
<tr>
<td>Apriso (mesalamine) 0.375g ER</td>
<td>NF</td>
<td>1500mg QD</td>
</tr>
<tr>
<td>Asacol HD (mesalamine) 800mg DR</td>
<td>NF</td>
<td>1600mg TID</td>
</tr>
<tr>
<td>Canasa (mesalamine) 1000mg Rectal Suppository</td>
<td>NF</td>
<td>1000mg QHS</td>
</tr>
<tr>
<td>Delzicol (mesalamine) 400mg DR</td>
<td>NF</td>
<td>Induction 800mg TID, Maintenance 800mg BID</td>
</tr>
<tr>
<td>Dipentum (olsalazine) 250mg</td>
<td>NF</td>
<td>500mg BID</td>
</tr>
<tr>
<td>Giazo (balsalazide) 1.1g</td>
<td>NF</td>
<td>3300mg BID</td>
</tr>
<tr>
<td>Lialda (mesalamine) 1.2g DR</td>
<td>NF</td>
<td>Induction: 2.4-4.8g QD, Maintenance: 2.4g QD</td>
</tr>
<tr>
<td>Pentasa (mesalamine) 250mg, 500mg CR</td>
<td>NF</td>
<td>1g QID</td>
</tr>
<tr>
<td>Rowasa (mesalamine) 4g/60mL Enema</td>
<td>NF</td>
<td>4g QHS</td>
</tr>
</tbody>
</table>

### References: