CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW

1Q17 – JANUARY – FEBRUARY

BRAND NAME
Stelara®

GENERIC NAME
ustekinumab

MANUFACTURER
Janssen Biotech, Inc.

DATE OF APPROVAL
September 26, 2016

PRODUCT LAUNCH DATE
January 25, 2010

REVIEW TYPE
☐ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☒ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants)

FDA APPROVED INDICATION(S)
Treatment of adult patients with:

- moderate to severe plaque psoriasis (Ps) who are candidates for phototherapy or systemic therapy
- active psoriatic arthritis (PsA), alone or in combination with methotrexate
- moderately to severely active Crohn's disease (CD) who have
    - failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker or
    - failed or were intolerant to treatment with one or more TNF blockers

OFF-LABEL USES
Not applicable

CLINICAL EFFICACY

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Stelara® was evaluated in three randomized, double-blind, placebo-controlled clinical studies in adult patients with moderately to severely active Crohn's disease (Crohn's Disease Activity Index [CDAI] score of 220 to 450). There were two 8-week intravenous induction studies (CD-1 and CD-2) followed by a 44-week subcutaneous randomized withdrawal maintenance study (CD-3) representing 52 weeks of therapy.

In studies CD-1 and CD-2, 1409 patients were randomized, of whom 1368 (CD-1, n=741; CD-2, n=627) were included in the final efficacy analysis. Induction of clinical response (defined as a reduction in CDAI score of greater than or equal to 100 points or CDAI score of less than 150) at Week 6 and clinical remission (defined as a CDAI score of less than 150) at Week 8 were evaluated. In both studies, patients were randomized to receive a single intravenous administration of Stelara® at either approximately 6 mg/kg, placebo, or 130 mg (a lower dose than recommended).

In Study CD-1, patients had failed or were intolerant to prior treatment with a TNF blocker: 29% patients had an inadequate initial response (primary non-responders), 69% responded but subsequently lost response (secondary non-responders) and 36% were intolerant to a TNF blocker. Of these patients, 48% failed or were intolerant to one TNF blocker and 52% had failed 2 or 3 prior TNF blockers. At baseline and throughout the study, approximately 46% of the patients were receiving corticosteroids and 31% of the patients were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 319 in the Stelara® approximately 6 mg/kg group and 313 in the placebo group.

In Study CD-2, patients had failed or were intolerant to prior treatment with corticosteroids (81% of patients), at least one immunomodulator (6-mercaptopurine, azathioprine, methotrexate; 68% of patients), or both (49% of patients). Additionally, 69% never received a TNF blocker and 31% previously received but had not failed a TNF blocker. At baseline, and throughout the study, approximately 39% of the patients were receiving corticosteroids and 35% of the patients were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 286 in the Stelara® and 290 in the placebo group.

In these induction studies (CD-1 and CD-2), a greater proportion of patients treated with Stelara® achieved clinical response at Week 6 with a statistically significant treatment difference of 12% and 27% in CD-1 and CD-2, respectively. Additionally, a greater proportion of treated patients achieved a clinical remission at Week 8 compared to placebo with statistically significant treatment difference of 14% and 21% in CD-1 and CD-2, respectively.

The maintenance study (CD-3), evaluated 388 patients who achieved clinical response (≥100 point reduction in CDAI score) at Week 8 of induction with Stelara® in studies CD-1 or CD-2. Patients were randomized to receive a subcutaneous maintenance regimen of either 90 mg Stelara® every 8 weeks or placebo for 44 weeks.

At Week 44, 47% of patients who received Stelara® were corticosteroid-free and in clinical remission, compared to 30% of patients in the placebo group. At Week 0 of Study CD-3, 34 out of 56 (61%) Stelara® treated patients who previously failed or were intolerant to TNF blocker therapies were in clinical remission and 23 out of 56 (41%) of these patients were in clinical remission at Week 44. In the placebo arm, 27 out of 61 (44%) patients were in clinical remission at Week 0 while 16 out of 61 (26%) of these patients were in remission at Week 44.

At Week 0 of Study CD-3, 46 out of 72 (64%) Stelara® treated patients who had previously failed immunomodulator therapy or corticosteroids (but not TNF blockers) were in clinical remission and 45 out of 72 (63%) of these patients were in clinical remission at Week 44. In the placebo arm, 50 out of 70 (71%) of these patients were in clinical remission at Week 0 while 31 out of 70 (44%) were in remission at Week 44. In the subset of these patients who were also naïve to TNF blockers, 34 out of 52 (65%) of Stelara® treated patients were in clinical remission at Week 44 as compared to 25 out of 51 (49%) in the placebo arm.

CONTRAINDICATIONS
Not applicable

BLACK BOX WARNINGS
Not applicable

DRUG INTERACTIONS
- Avoid use of live vaccines with Stelara®

ADVERSE REACTIONS
Most common adverse reactions are:
- Psoriasis (≥3%): nasopharyngitis, upper respiratory tract infection, headache, and fatigue
- Crohn's Disease, induction (≥3%): vomiting
- Crohn's Disease, maintenance (≥3%): nasopharyngitis, injection site erythema, vulvovaginal candidiasis/mycotic infection, bronchitis, pruritus, urinary tract infection, and sinusitis

DOSAGE AND ADMINISTRATION
Crohn's Disease Recommended Initial Adult Intravenous Dosage:
A single intravenous infusion using weight-based dosing:

Weight Range (kilogram)	Recommended Dosage
Up to 55 kg	260 mg (2 vials)
Greater than 55 kg to 85 kg	390 mg (3 vials)
Greater than 85 kg	520 mg (4 vials)

Crohn's Disease Recommended Maintenance Adult Subcutaneous Dosage:

A subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

PRODUCT AVAILABILITY

Subcutaneous Injection

- Injection: 45 mg/0.5 mL or 90 mg/mL in a single-dose prefilled syringe
- Injection: 45 mg/0.5 mL in a single-dose vial

Intravenous Infusion

- Injection: 130 mg/26 mL (5 mg/mL) solution in a single-dose vial

THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Cimzia (certolizumab pegol)	**Initial dose**: 400 mg SC initially and at weeks 2 and 4 **Maintenance dose:** In patients who obtain a clinical response, 400 mg SC every 4 weeks	
Entyvio (vedolizumab)	300 mg IV initially and at weeks 2 and 6, then Q8W	
Humira (adalimumab)	**Induction:** 160 mg SC (four 40mg injections) day 1 followed by 80 mg SC 2 weeks later (day15). 160mg can be given as 4 injections in one day or divided over 2 days. Two weeks later (day 29) begin maintenance dose of 40mg SC every other week **Maintenance:** 40 mg SC every other week	Also contains pediatric Crohn's disease indication.
Prednisone	40 mg PO QD for 2 weeks or IV 50-100 mg Q6H for 1 week	First-line therapy for moderate to severe Crohn's disease per ACG treatment guidelines
Remicade (infliximab)	5 mg/kg IV initially and at weeks 2 and 6, then Q8W	
Tysabri (natalizumab)	300 mg IV Q4W	

Boldface indicates generic availability

Utilization Management Recommendation
• There is significant potential for inappropriate use and utilization management should be considered for the following reason(s):

i) To ensure appropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcomes.
   (1) FDA indication is approved for moderate to severe Crohn's Disease who have:
      (a) failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker or
      (b) failed or were intolerant to treatment with one or more TNF blockers

ii) Recommended utilization management tool(s): (check all that apply)
   (1) ☒ Prior authorization
   (2) ☐ Quantity limits
   (3) ☐ Provider newsletter
   (4) ☐ Hard block (plan exclusion)
   (5) ☐ Messaging
   (6) ☐ Electronic step therapy
   (7) ☐ Clinical Program

Product Comparison

- Approve proposed utilization guidelines.

REFERENCES

1. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; September, 2016.
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3. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute Guideline on the Use of Thiopurines, Methotrexate, and Anti-TNF-α Biologic Drugs for the Induction and Maintenance of Remission in Inflammatory Crohn's Disease. Gastroenterology. 2013; 145:1459-1463
4. Lichtenstein GR, Hanauer SB, Sandborn WJ, et al. Management of Crohn's Disease in Adults. American Journal of Gasteroenterology. 2009; 104(2):465-83. Doi: 10.1038/ajg.2008.168.