TRUVEN HEALTH ANALYTICS

## COMPENDIA TRANSPARENCY TRACKING FORM

**DRUG:** Imatinib mesylate

**INDICATION:** Diffuse cutaneous systemic sclerosis

| COMPENDIA TRANSPARENCY REQUIREMENTS | |
|---|---|
| 1 | Provide criteria used to evaluate/prioritize the request (therapy) |
| 2 | Disclose evidentiary materials reviewed or considered |
| 3 | Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest |
| 4 | Provide meeting minutes and records of votes for disposition of the request (therapy) |

**EVALUATION/PRIORITIZATION CRITERIA:** **C, R, S**
*to meet requirement 1

| CODE | EVALUATION/PRIORITIZATION CRITERIA |
|---|---|
| **A** | Treatment represents an established standard of care or significant **advance** over current therapies |
| **C** | **Cancer** or cancer-related condition |
| **E** | Quantity and robustness of **evidence** for use support consideration |
| **L** | **Limited** alternative therapies exist for condition of interest |
| **P** | **Pediatric** condition |
| **R** | **Rare** disease |
| **S** | **Serious**, life-threatening condition |

**Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]**

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## EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

| CITATION | STUDY-SPECIFIC COMMENTS | LITERATURE CODE |
|---|---|---|
| Bournia,V.K., Evangelou,K., and Sfikakis,P.P.: Therapeutic inhibition of tyrosine kinases in systemic sclerosis: a review of published experience on the first 108 patients treated with imatinib. Semin.Arthritis Rheum Feb 2013; Vol 42, Issue 4; pp. 377-390. | Study methodology comments:<br>Literature analyst CB comments | 4 |
| Prey,S., Ezzedine,K., Doussau,A., et al: Imatinib mesylate in scleroderma-associated diffuse skin fibrosis: a phase II multicentre randomized double-blinded controlled trial. British Journal of Dermatology Nov 2012; Vol 167, Issue 5; pp. 1138-1144. | Study methodology comments:<br>This was a multicentre, randomized parallel-group double-blind trial. Overall, this study was at low risk for most of the key risk of bias criteria which included random sequence generation, lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with allocation concealment was unclear and not discussed in the paper. | S |
| Pope,J., McBain,D., Petrlich,L., et al: Imatinib in active diffuse cutaneous systemic sclerosis: Results of a six-month, randomized, double-blind, placebo-controlled, proof-of-concept pilot study at a single center. Arthritis & Rheumatism Nov 2011; Vol 63, Issue 11; pp. 3547-3551. | Study methodology comments:<br>This was a 6-month, randomized, double-blind, placebo-controlled, proof-of-concept pilot study. After randomizing 10 dcSSc patients (9 to the imatinib group and 1 to the placebo group), the principal investigator decided to stop enrollment because of poor tolerability of the study drug and two serious adverse events thought to be directly related to it. Overall, this study was at high risk of bias due to a high dropout rate and early study termination. | S |
| Pope,J., McBain,D., Petrilich,L., et al: A proof of concept trial of Gleevec (imatinib) in active diffuse scleroderma (DSSC). Clinical and Experimental Rheumatology 2010; Vol 28, Issue 2 SUPPL. 58; p. S94. | | S |

| | | |
|---|---|---|
| Fraticelli,P., Pomponio,G., Gabrielli,B., et al: Oral imatinib for the treatment of scleroderma pulmonary involvement: Preliminary results of a pilot study. Rheumatology Feb 2012; Vol 51 SUPPL. 2, p. ii25. | | 3 |
| Spiera,R.F., Gordon,J.K., Mersten,J.N., et al: Imatinib mesylate (Gleevec) in the treatment of diffuse cutaneous systemic sclerosis: results of a 1-year, phase IIa, single-arm, open-label clinical trial. Annals of the Rheumatic Diseases Jun 2011; Vol 70, Issue 6; pp. 1003-1009. | | 3 |
| Gordon,J.K., Davids,M.L., Doobay,K., et al: Imatinib mesylate (gleevec(trademark)) in the treatment of diffuse cutaneous systemic sclerosis: Results of a 24 month open label, extension phase. Arthritis and rheumatism Oct 2012; Vol 64 SUPPL. 10, p. S735. | | 3 |
| Khanna,D., Saggar,R., Mayes,M.D., et al: A one-year, phase I/IIa, open-label pilot trial of imatinib mesylate in the treatment of systemic sclerosis-associated active interstitial lung disease. Arthritis & Rheumatism Nov 2011; Vol 63, Issue 11; pp. 3540-3546. | | 3 |
| Divekar,A.A., Khanna,D., Abtin,F., et al: Treatment with imatinib results in reduced IL-4-producing T cells, but increased CD4(+) T cells in the broncho-alveolar lavage of patients with systemic sclerosis. Clinical Immunology Dec 2011; Vol 141, Issue 3; pp. 293-303. | | 2 |

**Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)**

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## CONTRIBUTORS:

*to meet requirement 3

| PACKET PREPARATION | DISCLOSURES | EXPERT REVIEW | DISCLOSURES |
|---|---|---|---|
| Margi Schiefelbein, PA | None | Edward P. Balaban, DO | None |
| Stacy LaClaire, PharmD | None | Jeffrey A. Bubis, DO | Other payments: Dendreon |
| Felicia Gelsey, MS | None | Keith A. Thompson, MD | None |
| | | Gerald J. Robbins, MD | None |
| | | John M. Valgus, PharmD | None |

## ASSIGNMENT OF RATINGS:

*to meet requirement 4

| | EFFICACY | STRENGTH OF RECOMMENDATION | COMMENTS | STRENGTH OF EVIDENCE |
|---|---|---|---|---|
| **MICROMEDEX** | --- | --- | | C |
| **Edward P. Balaban, DO** | Ineffective | Class III - Not Recommended | Imatinib appears ineffective in the therapy of systemic sclerosis | N/A |
| **Jeffrey A. Bubis, DO** | Ineffective | Class III - Not Recommended | Data does not demonstrate an outcomes benefit to Gleevec in diffuse cutaneous systemic sclerosis. | N/A |
| **Keith A. Thompson, MD** | Ineffective | Class III - Not Recommended | None | N/A |
| **Gerald J. Robbins, MD** | Ineffective | Class III - Not Recommended | Although theory attractive, small studies show lack of benefit and increased toxicity. Category B due to small numbers. | N/A |
| **John M. Valgus, PharmD** | Ineffective | Class III - Not Recommended | Studies demonstrate lack of efficacy compared with placebo with problematic side effect profile. Should not be used in clinical practice. | N/A |