Administration[6]:

- May be administered without regard to meals.
- NIOSH recommends appropriate precautions for receiving, handling, administration, and disposal.

Warnings/Precautions[6]:

Fluid retention/peripheral edema, Significant decreases in hemoglobin, Transaminase elevations, Hypersensitivity reactions, Pulmonary edema occur; Require further evaluation to determine cause and appropriate treatment or discontinuation of therapy.

Contraindications[6]:

Hypersensitivity to bosentan or any component of the formulation; concurrent use of cyclosporine or glyburide; women who are or may become pregnant, Pregnancy and breastfeeding.

Drug Interactions[6]:

Risk x: Cyclosporine, Glyburide, Mifepristone, CYP3A4 Inducers

Side effects[6]:

>10%: Edema, Headache, Increased serum ALT & AST, Respiratory tract infection

1% to 10%: Chest pain, Syncope, Flushing, Hypotension, Palpitations, Fluid retention, Anemia, Arthralgia, Sinusitis

<1%: Anaphylaxis, Angioedema, DRESS syndrome, Hepatic cirrhosis (prolonged therapy), Hepatic failure (rare), Hypersensitivity reaction, Jaundice, Leukopenia, Nasal congestion, Neutropenia, Peripheral edema, Severe anemia, Skin rash, Thrombocytopenia

Rx Code 62.5: 65524

Rx Code 125: 64923

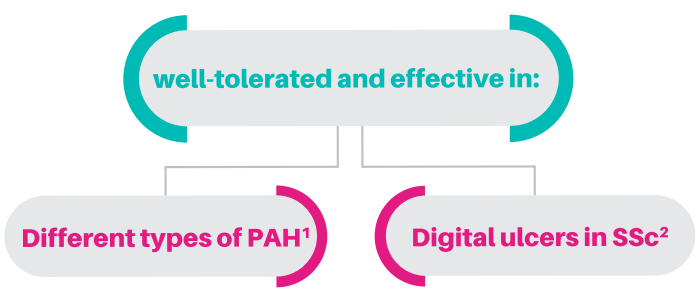
References:

1. Kuang, Hy., Li, Q., Du, Ha. et al. Efficacy and Safety of Long-Term Oral Bosentan in Different Types of Pulmonary Arterial Hypertension: A Systematic Review and Meta-Analysis. Am J Cardiovasc Drugs 21, 181–191 (2021).
2. Cristina N, Groseanu L, Berghea F, et alOP0270 LONG-TERM EFFICACY AND SAFETY OF BOSENTAN IN PATIENTS WITH DIGITAL ULCERS RELATED TO SYSTEMIC SCLEROSIS Annals of the Rheumatic Diseases 2021;80:164.
3. Kuang, Hy., Li, Q., Du, Ha. et al. Efficacy and Safety of Long-Term Oral Bosentan in Different Types of Pulmonary Arterial Hypertension: A Systematic Review and Meta-Analysis. Am J Cardiovasc Drugs 21, 181–191 (2021). https://doi.org/10.1007/s40256-020-00426-w
4. Beghetti M. Bosentan in pediatric patients with pulmonary arterial hypertension. Curr Vasc Pharmacol. 2009;7(2):225-233. doi:10.2174/157016109787455653
5. Lee KA, Kim H, Kim BY, et alAB0669 THE EFFECTS OF BOSENTAN FOR TREATMENT OF DIGITAL ULCER IN KOREAN PATIENTS WITH SYSTEMIC SCLEROSIS: PROSPECTIVE, MULTICENTER, OPEN-LABEL TRIAL. Annals of the Rheumatic Diseases 2019;78:1795-1796.
6. Uptodate /bosentan /2023

www.faranshimi.com Tel: +98 (21) 57941000 Patient Care: +98 (21) 57941444 Faranshimi

FARANTAN, a dual endothelin receptor antagonist ($ERA_{A/B}$), improves hemodynamics and exercise capacity in adults with PAH. clinical studies have shown bosentan is the one among ERAs that can significantly reduce in the mean number of digital ulcers in patients with systemic sclerosis.

- Decrease clinical deterioration and improve survival
- Improve pulmonary vascular resistance (PVR)
- Achieve a satisfactory exercise capacity
- Reduce the occurrence of new digital ulcers

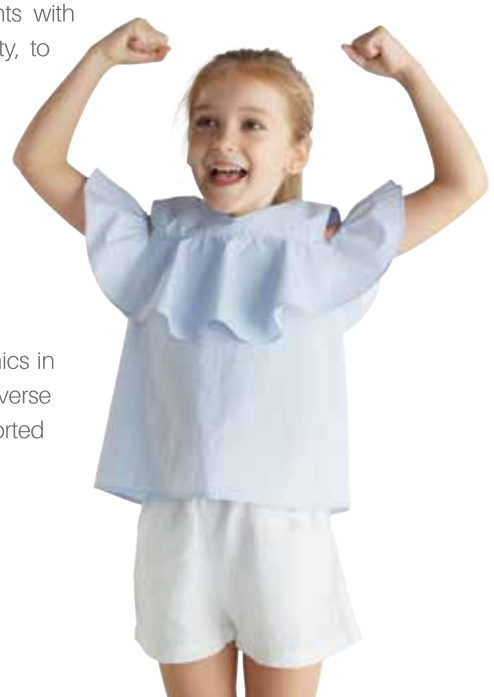


Efficacy and Safety of Long-Term Oral Bosentan in Different Types of PAH[3]: A Systematic Review and Meta-Analysis

In this systematic review and meta-analysis, long-term administration of oral bosentan has been identified as a well-tolerated and effective agent in different types of PAH. In addition, it has been concluded that long-term oral bosentan should be considered for patients with connective tissue disease (CTD) to achieve a satisfactory exercise capacity, to improve survivals, where more attention on adverse events is required.

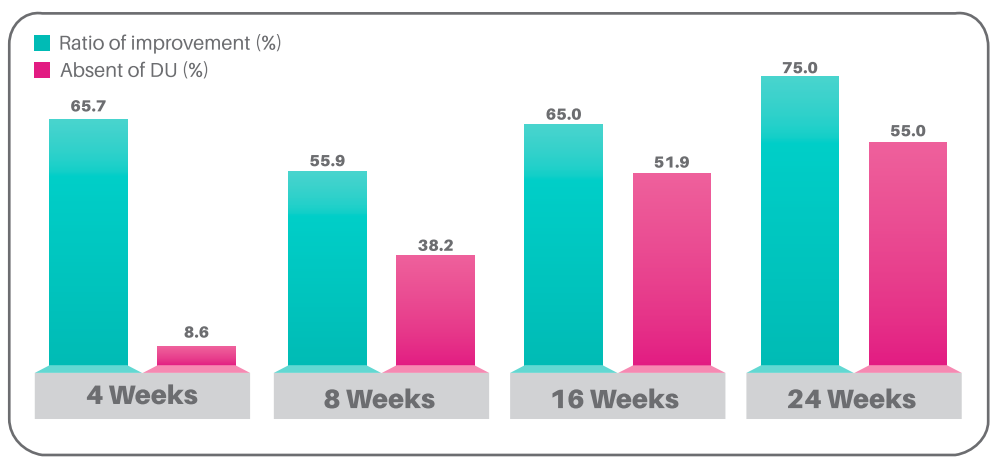
Bosentan in Pediatric Patients with Pulmonary Arterial Hypertension[4]:

Bosentan appears to improve long-term functional status and hemodynamics in children with PAH. Overall, no safety concern is raised by these studies; adverse events, including liver enzyme elevations, appear to be less frequent than reported in the adult PAH clinical trials.



The Efficacy and Safety of Bosentan in Digital Ulcer secondary to Systemic sclerosis[5]:

A 4-year prospective, multicenter, open-label trial was performed on 562 Patients with SSc to investigate the complete healing of DU and tolerability of bosentan. Administration of bosentan over 24 weeks was statistically associated with complete healing and significant reduction in number of DU in patients with SSc.



Dosing[6]:

Pulmonary Arterial Hypertension:

Adult:

<40 kg: 62.5mg - twice daily

>40 kg: 62.5mg - twice daily after ~4 Weeks 125mg - twice daily

Pediatric:

Infants and <12 Years:

1mg/kg/dose - twice daily then 2mg/kg/dose - twice daily

Digital ulcers in systemic sclerosis (off-label):

Adult:

62.5mg - twice daily after~4 Weeks 125mg - twice daily

Kidney Impairment:

No dosage adjustment necessary.

Hepatic Impairment:

- Treatment initiation; Moderate to severe impairment and/or baseline transaminase >3 times ULN: Avoid use.
- During treatment; dosing based on transaminase elevations accompanied by clinical symptoms of hepatotoxicity.
- AST / ALT > 8 Times ULN: stop treatment and do not reintroduce.