

Supplementary Material

Mobility and Quality of Life in Adults with Paediatric-Onset Hypophosphatasia Treated with Asfotase Alfa: Results from UK Managed Access Agreement

Authors: Katie E. Moss¹; Richard Keen²; Shona Fang³; Alexandros Zygouras⁴;
Muhammad K. Javaid⁵; Tarekegn Geberhiwot⁶; Kenneth E.S. Poole⁷; Peter Selby⁸;
Jennifer S. Walsh⁹; Judith S. Bubbear²

¹ St. George's University Hospitals, London, UK;

² Royal National Orthopaedic Hospital, Stanmore, UK;

³ Alexion, AstraZeneca Rare Disease, Boston, MA, USA;

⁴ Alexion, AstraZeneca Rare Disease, Middlesex, UK;

⁵ Oxford University, Oxford, UK;

⁶ Queen Elizabeth Hospital, Birmingham, UK;

⁷ Department of Medicine and NIHR Cambridge Biomedical Research Centre, University of Cambridge, Cambridge, UK;

⁸ Manchester Royal Infirmary, Manchester, UK;

⁹ University of Sheffield, Sheffield, UK

* Correspondence:

Author: Katie E. Moss

Address: St. George's University Hospitals, Blackshaw Rd, London, UK SW17 0QT

Phone: 0208-725-1419

E-mail: katie.moss@stgeorges.nhs.uk

Supplementary Table S1. Proportion of patients meeting specific inclusion criteria for UK MAA enrolment.

	Safety Analysis Population (N=28)	Effectiveness Analysis Population (n=24)
Fractures (both criteria below), n (%)	2 (7.1)	1 (4.2)
Fracture history prior to enrolment	5 (17.9)	4 (16.7)
Current fracture at time of enrolment	2 (7.1)	1 (4.2)
Pain (either of the criteria below), n (%)	28 (100)	24 (100)
BPI-SF severity ≥ 7 at time of enrolment	26 (92.9)	22 (91.7)
Reported use of ≥ 2 analgesics at time of enrolment	12 (42.9)	9 (37.5)
Bleck mobility score of 1 to 6, n (%)	25 (89.3)	22 (91.7)

BPI-SF, Brief Pain Inventory Short-Form.

Supplementary Table S2. Non-opioid medication use. Data cutoff: May 2023.

Patient	Drug name, dose and frequency	Started analgesic before or after starting asfotase alfa?	Duration of use before starting asfotase alfa	Duration of use after starting asfotase alfa treatment
1	Etoricoxib, 60 mg daily	Before	6.7 years	Unknown
	Etoricoxib, 30 mg daily	After	—	2.8 years
2	Aspirin, 2 tablets daily	Unknown	Unknown	Unknown
	Paracetamol, 1 g 3 times daily	Unknown	Unknown	Unknown, ongoing at end of data collection
3	Gabapentin, 300 mg 3 times daily	Unknown	Unknown	Unknown, ongoing at end of data collection
	Paracetamol, 1 g as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
4	Gabapentin, 100 mg 3 times daily	After	—	1.2 years
	Meloxicam, 15 mg daily	After	—	1.5 years, ongoing at end of data collection
5	Meloxicam, 15 mg daily	Before	1.1 years	3.5 years, ongoing at end of data collection
	Paracetamol, 1 g as needed	Same start date as asfotase alfa	—	3.5 years, ongoing at end of data collection
6	Naproxen, 500 mg daily	Before	3 months	3.3 years, ongoing at end of data collection
	Paracetamol, 500 mg	Unknown	NA	NA
	Paracetamol, 1 g as needed	After	—	3 months
	Amitriptyline, 10 mg	After	—	6 days
	Amitriptyline, 20 mg	After	—	4 days
	Amitriptyline, 30 mg	After	—	7 days
	Amitriptyline, 40 mg	After	—	2 months
7	Paracetamol, 500 mg daily	Unknown	Unknown	Unknown, ongoing at end of data collection
8	Ibuprofen, 400 mg 4 times daily	Before	6 months	6 months
	Paracetamol, 1 g 3 times daily	Before	6 months	3.3 years, ongoing at end of data collection
	Ibuprofen, 400 mg as needed	After	—	1.3 years, ongoing at end of data collection
	Ibuprofen gel, 5% in 100 g as needed	After	—	1.3 years, ongoing at end of data collection

Patient	Drug name, dose and frequency	Started analgesic before or after starting asfotase alfa?	Duration of use before starting asfotase alfa	Duration of use after starting asfotase alfa treatment
9	Paracetamol, 1 g 4 times daily	Unknown	Unknown	Unknown
	Ibuprofen, 400 mg 3 times daily	Unknown	Unknown	Unknown
	Diclofenac Slow Release, 75 mg daily	Unknown	Unknown	Unknown, ongoing at end of data collection
	Capsaicin cream, Unknown dose as needed	After	—	1.8 years
10	Aspirin, 300 mg once daily	Before	21.5 years	5 months
	Ibuprofen, 400 mg 4 times daily	Before	21.5 years	4.8 years, ongoing at end of data collection
	Paracetamol, 1 g	Before	21.5 years	4.8 years, ongoing at end of data collection
	Nortriptyline, 10 mg daily	Before	3.6 years	3.5 years
	Gabapentin, 600 mg 3 times daily	After	—	4.4 years, ongoing at end of data collection
	Amitriptyline, 50 mg daily	After	—	1.3 years, ongoing at end of data collection
11	Amitriptyline, 75 mg daily	Unknown	Unknown	Unknown, ongoing at end of data collection
	Pregabalin, 75 mg as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Diclofenac gel, Unknown as needed	Before	Unknown	Unknown, ongoing at end of data collection
	Paramax, 500/5 mg as needed	After	Unknown	Unknown, ongoing at end of data collection
	Gabapentin, 900 mg 3 times daily	Unknown	Unknown	Unknown
12	Amitriptyline, 10 mg daily	Before	1 month	5 days
	Ibuprofen, 200 mg as needed	After	—	0.9 years
	Arcoxia, 90 mg daily	After	—	1.5 years
	Indomethacin, 50 mg, unknown frequency	After	—	1.5 years
	THC:CBD, 5 mg 4 times daily	After	—	1 month

Patient	Drug name, dose and frequency	Started analgesic before or after starting asfotase alfa?	Duration of use before starting asfotase alfa	Duration of use after starting asfotase alfa treatment
13	Ibuprofen, 400 mg 3 times daily	Before	26.5 years	2.8 years, ongoing at end of data collection
	Paracetamol, 1 g 4 times daily	Before	26.5 years	2.8 years, ongoing at end of data collection
	Naproxen, 500 mg as needed	After	—	1.1 years
14	Amitriptyline, 10 mg daily	Unknown	Unknown	Unknown, ongoing at end of data collection
	Celebrex, 100 mg, unknown frequency	Unknown	Unknown	Unknown, ongoing at end of data collection
	Ibuprofen gel, 10% as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Ibuprofen, 400 mg as needed	Unknown	Unknown	Unknown
	Colchicine, 500 mg 2 times daily	Before	1 year	2.5 years, ongoing at end of data collection
15	Paracetamol, 1 g 3 times daily	Before	9 months	2.8 years, ongoing at end of data collection
	Naproxen, 250 mg daily	Before	6 months	7 months
16	Etoricoxib, 60 mg as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Paracetamol, 1 g as needed	Before	12.5 years	5 months
17	Etoricoxib, 30–60 mg, frequency unknown	Unknown	Unknown	Unknown, ongoing at end of data collection
	Diazepam, 2 mg as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Ibuprofen gel, 5% as needed	After	—	1.3 years, ongoing at end of data collection
18	Ibuprofen gel, 10% as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Ibuprofen, 400 mg 2 times daily	Unknown	Unknown	Unknown, ongoing at end of data collection
	Etoricoxib, 90 mg as needed	Before	1 year	1 month

Patient	Drug name, dose and frequency	Started analgesic before or after starting asfotase alfa?	Duration of use before starting asfotase alfa	Duration of use after starting asfotase alfa treatment
19	Amitriptyline, 10 mg daily	Unknown	Unknown	Unknown, ongoing at end of data collection
	Paracetamol, 500 mg as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Ibuprofen, 200 mg as needed	Unknown	Unknown	Unknown
	Diazepam, 2 mg as needed	Before	19.6 years	1.1 years, ongoing at end of data collection
	Etoricoxib, 60 mg daily	Before	11 months	3 months
20	Colchicine, 500 µg, unknown frequency	Unknown	Unknown	Unknown, ongoing at end of data collection
	Ibuprofen, 400 mg as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Paracetamol, 500 mg, unknown frequency	Unknown	Unknown	Unknown, ongoing at end of data collection
	Propranolol, unknown dose or frequency	Unknown	Unknown	Unknown, ongoing at end of data collection
21	Paracetamol, 500 mg every 4 hours	Unknown	Unknown	Unknown, ongoing at end of data collection
	Diazepam, unknown dose or frequency	Unknown	Unknown	Unknown
	Diclofenac, 1% gel as needed	Before	Unknown	Unknown, ongoing at end of data collection
	Proxicam, 10 mg daily	Before	Unknown	Unknown, ongoing at end of data collection
22	Naproxen, 1 g, unknown frequency	Before	Unknown	Unknown
	Paracetamol, 4 g, unknown frequency	Before	Unknown	Unknown
	Pregabalin, 600 mg, unknown frequency	Before	Unknown	2.7 years
	Amitriptyline, 20 mg, unknown frequency	After	Unknown	Unknown
	Pregabalin, 200 mg 2 times daily	After	—	1.3 years, ongoing at end of data collection

Patient	Drug name, dose and frequency	Started analgesic before or after starting asfotase alfa?	Duration of use before starting asfotase alfa	Duration of use after starting asfotase alfa treatment
23	Paracetamol, 1 g 4 times daily	Before	13.4 years	1.5 years, ongoing at end of data collection
	Ibuprofen, 1200 mg 3 times daily	Before	5.4 years	5 months
	Ibuprofen, 400 mg daily	After	—	8 months
	Ibuprofen, 200 mg 3 times daily	After	—	6 months, ongoing at end of data collection
24	Paracetamol, 1 g as needed	Unknown	Unknown	Unknown, ongoing at end of data collection
	Bupivacaine, 0.5%, 3 mL, once	After	—	1 day
	Lidocaine, 1%, 3 mL, once	After	—	1 day