Medicines Management Programme

Best-value medicine:

Teriparatide on the High Tech Arrangement

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List of Abbreviations

BVB	Best-value biological
BVM	Best-value medicine
EMA	European Medicines Agency
EPAR	European public assessment report
EU	European Union
HMA	Heads of Medicines Agencies
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
Mcg	Micrograms
MMP	Medicines Management Programme
NICE	National Institute for Health and Care Excellence
NOOG	National Osteoporosis Guideline Group
PCRS	Primary Care Reimbursement Service
PIL	Patient information leaflet
PFP	Pre-filled pen
PFS	Pre-filled syringe
SmPC	Summary of Product Characteristics
VAT	Value-added tax

1. Executive Summary

The Health Service Executive (HSE)-Medicines Management Programme (MMP) aims to promote safe, effective and cost-effective prescribing of biological medicines, including biosimilar medicines. The MMP recognises the potential savings arising from the availability of biosimilars. These savings, however, can only be realised by increased utilisation of best-value biological (BVB) medicines or best-value medicines (BVM), including biosimilars.

Medicinal products containing teriparatide accounted for expenditure[i] of approximately €4.2 million on the High Tech Arrangement in 2021.[1] There are now a number of medicinal products containing teriparatide available on the High Tech Arrangement. This provides the opportunity to identify a BVM for teriparatide in order to achieve efficiencies in this therapeutic area.

The aim of this initiative is to ensure cost-effective prescribing of teriparatide on the High Tech Arrangement. It identifies BVMs for teriparatide. It also aims to support the prescribing of the BVMs.

[i] Expenditure reflects the ingredient cost of the medicinal product, exclusive of value added tax and fees

The MMP recommends Movymia® and Sondelbay® as the BVMs for teriparatide on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Movymia® or Sondelbay® when issuing a prescription for teriparatide on the High Tech Arrangement.

Implementation of this recommendation will lead to significant savings for the health service.

Initiation

When initiating a patient on teriparatide, the clinician should prescribe Movymia® or Sondelbay®.

Switching

Patients currently on teriparatide should be considered for switching to Movymia® or Sondelbay® when their next repeat High Tech prescription is being issued.

2. Background

2.1 Teriparatide

Teriparatide is a biological medicine containing the active fragment (1 - 34) of endogenous human parathyroid hormone.[2] It is licensed for the treatment of:[2]

- osteoporosis in postmenopausal women and in men at increased risk of fracture. In postmenopausal women, a significant reduction in the incidence of vertebral and non-vertebral fractures but not hip fractures has been demonstrated.
- osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture.

The recommended dose of teriparatide is 20 micrograms (mcg) administered subcutaneously once daily. The maximum total duration of treatment with teriparatide should be 24 months. The 24-month course should not be repeated over a patient's lifetime.[2]

Expenditure[ii] on medicinal products containing teriparatide under the High Tech Arrangement accounted for approximately €4.2 million in 2021.[1]

There are currently five medicinal products containing teriparatide available on the High Tech arrangement:[3]

- the reference medicine, Forsteo®,
- three biosimilar medicines, Movymia®, Sondelbay® and Terrosa®, and
- a hybrid medicinal product, Tetridar®.

Teriparatide was ranked 14th in terms of prescribing frequency on the High Tech Arrangement in 2021, with a prescribing frequency of 13,653.[4] There are approximately 1,200 patients in receipt of teriparatide on the High Tech Arrangement on a monthly basis; the majority of these patients are currently on Forsteo®, with approximately 20% of patients in receipt of Movymia® or Tetridar®.[5]

The reference medicine, Forsteo®, first received a marketing authorisation from the European Commission in 2003. The patent for Forsteo® expired in August 2019, allowing for the availability of biosimilar medicines and hybrid medicinal products containing teriparatide.

[ii] Expenditure reflects the ingredient cost of the medicinal product, exclusive of value added tax and fees.

2.2 Biosimilar medicines

There is now considerable national and international experience with the usage of biosimilar medicines. They have been used safely in clinical practice in the European Union (EU) for over 15 years and have demonstrated similar efficacy, safety and immunogenicity with their reference medicine. Analysis of more than one million patient-treatment years of safety data for biosimilar medicines did not raise any safety concerns.[6,7]

The MMP has recommended BVB medicines for adalimumab and etanercept, all of which are biosimilar medicines. In August 2022, 76% of patients in receipt of adalimumab 40 mg pre-filled pen (PFP) or pre-filled syringe (PFS), and 68% of patients in receipt of etanercept 25/50 mg PFP or PFS were prescribed a BVB medicine.[5] Over 21,400 patients have been initiated on, or switched to a BVB medicine for adalimumab or etanercept since May 2019.[8] This represents a significant increase in the prescribing and utilisation of biosimilar medicines for adalimumab and etanercept under the High Tech Arrangement since 2019. This demonstrates that significant clinical experience is being obtained for biosimilar medicines of adalimumab and etanercept in a short timeframe.

There are four biosimilar medicines containing teriparatide that have been approved via the centralised procedure undertaken by the European Medicines Agency (EMA); Livogiva®, Movymia®, Sondelbay® and Terrosa®.[9]

2.3 Hybrid Medicinal Products

Tetridar® is a hybrid medicinal product containing teriparatide that has been produced by chemical synthesis. It, therefore, did not have to be licensed in the EU via the centralised procedure. Instead, Tetridar® was licensed using a decentralised procedure with Germany as the reference member state. Article 10(3) of Directive 2001/83/EC was considered by the reference member state to be the appropriate legal basis for consideration of the licensing application for Tetridar®, i.e. as an application as a hybrid medicinal product of the reference medicine Forsteo®. Following evaluation, Tetridar® was considered a legitimate hybrid form of the reference product, Forsteo®, and was granted a marketing authorisation.[10]

3. Scope

This document considers the medicinal products containing teriparatide that have a marketing authorisation that allows for supply in Ireland. It aims to achieve efficiencies by the identification of BVMs for teriparatide under the High Tech Arrangement.

4. Definitions

For the purposes of this document, the reimbursement price refers to the reimbursed price of the medicinal product as listed in the High Tech Drug File maintained by the HSE-Primary Care Reimbursement Service (PCRS). It may not represent the final acquisition cost to the HSE of the medicinal product, which may also include any rebates and commercial-in-confidence arrangements that are in place. Both the reimbursement price and the acquisition cost are exclusive of value added tax (VAT).

Only medicinal products containing teriparatide that have a marketing authorisation which allows for supply in Ireland as of 4 May 2022 are included in this review. All prices and costs are correct as of 31 January 2023.

5. Best-value medicine - Teriparatide

The MMP has identified BVMs for teriparatide under the High Tech Arrangement. The identification of the BVMs was carried out in accordance with the *Processes for the Assessment and Selection of Best-Value Biological Medicines*, as outlined in schedule 2 of the Framework Agreement on the Supply and Pricing of Medicines and schedule 1 of the Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines.[11,12] This involved a review period that included internal evaluation by the MMP and consideration of submissions received from the marketing authorisation holders of Forsteo®, Movymia®, Sondelbay®, Terrosa® and Tetridar®.

In line with the *MMP Roadmap for the prescribing of best-value biological medicines (BVB) medicines,* the MMP considered the following criteria when identifying BVMs for teriparatide:[13]

1. Acquisition cost
2. Therapeutic indications
3. Formulation considerations
4. Product range including pack sizes and strengths available
5. Product stability including storage requirements
6. Administration devices
7. Patient factors
8. Expenditure in the therapeutic area and potential for cost efficiencies
9. Clinical guidelines
10. Security of supply to the Irish Market

11. Utilisation and clinical experience with the biological medicine
12. Any other relevant factors with respect to the particular INN

The MMP recommends Movymia® and Sondelbay® as the BVMs for teriparatide on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Movymia® or Sondelbay® when issuing a prescription for teriparatide on the High Tech Arrangement. Implementation of this recommendation will lead to significant savings for the health service.

5.1 Consultation process

As part of the evaluation process, the MMP undertook a period of consultation during which submissions were invited from all relevant stakeholders, including the marketing authorisation holders of medicinal products containing teriparatide. The consultation phase commenced on Wednesday 23 March 2022. The closing date for receipt of submissions was 5pm on Wednesday 4 May 2022.

Five submissions were received during the consultation process. Submissions were received from the following:

- Accord Healthcare Ireland Ltd
- Clonmel Healthcare Limited
- Eli Lilly & Company (Ireland) Ltd
- Gedeon Richter Ireland Ltd
- Teva Pharmaceuticals Ireland

6. Evaluation

As of 1 January 2023, there are five medicinal products containing teriparatide available on the High Tech Arrangement:[3]

- Forsteo®
- Movymia®
- Sondelbay®
- Terrosa®
- Tetridar®

A medicinal product for which the EMA has issued a parallel distribution notice (Forsteo® PCO) is also available on the High Tech Arrangement.

Forsteo® is the reference medicinal product. Movymia®, Sondelbay® and Terrosa® are licensed as biosimilar medicines of the reference medicinal product, Forsteo®. Tetridar® is licensed as a hybrid medicinal product of the reference medicinal product, Forsteo®. All of these medicinal products were included in the evaluation to determine the MMP BVM for teriparatide under the High Tech Arrangement.

The distributors for Livogiva® in Ireland, Consilient Health, confirmed to the MMP that they do not plan to launch this biosimilar medicine containing teriparatide in Ireland. It was, therefore, not considered as part of the evaluation process.

6.1 Acquisition cost

The acquisition cost, annual cost and reimbursement price of the medicinal products containing teriparatide that are available on the High Tech Arrangement as of 31 January 2023 are outlined in table 1.

Table 1: Acquisition cost, annual cost and reimbursement price of medicinal products containing teriparatide available on the High Tech Arrangement as of 31 January 2023[3]

Medicinal Product	Reimbursement Price per pack*	Rebate per pack*	Acquisition Cost per pack* (ex VAT)	Acquisition Cost per pack* (inc VAT)	Annual Cost (ex VAT)	Annual Cost (inc VAT)
Forsteo® 20 mcg/80 microliter PFP	€245.14	€28.37	€216.77†	€273.15	€2,827.63	€3,563.11
Forsteo® (PCO) 20 mcg/80 microliter PFP	€237.78	€27.52	€210.26†	€264.95	€2,742.80	€3,456.21
Movymia® starter pack (20 mcg/80 microliter cartridge + pen)	€214.49	-	€214.49	€263.82	€2,797.92	€3,441.44
Movymia® 20 mcg/80 microliter cartridge	€214.49	-	€214.49	€263.82	€2,797.92	€3,441.44
Sondelbay® 20 mcg/80 microliter PFP	€171.59	-	€171.59	€211.06	€2,238.34	€2,753.15
Terrosa® starter pack (20 mcg/80 microliter cartridge + pen)	€214.49	-	€214.49	€263.82	€2,797.92	€3,441.44
Terrosa® 20 mcg/80 microliter cartridge	€214.49	-	€214.49	€263.82	€2,797.92	€3,441.44
Tetridar® 20 mcg/80 microliter PFP	€214.49	-	€214.49	€263.82	€2,797.92	€3,441.44

ex: excluding; inc: including; mcg: micrograms; PFP: Pre-filled pen; VAT: value-added tax

Prices correct as of 31 January 2023

** Each pack contains a 28-day supply of teriparatide*

†The acquisition cost of the reference medicinal product, Forsteo®, takes account of the automatic price reduction for patent-expired non-exclusive biological medicines on 1 January 2022 to 62.86% of the 31 July 2016 ex-factory price, and the rebate of 12.5% that is applied to patent-expired non-exclusive biological medicines.

Submissions received during the consultation process included revised commercial terms for some of the medicinal products listed in table 1, resulting in significant reductions in the acquisition costs to the HSE.[14-18]

Recommendation

Movymia® and Sondelbay® have the lowest acquisition cost to the HSE across all of the proposed revised commercial terms that were contained within submissions received as part of the consultation process.

6.2 Therapeutic indications

The reference biological medicine, Forsteo®, is licensed for the treatment of:[2]

- osteoporosis in postmenopausal women and in men at increased risk of fracture. In postmenopausal women, a significant reduction in the incidence of vertebral and non-vertebral fractures but not hip fractures has been demonstrated.
- osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture.

The biosimilar medicines, Movymia®, Sondelbay® and Terrosa®, and the hybrid medicinal product, Tetridar® are all licensed for the full range of therapeutic indications in line with the reference biological medicine.[19-22]

Recommendation

In relation to the criterion of therapeutic indications, the MMP is of the opinion that the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide are equivalent.

6.3 Formulation considerations

Forsteo®, Movymia®, Sondelbay®, Terrosa® and Tetridar® are all formulated as colourless, clear solutions for injection.[2,19-22] Each of the medicinal products contains the following excipients: [2,19-22]

- glacial acetic acid
- sodium acetate
- mannitol
- metacresol
- hydrochloric acid
- sodium hydroxide
- water for injections

All of the medicinal products contain 2.4 ml of solution per pack, corresponding to 600 mcg of teriparatide (i.e. 250 mcg/ml). Each medicinal product delivers a dose of 80 microliters of solution, containing 20 mcg of teriparatide. There are 28 doses of teriparatide 20 mcg within one pack of each product. [2,19-22]

All of the medicinal products containing teriparatide that are under evaluation contain less than 1 mmol sodium (23 mg) per dose, i.e. they are essentially 'sodium-free'.[2,19-22]

Administration site conditions are reported in the section on undesirable effects in the Summary of Product Characteristics (SmPC) of Forsteo®. Mild and transient injection site events, including pain, swelling, erythema, localised bruising, pruritus and minor bleeding at the injection site were reported as common adverse reactions associated with the use of Forsteo® in clinical trials and post-marketing exposure. Injection site erythema and injection site reaction were reported as uncommon adverse events.[2]

The SmPCs for the three biosimilar medicines containing teriparatide (Movymia®, Sondelbay® and Terrosa®) and the hybrid medicinal product containing teriparatide (Tetridar®) all carry the same statements as Forsteo® in relation to administration site conditions.[19-22]

6.3.1 European Public Assessment Report – Movymia®

In the clinical safety section of the European public assessment report (EPAR) for Movymia®, the EMA report that injection site erythema was seen more often in the Movymia® group in comparison to the Forsteo® group in the phase I study that was undertaken (nine [17%] versus six [11%] subjects, respectively). The EMA also note that all of the described erythema were very mild, and thus the observed difference was regarded as of no relevance.[23]

6.3.2 European Public Assessment Report – Sondelbay®

In the clinical safety section of the EPAR for Sondelbay®, the EMA report that there was only one report of injection site reaction in the phase 1 study that was undertaken; this related to a patient who had been administered Forsteo®.[24]

6.3.3 European Public Assessment Report – Terrosa®

In the clinical safety section of the EPAR for Terrosa®, the EMA report that injection site erythema was seen more often in the Terrosa® group in comparison to the Forsteo® group in the phase I study that was undertaken (nine [17%] versus six [11%] subjects, respectively). The EMA also note that all of the

described erythema were very mild, and thus the observed difference was regarded as of no relevance.[25]

6.3.4 Public Assessment Report – Tetridar®

In the clinical safety section of the public assessment report for Tetridar®, injection site erythema was observed in one patient in both the Tetridar® and the Forsteo® treatment groups.[10]

Recommendation

In relation to the criterion of formulation considerations, the MMP is of the opinion that the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide are equivalent.

6.4 Product range including pack sizes and strengths available

Table 2 outlines the various presentations of the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide.

Table 2: Product range of medicinal products containing teriparatide[2,19-22]

Medicinal Product	**Product range**		
	20 mcg/80 microliter PFP	20 mcg/80 microliter cartridge + re-usable pen	20 mcg/80 microliter cartridge
Forsteo®	✓		
Movymia®		✓	✓
Sondelbay®	✓		
Terrosa®		✓	✓
Tetridar®	✓		

mcg: micrograms; PFP: Pre-filled pen

Forsteo® is available as a disposable PFP device containing multiple doses; the patient is supplied with a new PFP on each occasion a new supply is needed. Sondelbay® and Tetridar® have the same presentations, i.e. a disposable PFP device. Movymia® and Terrosa® are available as re-usable pen devices with replaceable cartridges, which contain the solution for injection. A starter pack, containing the re-usable pen and a cartridge, should be supplied to the patient when they are initiated on treatment with teriparatide. For further supplies, a cartridge should be provided to the patient for use with the re-usable pen device.

Each cartridge or disposable PFP contains 2.4 ml of solution per pack, corresponding to 600 mcg of teriparatide (i.e. 250 mcg/ml). Both pen devices (disposable and re-usable) deliver a dose of 80 microliters of solution, containing 20 mcg of teriparatide. Each cartridge or disposable PFP contains 28 doses of teriparatide 20 mcg.[2,19-22]

Recommendation

In relation to the criterion of product range, the MMP is of the opinion that the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide provide a similar offering.

6.5 Product stability including storage requirements

Forsteo® 20 mcg/80 microliter PFP, Movymia® 20 mcg/80 microliter cartridge, Sondelbay® 20 mcg/80 microliter PFP and Terrosa® 20 mcg/80 microliter cartridge each have a shelf life of two years. Tetridar® 20 mcg/80 microliter PFP has a shelf life of 18 months. All five medicinal products must be stored in a refrigerator between 2°C and 8°C, and should not be frozen.[2,19-22]

Once opened, Forsteo® 20 mcg/80 microliter PFP, Sondelbay® 20 mcg/80 microliter PFP and Tetridar® 20 mcg/80 microliter PFP should be returned to the refrigerator immediately after use. After insertion of Movymia® 20 mcg/80 microliter cartridge and Terrosa® 20 mcg/80 microliter cartridge into their re-usable pen, the combined pen and cartridge should be returned to the refrigerator immediately after use. The cartridge should not be removed from the pen after first use.[2,19-22]

After first use, all five medicinal products should be stored for a maximum of 28 days at 2°C and 8°C, after which time they should be disposed of, even if they are not completely empty.[2,19-22]

In addition, Sondelbay® 20 mcg/80 microliter PFP can be stored at temperature conditions up to 25°C for a maximum of three days when refrigeration is not available, after which it should be returned to the refrigerator and used within 28 days of the first injection. The Sondelbay® 20 mcg/80 microliter PFP should be discarded if it has been kept out of the refrigerator at temperature conditions up to 25°C for more than three days.[20]

For all medicinal products, the pen device (PFP or re-usable) should not be stored with the needle attached.[2,19-22]

Recommendation

In relation to the criterion of product stability, MMP is of the opinion that the Forsteo®, Movymia®, Sondelbay® and Terrosa® provide a similar offering. The MMP notes the shorter shelf life of Tetridar® in comparison to the other medicinal products containing teriparatide.

6.6 Administration devices

From examination of the patient information leaflets (PIL), SmPCs and submissions received for each of the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide, there are two different types of administration devices; a disposable PFP device (Forsteo®, Sondelbay® and Tetridar®) and a re-usable pen device with replaceable cartridges (Movymia® and Terrosa®). Table 3 provides a summary of various properties for the administration devices of the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide.

Table 3: Characteristics of administration devices for medicinal products containing teriparatide available on the High Tech Arrangement

	Forsteo®	Movymia®	Sondelbay®	Terrosa®	Tetridar®
Disposable PFP	✓		✓		✓
Re-usable pen device		✓		✓	
Pen requires priming		✓		✓	
Dose delivery indicator	✓	✓	✓	✓	✓
Dose counter			✓		

PFP: Pre-filled pen

The disposable PFPs do not need to be primed; the re-usable pen devices need to be primed each time a new cartridge is inserted. A dose counter is only present on the Sondelbay® PFP; none of the other medicinal products have a dose counter on their pen and therefore, it is not possible to accurately determine how many doses of teriparatide have been administered or how many remain.

The re-usable pen devices that are employed with Movymia® (indicator window) and Terrosa® (indicator window), and the disposable PFP employed with Forsteo® (yellow shaft not visible), Sondelbay® (indicator window) and Tetridar® (yellow shaft not visible) all contain mechanisms to indicate when the full dose of teriparatide has been administered.

There is no latex present in the administration devices for Movymia®, Sondelbay®, Terrosa® and Tetridar®.[14,15,17,18]

None of the medicinal products are supplied with injection needles attached. All of the medicinal products require the patient to attach and dispose of an injection needle each time a dose is administered. Injection needles are not supplied with any of the medicinal products, and therefore must be provided separately to the patient. Table 4 provides details of the needles that are suitable for use with each of the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide.

Table 4: Details of needles suitable for use with medicinal products containing teriparatide available on the High Tech Arrangement

Medicinal Product	Type of needles suitable for use with pen
Forsteo®[2]	Becton, Dickinson and Company pen needles can be used
Movymia®[15,19]	Injection needles developed according to the pen needle ISO standard of a gauge between 29 G and 32 G (diameter 0.23 – 0.33 mm) and a length between 4 mm to 12.7 mm
Sondelbay®[14,20]	Pen needles of a gauge of 31 G or 32 G and a length of 4, 5 or 8 mm
Terrosa®[17,21]	Injection needles developed according to the pen needle ISO standard of a gauge between 29 G and 31 G (diameter 0.25 – 0.33 mm) and a length between 5 mm to 12.7 mm
Tetridar®[18,22]	Becton, Dickinson and Company pen needles of a gauge between 29 G and 31 G (diameter 0.25 – 0.33 mm) and a length of 5, 8 or 12.7 mm

G: gauge; ISO: International Organisation for Standardisation; mm: millimetre

There is a variety of needles available on the Community Drug Schemes, all supplied in packs of 100. The reimbursement price per pack varies from €6.23 to €17.23.[26] A full 24-month course of teriparatide would require eight packs of needles.

None of the medicinal products include a safety feature upon administration of the injection; in all cases, the patient is required to remove the needle from the pen after administration of the dose of teriparatide, and dispose of it.

The re-usable pen devices supplied with Movymia® and Terrosa® both have a service life of two years.

The instructions, within each of the PILs and accompanying pen user manuals, for the administration of a dose from the pen devices of medicinal products containing teriparatide are clear and easy to follow. In all cases, the instructions are presented in the form of text with accompanying pictograms.

Recommendation

In relation to the criterion of administration devices, the MMP is of the opinion that the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide provide a similar offering.

6.7 Patient factors

In their submissions, Accord Healthcare Ireland Ltd, Clonmel Healthcare Limited, Eli Lilly & Company (Ireland) Ltd, Gedeon Richter Ireland Limited and Teva Pharmaceuticals Ireland outlined the support services that are available when patients are prescribed a medicinal product containing teriparatide.[14-18]

A number of studies were identified that investigated the effect of the provision of a patient support programme on persistence with teriparatide treatment. High persistence rates were observed in these studies when teriparatide was administered in conjunction with a patient support programme, with one-year persistence rates of 75, 77 and 87%, a 15-month persistence rate of 82%, 18-month persistence rates of 79 and 86%, and two-year persistence rates of 63, 64, 69 and 78%.[27-32] The patient support programmes contained different elements, including one or more of the following:[27-32]

- delivery of the medicinal product containing teriparatide to the patient's home
- provision of education and training on injection technique by nurses
- provision of a waste management service, including collection of used pre-filled pens and needles
- provision of a patient support helpline to address any potential queries
- provision of patient educational material on the injection device and osteoporosis
- regular scheduled telephone calls to motivate patients to complete full course of teriparatide treatment and address any potential queries.

In addition, one study also investigated the effect of the provision of a patient support programme on adherence to teriparatide treatment, with good to very good (> 75%) adherence reported for 54% of patients enrolled in a patient support programme, compared with 48% of patients not enrolled in the programme.[31]

There are a number of common limitations observed in these studies. The majority of studies did not have a control group, and therefore the lack of randomisation does not allow for any definite conclusions to be drawn about the impact of patient support programmes on adherence and persistence. Some of the studies were retrospective in nature. Enrolment in the patient support

programmes was voluntary, which could introduce an element of bias as those patients who chose to be included in a programme may be more motivated than non-participants to adhere to and persist with their treatment. Persistence was not measured consistently across all of the studies; in some cases it was self-reported by patients. The patient support programmes involved different elements across all of the studies, therefore presenting a challenge in making any definite conclusions about the benefit of patient support programmes in general. A number of the studies were sponsored by the marketing authorisation holder for Forsteo®.[27-32]

Overall, the evidence supporting the benefits of manufacturer-provided patient support programmes for patients who are prescribed teriparatide is limited and of low-quality.

The MMP did not identify any published evidence that compared the patient support programmes/services that are offered by the marketing authorisation holders of medicinal products containing teriparatide with each other.

The offerings that are available to patients who are prescribed the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide are all similar in nature, based on the information provided to the MMP as part of the consultation process. No robust clinical evidence was identified by the MMP that compared patient support programmes with each other.

Recommendation

In relation to the criterion of patient factors, the MMP is of the opinion that the patient support programmes offered by Accord Healthcare Ireland Ltd, Clonmel Healthcare Limited, Eli Lilly & Company (Ireland) Ltd, Gedeon Richter Ireland Limited and Teva Pharmaceuticals Ireland are all similar in nature.

6.8 Expenditure in the therapeutic area and potential for cost savings

Expenditure[iii] on medicinal products containing teriparatide accounted for approximately €4.2 million in 2021.[1] Teriparatide was ranked 14th in terms of prescribing frequency on the High Tech Arrangement in 2021, with a prescribing frequency of 13,653.[4] There are approximately 1,200 patients in receipt of teriparatide on the High Tech Arrangement on a monthly basis.[5]

[iii] Expenditure reflects the ingredient cost of the medicinal product, exclusive of value added tax and fees.

The Framework Agreement on the Supply and Pricing of Medicines (2021) contains a number of clauses in relation to the pricing of patent-expired non-exclusive biological medicines that are relevant to medicinal products containing teriparatide. Clause 8 applies to patent-expired biologic medicines for which a biosimilar medicine is available for supply. In relation to price reductions, clause 8.2.1 states that, on the 1st of January 2022, the price of existing patent-expired non-exclusive biologic medicines shall be reduced to 62.86% of the 31st of July 2016 ex-factory price. In addition to this price reduction, clause 8.2.3 states that a rebate to the HSE of a sum equal to 12.5% of the reduced price as of the 1st of January 2022, is applied to the patent-expired, non-exclusive biological medicine.[11] This is reflected in the current acquisition and annual costs of Forsteo® that are included in table 1.

The Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines (2021) also contains a number of clauses in relation to the pricing of biosimilar and hybrid medicines that are relevant to medicinal products containing teriparatide. Clause 8.2.1 states that, on the 1st of March 2022, the price of each existing biosimilar medicine shall be reduced to 55% of the 31st July 2016 price of the reference originator. This price reduction is reflected in the current acquisition and annual costs of Movymia® and Terrosa® that are included in table 1. Clause 9.2.1 states that, on the 1st of March 2022, the price of each existing hybrid medicine shall be reduced to 50% of the original ex-factory price of the reference originator. In addition, clause 8.2.2 states that the price that a supplier shall submit to the HSE of a new biosimilar medicine for which an application is made for its addition to the reimbursement list shall be no greater than 55% of the 1st of October 2021 price of the equivalent branded original medicine.[12] This clause applied in the case of the application for the pricing and reimbursement of Sondelbay® that was submitted by Accord Healthcare Ireland Ltd.

The current acquisition and annual costs of medicinal products containing teriparatide as of 31 January 2023 are outlined in Table 1. The acquisition and annual costs of the biosimilar medicines Movymia®, Sondelbay® and Terrosa®, and the hybrid medicinal product Tetridar® are less than that of Forsteo®; efficiencies can therefore be achieved through the prescribing and utilisation of biosimilar medicines and hybrid medicinal products containing teriparatide on the High Tech Arrangement. Data from the HSE-PCRS indicates that the majority of patients receiving teriparatide on the High Tech Arrangement are currently on Forsteo®, with approximately 20% of patients in receipt of Movymia® or Tetridar®.[5] Any additional savings that could have been achieved through the use of biosimilar medicines and hybrid medicinal products containing teriparatide, which have a lower acquisition cost than Forsteo®, have not been realised.

Submissions received during the consultation process included revised commercial terms for some of the medicinal products containing teriparatide, resulting in significant reductions in the acquisition costs to the HSE.

Recommendation

In relation to the criterion of expenditure in the therapeutic area and potential for cost savings, the MMP is of the opinion that Movymia® and Sondelbay® are the BVMs of choice due to the potential for significant cost savings based on the revised commercial terms proposed in the submissions received as part of the consultation process.

6.9 Clinical guidelines

There is currently no national clinical guideline available in Ireland for the treatment of osteoporosis. The Irish Osteoporosis Society has published guidelines on the management of osteoporosis. These guidelines were last updated in 2012, prior to the availability of biosimilar medicines and hybrid medicinal products containing teriparatide. The guidelines include teriparatide as a treatment option for osteoporosis in line with its licensed indications.[33]

The United Kingdom National Osteoporosis Guideline Group (NOOG) has published an updated version of its clinical guideline for the prevention and treatment of osteoporosis in 2021. The National Institute for Health and Care Excellence (NICE) have accredited the process used by the NOOG to produce this guideline. With respect to biosimilar medicines, this guideline states that biosimilar medicines containing teriparatide are now available, which is expected to improve the cost-effectiveness of the use of teriparatide.[34]

Recommendation

In relation to the criterion of clinical guidelines, no relevant information was identified by the MMP.

6.10 Security of supply to Irish Market

Accord Healthcare Ireland Ltd, Clonmel Healthcare Limited, Eli Lilly & Company (Ireland) Ltd, Gedeon Richter Ireland Limited and Teva Pharmaceuticals Ireland outlined the processes that they have in place for supply of their medicinal product containing teriparatide to the Irish market.

Accord Healthcare Ireland Ltd outlined the distribution model that they have in place nationally for Sondelbay®. They also outlined the arrangements that they have in place to ensure sufficient supply

of Sondelbay® to the Irish market, including internal processes. Accord Healthcare Ireland Ltd also outlined the actions that they have taken to deal with Brexit.[14]

Clonmel Healthcare Limited outlined the arrangements that they have in place for the supply chain management of Movymia® to the Irish market, including the distribution model that they employ. They also outlined the actions that they have taken to deal with Brexit.[15]

Eli Lilly & Company (Ireland) Ltd outlined the arrangements that they have in place for the supply chain management of Forsteo® to the Irish market, including the distribution model that they employ. They also outlined the actions that they have taken to deal with Brexit.[16]

Gedeon Richter Ireland Limited outlined the arrangements that they have in place for the supply chain management of Terrosa® to the Irish market, including the distribution model that they employ. They also outlined the actions that they have taken to deal with Brexit.[17]

Teva Pharmaceuticals Ireland outlined the arrangements that they have in place for the supply chain management of Tetridar® to the Irish market, including the distribution model that they employ. They also outlined the actions that they have taken to deal with Brexit.[18]

Recommendation

In relation to the criterion of security of supply to the Irish market, the MMP is of the opinion that Accord Healthcare Ireland Ltd, Clonmel Healthcare Limited, Eli Lilly & Company (Ireland) Ltd, Gedeon Richter Ireland Limited and Teva Pharmaceuticals Ireland have all provided evidence of their capacity to meet the ongoing needs of Irish patients with respect to the supply of medicinal products containing teriparatide, including the measures they are taking to mitigate the impact of Brexit. The MMP also note the significant experience of Eli Lilly & Company (Ireland) Ltd in ensuring security of supply of Forsteo® to Irish patients.

6.11 Utilisation and clinical experience with the biological medicine

There is significant clinical experience with the use of Forsteo® in the Irish setting, with approximately 950 patients in receipt of Forsteo® on the High Tech Arrangement on a monthly basis.[5] Market exclusivity for Forsteo® lapsed in August 2019, and the first biosimilar medicine containing teriparatide was added to the High Tech Arrangement on 1 September 2019.[35]

There has been limited uptake of biosimilar medicines and hybrid medicinal products containing teriparatide in Ireland to date. Approximately 20% of patients in receipt of teriparatide on the High Tech Arrangement are prescribed Movymia® or Tetridar®.[5] Other European healthcare systems have seen significant uptake in the utilisation of biosimilar medicines containing teriparatide.[36]

Manufacturers of biosimilars must perform an extensive head-to-head comparability with the reference medicine and demonstrate to regulators that they have similar quality, safety and efficacy to the reference medicine such that there are no clinically meaningful differences between the two.[37] The EMA and Heads of Medicines Agencies (HMA), in a joint statement, have confirmed that biosimilar medicines approved in the EU are interchangeable with their reference medicine or with an equivalent biosimilar. Interchangeability in this context means that the reference medicine can be replaced by a biosimilar without a patient experiencing any changes in the clinical effect.[7] The clinical experience, therefore, obtained with Forsteo® is transferable to the biosimilar medicines of teriparatide.

Tetridar® is licensed as a hybrid medicinal product, i.e. following evaluation, Tetridar® was considered a legitimate hybrid form of the reference product, Forsteo®, and was granted a marketing authorisation.[10] Tetridar® was shown to be analytically and functionally comparable to Forsteo®. In addition, bioequivalence of Tetridar® to the reference product was also demonstrated.[10] The MMP are, therefore, of the opinion that the clinical experience obtained with Forsteo® is transferable to Tetridar®.

Recommendation

The MMP acknowledge the significant clinical experience that has been obtained in Ireland with the reference biological medicine, Forsteo®. Biosimilar medicines and hybrid medicinal products of teriparatide have only recently become available in Ireland and uptake of these is limited to date. The situation is different in other European countries where there has been significant uptake of biosimilar medicines of teriparatide. This demonstrates that significant clinical experience is being obtained for biosimilar medicines of teriparatide in a short timeframe.

Overall, in relation to the criterion of utilisation and clinical experience with the biological medicine, the MMP is of the opinion that the medicinal products containing teriparatide that are under evaluation for a BVM for teriparatide provide a similar offering.

6.12 Any other relevant factors with respect to the particular INN

A variety of material was submitted under this criterion including information on:

- comparison of the properties of the administration devices for medicines containing teriparatide
- pen demonstration devices.

The MMP is of the opinion that no new relevant material was submitted under this criterion that had not been considered under any of the other criteria.

6.12.1 Position papers

No published position papers on the usage of biosimilar medicines or hybrid medicinal products, either in general or specifically in relation to teriparatide, were identified from the Irish clinical societies for the specialities for which teriparatide is prescribed (i.e. Irish Gerontological Society, Irish Society of Physicians in Geriatric Medicine and Irish Society of Rheumatology). The HSE-National Clinical Programme for Rheumatology published a model of care for rheumatology in Ireland in 2018. This proposes the development of evidence-based national guidelines for the use of biologic therapies, including biosimilar medicines, in a cost-effective manner in conjunction with the MMP.[38]

6.12.2 Legislation/Guidance from Medicines Regulators

The MMP also felt there was merit in reviewing any legislation or guidelines from medicines regulators that relate to the prescribing and utilisation of biosimilars. Pharmacist-led substitution of biological medicines is not permitted under the Health (Pricing and Supply of Medical Goods) Act 2013.[39]

The Health Products Regulatory Authority (HPRA) published an updated version of their Guide to Biosimilars for Healthcare Professionals in August 2020. This guide defines interchangeability as "the possibility of exchanging one medicine with another that is expected to have the same effect. This could mean replacing a reference medicine with a biosimilar (or vice versa), or replacing one biosimilar with another". The guide states that, once approved, biosimilars can be used interchangeably with the reference medicine, or with biosimilars of that reference medicine.[37]

The EMA and HMA, in a joint statement issued on 19 September 2022, have confirmed that biosimilar medicines approved in the EU are interchangeable with their reference medicine or with an equivalent biosimilar. Interchangeability in this context means that the reference medicine can be replaced by a biosimilar without a patient experiencing any changes in the clinical effect.[7]

Recommendation

In relation to the criterion of any other relevant factors with respect to the particular INN, the MMP is of the opinion that no new relevant material was submitted under this criterion that had not been considered under any of the other criteria.

Overall Recommendation

The MMP recommends Movymia® and Sondelbay® as the BVMs for teriparatide on the High Tech Arrangement.

7. MMP Recommendations

The MMP recommends Movymia® and Sondelbay® as the BVMs for teriparatide on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Movymia® or Sondelbay® when issuing a prescription for teriparatide on the High Tech Arrangement.

Implementation of this recommendation will lead to significant savings for the health service.

Initiation

When initiating a patient on teriparatide, the clinician should prescribe Movymia® or Sondelbay®.

Switching

Patients currently on teriparatide should be considered for switching to Movymia® or Sondelbay® when their next repeat High Tech prescription is being issued.

The MMP recommends that all new patients being initiated on a medicinal product containing teriparatide should be prescribed the MMP BVMs, Movymia® or Sondelbay®. Patients currently on teriparatide should be considered for switching to Movymia® or Sondelbay® when their next repeat High Tech prescription is being issued.

8. References

1. HSE-Primary Care Reimbursement Service (PCRS). Reporting and Open Data Area. Pharmacy Reports. Top 100 Products by Year Cost. HTS 2021. Accessed at https://www.sspcrs.ie/analytics/saw.dll?PortalPages on 28/10/2022.
2. Forsteo® 20 micrograms/80 micoliters solution for injection in pre-filled pen. Summary of Product Characteristics. Last revised 20/01/2022. Accessed at www.ema.europa.eu on 31/01/2023.
3. HSE-Primary Care Reimbursement Service (PCRS). Complete List of High Tech Products By Non-Proprietary Name as at 1st January 2023. Accessed at www.pcrs.ie on 31/01/2023.
4. HSE-Primary Care Reimbursement Service (PCRS). Reporting and Open Data Area. Pharmacy Reports. Top 100 Prescribing Products by Year. HTS 2021. Accessed at https://www.sspcrs.ie/analytics/saw.dll?PortalPages on 28/10/2022.
5. HSE-Primary Care Reimbursement Service (PCRS). Reimbursement report. On file.
6. European Medicine Agency (EMA) and the European Commission. Biosimilars in the EU. Information guide for healthcare professionals. 2019. Accessed at https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf on 28/10/2022.
7. European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA). Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU. 19 September 2022. Accessed at https://www.ema.europa.eu/en/documents/public-statement/statement-scientific-rationale-supporting-interchangeability-biosimilar-medicines-eu_en.pdf on 28/10/2022.
8. HSE-Primary Care Reimbursement Service (PCRS). High Tech Update for Dermatology, Gastroenterology & Rheumatology National Gainshare. 25 October 2022. On file.
9. European Medicines Agency (EMA). Biosimilar Medicines: Overview. Accessed at https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview on 28/10/2022.
10. Bundesinstitut für Arzneimittel und Medizinprodukte. Public Assessment Report. Teriparatid-ratiopharm 20 µg / 80 ml mg/ml, Solution for injection. Last revised 8 May 2017. Accessed at https://mri.cts-mrp.eu/portal/home?domain=h on 28/10/2022.
11. DoH/DPER/HSE/IPHA. Framework Agreement on the Supply and Pricing of Medicines. 6 December 2021. Accessed at https://www.hse.ie/eng/about/who/cpu/ on 28/10/2022.
12. DoH/DPER/HSE/MFI. Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines. 13 December 2021. Accessed at https://www.hse.ie/eng/about/who/cpu/ on 28/10/2022.
13. HSE-Medicines Management Programme (MMP). MMP roadmap for the prescribing of best-value biological (BVB) medicines in the Irish healthcare setting. Version 3, March 2022. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-roadmap-for-the-prescribing-of-best-value-biological-bvb-medicines-in-the-irish-healthcare-setting.pdf on 28/10/2022.
14. Accord Healthcare Ireland Ltd. Submission. On file.
15. Clonmel Healthcare Limited. Submission. On file.
16. Eli Lilly & Company (Ireland) Ltd. Submission. On file.
17. Gedeon Richter Ireland Ltd. Submission. On file.

18. Teva Pharmaceuticals Ireland. Submission. On file.
19. Movymia® 20 micrograms/80 microliters solution for injection. Summary of Product Characteristics. Last revised 20/01/2022. Accessed at www.ema.europa.eu on 31/01/2023.
20. Sondelbay® 20 micrograms/80 microliters solution for injection in pre-filled pen. Summary of Product Characteristics. Last revised 16/06/2022. Accessed at www.ema.europa.eu on 31/01/2023.
21. Terrosa® 20 micrograms/80 microliters solution for injection. Summary of Product Characteristics. Last revised 03/11/2021. Accessed at www.ema.europa.eu on 31/01/2023.
22. Tetridar® 20 micrograms/80 microliters solution for injection in pre-filled pen. Summary of Product Characteristics. Last revised August 2022. Accessed at www.hpra.ie on 31/01/2023.
23. European Medicines Agency (EMA). European Public Assessment Report. Movymia®. 16 March 2017. Accessed at www.ema.europa.eu on 28/10/2022.
24. European Medicines Agency (EMA). European Public Assessment Report. Sondelbay®. 20 June 2022. Accessed at www.ema.europa.eu on 28/10/2022.
25. European Medicines Agency (EMA). European Public Assessment Report. Terrosa®. 16 March 2017. Accessed at www.ema.europa.eu on 28/10/2022.
26. HSE-Primary Care Reimbursement Service (PCRS). List of Reimbursable Items. Accessed at www.pcrs.ie on 28/10/2022.
27. Arden NK, Earl S, Fisher DJ *et al*. Persistence with teriparatide in patients with osteoporosis: the UK experience. *Osteoporos Int* 2006;17:1626-1629.
28. Briot K, Ravaud P, Dargent-Molina P *et al*. Persistence with teriparatide in postmenopausal osteoporosis; impact of a patient education and follow-up program: the French experience. *Osteoporos Int* 2009;20:625-630.
29. Tamone C, Fonte G, Panico A *et al*. Impact of a phone follow-up program on persistence with teriparatide or PTH (1-84) treatment. *Calcif Tissue Int* 2012;90:272-278.
30. Nogues X, Rentero ML, Rodriguez AL. Use of an educational support program to assist patients receiving injectable osteoporosis treatment: experience with teriparatide. *Curr Med Res Opin* 2014;30:287-296.
31. Sato M, Tsujimoto M, Kajimoto K *et al*. Effect of a patient-support program on once-daily teriparatide adherence and persistence in the Japan Fracture Observational Study (JFOS). *Arch Osteoporos* 2018;13:74.
32. Van Maren MA, Wyers CE, Driessen JHM *et al*. Two-year persistence with teriparatide improved significantly after introduction of an educational and motivational support program. *Osteoporos Int* 2019;30:1837-1844.
33. Irish Osteoporosis Society. Osteoporosis Guidelines 2 for Health Professionals. October 2012. Accessed at www.icgp.ie on 28/10/2022.
34. National Osteoporosis Guideline Group (NOOG). Clinical guideline for the prevention and treatment of osteoporosis. 2021. Accessed at https://www.nogg.org.uk/ on 28/10/2022.
35. HSE-Primary Care Reimbursement Service. Updates to the List of Reimbursable Items and High Tech Scheme List. Accessed at www.pcrs.ie on 28/10/2022.
36. IQVIA. The Impact of Biosimilar Competition in Europe. December 2021. Accessed at www.iqvia.com on 28/10/2022.
37. Health Products Regulatory Authority (HPRA). Guide to Biosimilars for Healthcare Professionals. 5 August 2020. Accessed at www.hpra.ie on 28/10/2022.

38. HSE National Clinical Programme for Rheumatology. Model of Care for Rheumatology in Ireland. 2018. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/rheumatology/achievements/model-of-care-for-rheumatology-in-ireland.pdf on 28/10/2022.
39. Government of Ireland. Health (Pricing and Supply of Medical Goods) Act 2013. S.I. No 14/2013.