VOLUNTARY COMPLIANCE UNDERTAKING
OF
ULTRAGENYX PHARMACEUTICALS INC.
TO
THE PATENTED MEDICINE PRICES REVIEW BOARD

1.0 Product Summary

1.1. Crysvita (burosumab) is a fibroblast growth factor 23 (FGF23) inhibitor indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 6 months of age and older. Crysvita is also indicated for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with tumors that cannot be curatively resected or localized in adult patients.

1.2. Health Canada first issued a Notice of Compliance for Crysvita on December 5, 2018, and the medicine was first sold in Canada on January 28, 2019.

1.3. Crysvita is available as a solution for subcutaneous injection in single-use vials. The medicine is presented in strengths of 10 mg/milliliter (DIN 02483629), 20 mg/milliliter (DIN 02483637), and 30 mg/milliliter (DIN 02483645).

1.4. The first reported patent pertaining to Crysvita was granted on July 31, 2012. The last reported patent pertaining to Crysvita is set to expire on February 14, 2028. Ultragenyx Pharmaceuticals Inc. ("Ultragenyx") is the rights holder for the purposes of the *Patent Act* and the Patented Medicine Prices Review Board (PMPRB).

2.0 Application of the Guidelines

2.1 The Human Drug Advisory Panel (HDAP) recommended that Crysvita be classified as a Moderate Improvement based on primary factors.

2.2 Crysvita has been sold in Canada at prices of $4,992.2900 per milliliter, $9,984.5800 per milliliter, and $14,976.8700 per milliliter for Crysvita 10 mg, 20 mg, and 30 mg, respectively. It was determined by PMPRB Staff that these prices exceeded the thresholds set out in the Guidelines by an amount which triggered the investigation criteria.

3.0 Position of the Rights Holder

3.1 This Voluntary Compliance Undertaking (VCU) constitutes no admission by Ultragenyx that the prices of Crysvita are now, or were at any time since the date of first sale, excessive for the purposes of the *Patent Act*, nor is this VCU binding upon any panel of the Board for the purposes of the *Patent Act*.

4.0 Terms of the Voluntary Compliance Undertaking

4.1 Pursuant to this VCU, Ultragenyx will undertake:

A Voluntary Compliance Undertaking (VCU) is a voluntary and unilateral written promise by a rights holder to comply with the Board's Guidelines to close an investigation initiated by PMPRB Staff pursuant to those Guidelines. Consideration of a VCU is an administrative procedure and does not constitute an admission or determination by the PMPRB that the price submitted by the rights holder, or used to calculate a revenue offset, is not excessive. VCUs do not have precedential value.

4.1.1 To accept the Lowest International Price Comparison (LIPC) as the price test in the determination of the Maximum Average Potential Prices (MAPPs) for Crysvita;

4.1.2 To agree that that the MAPPs and 2020, 2021, and 2022 Non-Excessive Average Prices (NEAPs) for Crysvita are as follows:

Year	10 mg/milliliter (DIN 02483629)	20 mg/milliliter (DIN 02483637)	30 mg/milliliter (DIN 02483645)
2019	$4,414.8476	$8,829.7018	$13,244.5494
2020	$4,514.9476	$9,029.9018	$13,544.8494
2021	$4,514.9476	$9,029.9018	$13,544.8494
2022	$4,514.9476	$9,029.9018	$13,544.8494

4.1.3 To reduce the list prices of Crysvita to 2022 NEAPs described in 4.1.2 within 60 days of the acceptance of this VCU;

4.1.4 To file evidence with PMPRB Staff within 30 days of the price reduction that customers have received notification that the price has been reduced; and

4.1.5 To ensure that the prices of Crysvita remain within the PMPRB's Guidelines in all future periods in which it is under the PMPRB's jurisdiction.

Signature: _____

Name: Monty Keast

Position: Vice President & General Manager

Rights Holder: Ultragenyx Pharmaceutical Inc.

Date: February 2, 2022

A Voluntary Compliance Undertaking (VCU) is a voluntary and unilateral written promise by a rights holder to comply with the Board's Guidelines to close an investigation initiated by PMPRB Staff pursuant to those Guidelines. Consideration of a VCU is an administrative procedure and does not constitute an admission or determination by the PMPRB that the price submitted by the rights holder, or used to calculate a revenue offset, is not excessive. VCUs do not have precedential value.