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SCHEDULING DELEGATES' INTERIM DECISION

Response to Invitation to Comment:
HYALURONIC ACID

Date: 5 March 2018 Total number of pages: 5

1 INTRODUCTION

This submission is in response to the notice published on 5 February 2018, relating to the Scheduling Delegate's interim decision to amend the Schedule 4 entry for Hyaluronic acid as outlined in Table 1.

Table 1 - Schedule 4 entry- Hyaluronic acid

Current	Proposed
HYALURONIC ACID AND ITS POLYMERS in preparations for injection or implantation: a. for tissue augmentation: b. for cosmetic use; or c. for the treatment of animals	HYALURONIC ACID AND ITS POLYMERS in preparation for injection or implantation

Sanofi is the Sponsor of two Class III medical devices Synvisc (ARTG 159219) and Synvisc-One (ARTG 145345) that contain Hylan G-F-20. The component materials are hylan A and hylan B polymers that are derivatives of hyaluronan [sodium salt of hyaluronic acid (HA)].

As per the approved GMDN code, HA is a synovial fluid supplementation substance, as it has no defined active drug substance with biological activity. Articulation of the knee joint relies on the synovial fluid to assist with lubrication and mechanical support which can be impacted when either damage or chronic disease such as osteoarthritis (OA) is present. Synvisc achieves its intended purpose solely by the process of viscosupplementation, where the physiological and rheological states of the joint tissues are restored. No pharmacological or chemical interactions occur. Intra-articular injection is used to access the joint space. Synvisc products are used predominantly by orthopedic surgeons and sports physicians in patients with OA to improve mechanical movement of the joint. This in turn provides pain relief which may allow patients to delay more invasive surgical interventions as the joint continues to deteriorate. HA intra-articular injections for the purposes of viscosupplementation have been regulated in Australia; EU, US and Canada as medical devices for many years without any restrictions that require a prescription for supply.

The Sponsor did not receive any notification advising that they may be significantly affected by a proposal to amend the Schedule 4 entry for hyaluronic acid for which a notice inviting public submissions was published on 6 September 2017. Consequently, only following publication of the Delegate's interim decision which included the full background information, was it clearly identified that the focus of the proposed amendment was existing Class III devices. The Sponsor notes the Scheduling Handbook published in December 2017 includes the requirements for affected Sponsors to be notified, reflecting feedback from the MMDR review.

The Sponsor fully acknowledges the Delegate's rationale for the amendment to the Schedule 4 entry as outlined in the Interim decision is to allow alignment with the existing subclause e of Appendix A. It is also noted that the referenced historical discussions of the prior advisory committee were more than a decade ago and that no consultation with stakeholders was undertaken prior to the proposal being submitted. This step would have provided perspective on experience of use of the product in current clinical practice and an understanding of the impact on supply logistics and communication needs that would warrant a significantly longer transition time than indicated by the proposed implementation date of 1 June 2018.

The importance of stakeholder engagement to ensure impacts are understood is also reflected in the TGA key performance indicators. The recent amendments to the scheduling of codeine serves as a benchmark for best practice regulation in terms of stakeholder engagement, communication and establishing a realistic transition timeframe to manage change. This approach should become the default business as usual model for future Delegate initiated scheduling amendments.

2 SPONSOR COMMENTS ON PROPOSED AMENDMENT

The Australian regulatory framework for devices is based on that in the EU. In other major markets where the product has been available for many years including the EU, Canada and US, the largest markets in the world, there are no restrictions on supply of Synvisc and no evidence of any risk to public safety as a result of the current means of supply.

The scheduling framework is designed to ensure the safe handling of medicines and poisons in Australia and allows restrictions to be placed on supply in the interests of public health and safety, with a particular focus on minimising the risks from poisoning, misuse and abuse. As acknowledged in the Delegate's interim decision in consideration of the Scheduling factors relevant to an entry in Schedule 4 there are no relevant risks to the public based on:

1. The ailments or symptoms that the substance is used for require medical intervention.
    - Synvsic is used as part of routine clinical practice by physicians such as orthopedic surgeons, sports physicians and rhematologists to manage pain associated with osteoarthritis of the knee
2. The use of the substance requires adjunctive therapy or evaluation or specialised handling for administration.
    - Synvisc is used as part of routine clinical practice by relevant physicians such as orthopedic surgeons, sports physicians and rheumatologists specialising in the management of of osteoarthritis, and who are experienced in its use. It does not require any adjunctive therapy to administer and may be an intervention used prior to more invasive surgical procedures.
3. the lack of any potential for dependency or misuse, abuse or illicit use
    - as the effect of Synvisc is mechanical in nature, there is no potential for dependency, abuse or illicit use. Access is only available from a medical practitioner with the majority of supply (>95%) being sent directly to the treating physician. The small amount of product sent to pharmacy is labelled for an individual patient to collect, for

subsequent administration by a treating physician. No product is available for purchase directly from a pharmacy by a patient, and self-administration has never occurred and is exceedingly unlikely.

4. the lack of any serious, severe and/or frequent adverse events that require monitoring or intervention by a medical practitioner
   - Extensive clinical experience has demonstrated that there are no adverse events of a seriousness, severity and frequency that require monitoring or intervention by a medical practitioner to minimise the risk of using the substance.
5. The margin of safety between the therapeutic and toxic dose of the substance is such that it requires medical intervention to minimize the risk of using the substance
   - as Synvisc has no active ingredients there is no risk relating to the margin of safety between the therapeutic and toxic dose of the substance that requires intervention by a medical practitioner to reduce its risk in use
6. the lack of any serious, severe and/or frequent interactions of the substance that require monitoring or intervention by a medical practitioner
   - as Synvisc has no active ingredients there is no potential for interactions with medicines that may require monitoring or intervention by a medical practitioner.
7. the lack of any potential for communal harm
   - as Synvisc is administered to an individual and its effect is mechanical in nature there is no potential that it will contribute to communal harm
8. the extensive experience under normal clinical conditions of use
   - Synvisc has a long history of clinical use both in Australia and globally. There is no evidence that the current methods of distribution and use in clinical practice pose a risk to the public.

Based on consideration of the scheduling factors, the extensive experience of use in clinical practice and the fact that the vast majority of supply already goes direct to the treating physican, the Sponsor considers that the current method of product access is appropriate and does not pose any risks to public health that require further mitigation.

3 SUMMARY AND SPONSOR RECOMMENDATIONS

In summary, there is no evidence of any safety risk with Synvisc based on extensive use over many years not only in Australia but in other major markets including EU, USA and Canada where the product has been and continues to be available without any restrictions.

The TGA Delegate’s assessment against the scheduling factors has also confirmed the lack of any safety risk and the potential benefits of HA when used for its intended purpose. The Sponsor fully agrees that cosmetic or tissue augmentation use has a completely different benefit/risk framework, and is appropriately included in Schedule 4.

As noted, the vast majority of current supply of Synvisc goes directly to medical practitioners (>95%). Pharmacy supply is used only where the practitioner does not have any facilities for storage or is mobile.

- Product is supplied to pharmacies specifically for a named patient to collect
- Pharmacies do not maintain a general stock of product that could be made available to the public. The Sponsor is not aware of any request from pharmacies to begin maintaining a general stock nor does the Sponsor intend to begin supply to pharmacies on that basis.

Since no safety risk has been identified and the vast majority of supplies are sent directly to medical practitioners, hence not requiring a prescription, the proposal to change the Schedule 4 entry for HA will not provide any additional risk reduction that will benefit patients. In addition, the transition period of 1 June 2018 is unrealistic to allow for supply logistics and appropriate stake holder communications to be managed. A period of 12-18 months would be the minimum time period required.

The proposal will however, **add** the risk of potentially increasing costs for patients due to dispensing fees being incurred, result in delays in accessing treatment if the product is not routinely held in stock by the pharmacy, increase administrative burden 'for prescribers', and additional logistic impacts for wholesalers and suppliers. As such the proposal is counter to the principal of red tape reduction that supports best practice regulation. In addition, the Delegate noted the potential benefits of Synvisc include the potential to reduce pain medication use, particularly in the elderly population that have higher associated risks from chronic pain therapy which may be used whilst patients await joint replacement surgery. Any change in access that serves as a disincentive to consider an intervention that may reduce pain medication use, will thus increase the risk of adverse clinical sequelae.

On this basis the Sponsor can see no reason why the Delegate proposal will bring a positive benefit to the health of the Australian public. The Sponsor therefore **does not support** the Schedule 4 entry being amended. In alignment with overseas jurisdictions with comparable regulatory standards and similar healthcare practices to those in Australia the status quo should remain.