



24.08.2020 Joint Injections – Market Evaluation

The aim of this study is to summarize the current market status of the intra-articular Hyaluronic acid injections in Turkey, compile evidence for their short and long term efficacy, and discuss details about safety profiles.

JOINT INJECTIONS - MARKET EVALUATION

OUR COMPANY

Our company, **Sector** is a healthcare company working in various fields within Medical Devices, Pharmaceuticals and Nutrition supplements. Our medical device range consists of various products within Bariatrics, Urology, Orthopedia, Plastic Surgery, Weight Loss Treatment, Dental and IVD. We are distributing and promoting through our strong sales force and through a wide network of sub-distributors. Our portfolio includes Various vitamin&mineral supplements such as Chondroitin, MSM, Glucoseamine and much more, these products enable us to reach most of the MDs and experts throughout Turkey.

'To serve as the most trusted, convenient multichannel provider of innovative health solutions, products and services by enabling access to high quality medical devices.'

Our core values put our customers into the first place. We aim to establish long term business relationships with our business partners and providing our customers the most desired level of health care solutions.

A glance over Turkey

Osteoarthritis

Osteoarthritis (OA) is a progressive disease caused by the destruction of joint cartilage and remodeling of the adjacentbone. These disturbances are consequence of stresses that maybe the beginning of joint damage. In particular, the destruction of cartilage is usually located in two or more joints such as knees, hips, lower back, neck, or small joints of the fingers, being the knee the most frequently affected in approximately up to 83% of total OA patients (Lane et al., 2011; Vos et al., 2012). Osteoarthritis is a major cause for a reduction in quality of life due to restriction in activity and disability, without a curative treatment option by leading to total joint replacement (Hellevik et al., 2018).

The current non-surgical treatments for knee OA are focused on relieving symptoms, minimizing functional impairment, and preserving quality of life. For patients with knee OA, the initial treatment is mainly based in theuse of oral non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular injections and collagen/mineral/Chondrin derivative/Glucosamine-based supplements (Hochberg et al., 2012).

Risk factors for osteoarthritis and prevalence

Diabetes mellitus and osteoarthritis (OA) are common diseases that frequently co-exist, along with overweight/obesity (Sevinç, 2014). On a pathophysiological level of osteoarthritis, it is believed that adipose tissue and chondrocytes produce adipokines, which regulate adipocyte metabolism, the immune and inflammatory response. These adipokines were identified in osteoarthritic joints and in vitro to produce comparable chondrocyte activation as seen in pro-inflammation and mechanical stress.

Furthermore, high levels of glucose (in DM patients) may disturb the homeostatic state of chondrocytes (metabolic osteoarthritis) due to multiple mechanisms such as failed regulation of glucose transporters (GLUT-1) receptors oraccumulated advanced glycation products (Walter et al., 2020). The prevalence of OA is estimated to be between 30–50% global, leading to stiffness, general joint pains, reduced range of motion and increased morbidity and mortality (Schett et al., 2013).

The prevalence of diabetes and obesity is increasing day by day in our country (Figure 1), as in other countries of the world (Erem, 2015). According to the study report (2016) made by our Health Ministry:

- 20 years and over population: 47,467,350 (65.4%)
- Diabetes rate in TURDEP-II: 13.7%
- Number of people with diabetes: 6.503.027 people
- Known number of people with diabetes (54.55%): 3,547,401 people
- Number of new people with diabetes (45.45%): 2,955,626 people
- Prediabetic population (28.7%): 13,812,899 people
- Obese population (31.2%): 15.237.019 people
- Overweight population (37.5%): 17.088.246 people



Figure 1

In a prevalence study conducted in Turkey, in the population aged 50 and older, symptomatic knee OA prevalence is 14,8% (2.985.288), 22,5% in women, while men were reported as 8% (Kaçar et al., 2005). Population aged 50 and older is 20.170.866 in Turkey (*Türkiye Nüfusu Yaş Gruplarına Göre Dağılımı* 2019, n.d.).

Intraarticular HA therapy

Hyaluronic acid and steroids are the two main treatments used in intraarticular applications. Hyaluronic acid is a natural component of cartilage and plays a very important role in the viscoelastic properties of synovial fluid. Hyaluronic acid concentrations were lower in degenerative joint fluid than in the healthy joint. It is thought that hyaluronic acid injections protect the joint cartilage and soft tissue surfaces of the joint by improving the viscoelastic properties of the joint. It also shows anti-inflammatory and antinociceptive effects (Bilge et al., 2018). The first and most commonly used HA therapy is for the knee joint. Other joints where HA can find usage area; shoulder, hand joints, hip joints, temporomandibular joint (TMJ), spine, foot and ankle joints.

Intra-articular hyaluronic acid injection treatment aims, symptom relief that continues for at least a year (Nelson et al., 2015).

Studies showes that HA preparations with molecular weights above 500.000 Daltons can stimulate endogenous HA synthesis. At this point, the concept of molecular weight is important. Theoretically, it is an advantageous situation if the exogenous HA (injection) given has a higher molecular weight than the endogenous HA (Last, 2007).

Intraarticular HA injections that currently in Turkish Market

There is currently lots of HA preparations in Turkey, we've listed some of them. The available data may contain errors, it's because same manufacturers are supplying different distributors in Turkey, some of the products' licences have been deactivated by the Medicine and Medical Device Agency (TITCK) and some brands have been transferred to other distributors.



To summarize; the products effectiveness continue from six months to two years (symptom suppression), and their retail price (end-user price / VAT included) ranges between **second and second for each** injection.

Conclusion

Ministry of Health has ended the reimbursement program for HA intraarticular injection therapy in 2017 because of companies and doctors were abusing the re-payment program. Also Turkish Medicine and Medical Device Ministry has banned the sales from pharmacies about 8 months ago. Because of this

alteration companies needs a strong sales force dedicated to the sale of intraarticular injections to doctors and a well organized marketing throughout Turkey.

We want our influence to increase with **Exercise 1** in the Turkish market. Gripping point to our current market for us can be it's ease of use, price and customer support that we will be providing.

The possible agreement between us can to turn into a long partnership. We aim to establish sustainable business model.

REFERENCES

- Bilge, A., Ulusoy, R. G., Üstebay, S., & Öztürk, Ö. (2018). Osteoarthritis. Kafkas Journal of Medical Sciences, 8(50), 133–142. https://doi.org/10.5505/kjms.2016.82653
- Erem, C. (2015). Prevalence of Overweight and Obesity in Turkey. IJC Metabolic & Endocrine, 8, 38–41. https://doi.org/10.1016/j.ijcme.2015.07.002
- Hellevik, A. I., Johnsen, M. B., Langhammer, A., Baste, V., Furnes, O., Storheim, K., Zwart, J. A., Flugsrud, G.
 B., & Nordsletten, L. (2018). Metabolic syndrome as a risk factor for total hip or knee replacement due to primary osteoarthritis: A prospective cohort study (the HUNT study and the Norwegian Arthroplasty Register). *Clinical Epidemiology*, Volume 10, 83–96.
 https://doi.org/10.2147/CLEP.S145823
- Hochberg, M. C., Altman, R. D., April, K. T., Benkhalti, M., Guyatt, G., McGowan, J., Towheed, T., Welch,
 V., Wells, G., & Tugwell, P. (2012). American College of Rheumatology 2012 recommendations
 for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip,
 and knee. Arthritis Care & Research, 64(4), 465–474. https://doi.org/10.1002/acr.21596
- Kaçar, C., Gilgil, E., Urhan, S., Arıkan, V., Dündar, Ü., Öksüz, M. C., Sünbüloglu, G., Yıldırım, Ç., Tekeoglu,
 İ., Bütün, B., Apaydın, A., & Tuncer, T. (2005). The prevalence of symptomatic knee and distal interphalangeal joint osteoarthritis in the urban population of Antalya, Turkey. *Rheumatology International*, 25(3), 201–204. https://doi.org/10.1007/s00296-003-0415-z
- Lane, N. E., Brandt, K., Hawker, G., Peeva, E., Schreyer, E., Tsuji, W., & Hochberg, M. C. (2011). OARSI-FDA initiative: Defining the disease state of osteoarthritis. Osteoarthritis and Cartilage, 19(5), 478– 482. https://doi.org/10.1016/j.joca.2010.09.013
- Last, N. (2007). Osteoartritte intraartiküler hyalüronik asit tedavisi. Türkiye Fiziksel Tıp ve Rehabilitasyon Dergisi, 53(4), 154-159–15.

- Nelson, F. R., Zvirbulis, R. A., Zonca, B., Li, K. W., Turner, S. M., Pasierb, M., Wilton, P., Martinez-Puig, D., & Wu, W. (2015). Erratum to: The effects of an oral preparation containing hyaluronic acid (Oralvisc®) on obese knee osteoarthritis patients determined by pain, function, bradykinin, leptin, inflammatory cytokines, and heavy water analyses. *Rheumatology International*, 35(1), 53–53. https://doi.org/10.1007/s00296-014-3078-z
- Schett, G., Kleyer, A., Perricone, C., Sahinbegovic, E., Iagnocco, A., Zwerina, J., Lorenzini, R., Aschenbrenner, F., Berenbaum, F., D'Agostino, M.-A., Willeit, J., & Kiechl, S. (2013). Diabetes Is an Independent Predictor for Severe Osteoarthritis: Results from a longitudinal cohort study. *Diabetes* Care, 36(2), 403–409. https://doi.org/10.2337/dc12-0924
- Sevinç, S. (2014). KISIR DÖNGÜ: OSTEOARTRİT ve OBEZİTE (OLGU SUNUMU). ERÜ Sağlık Bilimleri Fakültesi Dergisi, 2(2), 80–88.
- Türkiye Nüfusu Yaş Gruplarına Göre Dağılımı 2019. (n.d.). Retrieved August 24, 2020, from https://www.nufusu.com/turkiye-nufusu-yas-gruplari
- Vos, T., Flaxman, A. D., Naghavi, M., Lozano, R., Michaud, C., Ezzati, M., Shibuya, K., Salomon, J. A.,
 Abdalla, S., Aboyans, V., Abraham, J., Ackerman, I., Aggarwal, R., Ahn, S. Y., Ali, M. K., AlMazroa,
 M. A., Alvarado, M., Anderson, H. R., Anderson, L. M., ... Murray, C. J. (2012). Years lived with
 disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: A systematic
 analysis for the Global Burden of Disease Study 2010. *The Lancet*, 380(9859), 2163–2196.
 https://doi.org/10.1016/S0140-6736(12)61729-2
- Walter, S. S., Wintermeyer, E., Klinger, C., Lorbeer, R., Rathmann, W., Peters, A., Schlett, C. L., Thorand, B., Gatidis, S., Nikolaou, K., Bamberg, F., & Notohamiprodjo, M. (2020). Association between metabolic syndrome and hip osteoarthritis in middle-aged men and women from the general population. *PLOS ONE*, 15(3), e0230185. https://doi.org/10.1371/journal.pone.0230185



Pharm. Ahmet Ozan ÖZGEN

Business Development Executive

+90 505 759 20 56
 A Ø

This document, with all it's attachments, will be deemed the confidential property of the third parties' confidentiality obligations.