Consolidated stakeholder feedback

HTA protocol

Intra-articular glucocorticoid injections for osteoarthritis of the hip or knee

Stakeholders (SH; in alphabetical order) that have provided comments:

1	Mepha Pharma AG
2	santésuisse
3	Schweizerische Gesellschaft für Rheumatologie
4	Swiss Orthopaedics

SH	SH comment	Reply authors / BAG & implemented changes
1	The defined population in the PICO (section 4) is very broad and does not include the severity of OA. Since IAGI are usually used for treating OA symptoms at a later stage of the disease (e.g. after paracetamol and NSAIDs; see section 3), the population should be narrowed down by severity of disease.	We acknowledge that the population is broad. However, Section 6.2.6 of the protocol (subgroup and sensitivity analysis) mentioned that subgroup analysis will be conducted to investigate the impact of the following patient and intervention characteristics such as the severity of OA on the results of the meta-analyses. No change needed.
2	Das HTA Protokoll ist übersichtlich und gut strukturiert. Es finden sich jedoch ungenügende Angaben zu Evidenzlücken betreffend die intraartikuläre Injektion von Glukokortikoiden (IAGI) zur Behandlung der Arthrose von Knie- und Hüftgelenk (OA). Dies erstaunt insofern, als mehrere aktuelle internationale Guidelines die IAGI aufgrund der vorhandenen Evidenz als eine von mehreren therapeutischen Optionen empfehlen (z.B. ACR, EULAR, ESCE etc.). Translation: The HTA protocol is clear and well structured. However, there is insufficient information on evidence gaps regarding the intra-articular injection of glucocorticoids (IAGI) for the treatment of osteoarthritis of the knee and hip (OA). This is surprising in that several current international guidelines recommend IAGI as one of several therapeutic options based on the available evidence (e.g. ACR, EULAR, ESCE etc.).	Thank you for this feedback. Evidence gaps will be addressed in the HTA phase. No change needed.

2	Im HTA-Protokoll fehlt eine Beschreibung des schrittweise aufbauenden Behandlungs-Algorithmus mit unterschiedlichen therapeutischen Optionen, Kombinationen und therapeutischen Phasen (z.B. Basic, Background, Advanced etc.), welche sich an individueller Ausgangslage (z.B. klinischer Status, Risikofaktoren, Komorbiditäten, Alter etc.), Verlauf und weiteren Rahmenbedingungen orientieren. Für das HTA sowie für die Diskussion der PICO-Kriterien ist das Verständnis des Algorithmus wichtig. Gemäss internationalen Guidelines umfasst die optimale Behandlung der OA eine angepasste Kombination von unterschiedlichen pharmakologischen und nicht-pharmakologischen Massnahmen. Translation: The HTA protocol lacks a description of the step-by-step treatment algorithm with different therapeutic options, combinations and therapeutic phases (e.g. basic, background, advanced, etc.), which are based on the individual starting point (e.g. clinical status, risk factors, comorbidities, age, etc.), course and other framework conditions. Understanding the algorithm is important for the HTA as well as for the discussion of the PICO criteria. According to international guidelines, the optimal treatment of OA includes an adapted combination of different pharmacological and non-pharmacological measures.	The original protocol draft included an expanded version of the treatment algorithm. However, the section was simplified due to discordance among the guidelines and clinical reviewers, which made it difficult to define a single treatment pathway. Section 2.3 of the protocol states that there is discordance in the recommendations from guidelines on the management of hip and knee OA. While it is acknowledged that a range of treatment options exist in this population (including but not limited to oral pain medication, non-steroidal anti-inflammatory drugs (NSAIDs) and physical therapy), this HTA will focus on evaluating the efficacy of IAGI in relation to placebo (including oral placebo and sham injection) or no treatment.
2	Obwohl zahlreiche Studien die IAGI mit anderen therapeutischen Optionen vergleichen, ist dies in der vorgeschlagenen isolierten Untersuchung der IAGI nicht vorgesehen. Ausgangslage, Rahmenbedingungen oder andere vorgängige oder begleitende Therapien werden nicht (Comparatoren) oder ungenügend (Subgruppenanalysen) berücksichtigt. Potentielle Unterschiede in Studienpopulationen bzw. Vergleichsgruppen könnten Aussagekraft und Übertragbarkeit der Ergebnisse erschweren (z.B. Validität, Effektstärke, Inhomogenität etc.; s.a. Jüni 2015). Translation: Although numerous studies compare IAGI to other therapeutic options, the proposed isolated review of IAGI does not do so. Initial situation, framework conditions or other previous or accompanying therapies are not (comparators) or insufficiently (subgroup analyses) taken into account. Potential differences in study populations or comparison groups could make it difficult to provide meaningful information and transfer the results (e.g. validity, effect size, inhomogeneity, etc.; see also June 2015).	We acknowledged that the proposed reviews did not include other therapeutic options as comparators for patients with knee and hip OA. However, due to the discordance among the clinicians and guidelines on the interventions for OA of the knee and hips, as well as the controversial nature of some of the comparators, it was preferred that the comparator list be limited to placebo/sham and no treatment only. No change needed.
2	Alternativ wäre eine Netzwerk-Metaanalyse der IAGI im Vergleich mit anderen therapeutischen Optionen zu prüfen. Translation: Alternatively, a network meta-analysis of the IAGI in comparison with other therapeutic options could be examined.	The comparator list was limited to placebo/sham and no treatment. The use of network meta-analysis in this case is not needed. No change needed.
2	Die Ausführungen zur ökonomischen Beurteilung der IAGI können nachvollzogen werden. Der Aufbau eines neuen Modells für die Beurteilung der Wirtschaftlichkeit der IAGI wird unterstützt falls Studien nicht die relevanten Evidenzgrundlagen liefern. Translation:	Thank you for this feedback, it is noted. No change needed.

	The statements on the economic assessment of the IAGI can be understood. The development of a new model for assessing the economic efficiency of IAGI is supported if studies do not provide the relevant evidence base.	
3	Die Indikationen für Steroidinfiltration der Gon- und Coxarthrose sind vielfältig und sollten separat analysiert werden: Translation: The indications for steroid infiltration of gonarthrosis and coxarthrosis are diverse and should be analysed separately.	Thank for the feedback. The outcomes for hip and knee OA will be analysed separately.
3	Grundsätzlich werden lediglich «aktivierte Arthrose», mit oder ohne Gelenkerguss, infiltriert, schmerzhafte Arthrose-Gelenke hingegen kaum. Translation: Basically, only "activated arthrosis", with or without joint effusion, is infiltrated, painful arthrosis joints, on the other hand, are hardly ever infiltrated.	Thank you for this feedback. We acknowledge that activated arthrosis is included as an indication for some IAGIs approved by Swissmedic. The applicability of identified literature to Swiss practice will be evaluated in the HTA. No change needed.
3	Eine weitere wichtige Indikation/Untergruppe ist die assoziierte mikrokristalline Arthritis (z.B. Chondrokalzinose /CPPD, Hydroxylapatit), die sehr häufig zusammen mit Osteoarthritis auftritt. Translation: Another important indication/subgroup is associated microcrystalline arthritis (e.g. chondrocalcinosis/CPPD, hydroxyapatite), which very often occurs together with osteoarthritis.	Thank you for this feedback. The population included in the assessment includes patients with OA. Studies which include OA with and without calcium pyrophosphate crystal deposition will be captured in the search. No change needed.
3	Steroidinjektionen bei der nicht aktivierten Arthrose und die repetitiven Steroidinjektionen (mit fixen Intervallen) entsprechen keiner gängigen Praxis in der Schweiz und sind deswegen nicht von Interesse. In der Praxis nehmen Schweizer Ärzte keine systematischen Steroidinjektionen nach 3, 6 und 12 Monaten vor, weswegen diese Zeitpunkte aus Sicht der SGR nicht zu untersuchen sind. Translation: Steroid injections in non-activated arthrosis and repetitive steroid injections (at fixed intervals) do not correspond to common practice in Switzerland and are therefore not of interest. In practice, Swiss physicians do not carry out systematic steroid injections after 3, 6 and 12 months, which is why the SGR does not consider these points in time to be examined.	Thank you for this feedback. We acknowledge that IAGI on non-activated arthrosis and repetitive injections might not be a common practice in Switzerland. Analysis at the proposed timepoints will determine duration of IAGI effectiveness (short term vs long term effectiveness), and is not related to the frequency of the injections but rather duration of follow-up. The applicability of evidence to Swiss practice will be evaluated in the HTA. No change needed.
4	To the Knee Expert Group of the Swiss Orthopaedics, the necessity of an HTA regarding glucocorticoid injections in the knee and hip is questionable. To our knowledge, there have been no conflicting discussions with health insurance providers about the reimbursement of this cost-effective intervention in the past. As such, an infiltration of the knee joint with local anesthetics and corticoids costs approximately CHF 54. It is well known that there are conflicting results about the clinical efficacy of corticoid injections in osteoarthritis. However, such injections are not only a therapeutic but also a diagnostic tool during the decision-making process concerning a potential surgical treatment of osteoarthritis, e.g. the implantation of a joint arthroplasty.	Thank you for this feedback, it is noted. However, the main objective of this assessment it to determine the therapeutic effectiveness of IAGI in OA patients. In this assessment, the purpose of the injection is not to determine the cause or source of hip/knee pain, nor to determine if the pain is intra or extra-articular in origin. The patients were diagnosed to have OA with pain as one of the presentations. The diagnostic effect of IAGI is outside the scope of this assessment. No change needed.
4	In young patients with osteoarthritis, where the implantations of an arthroplasty should be delayed, there is often no alternative to corticoid injections available. This	Thank you for this feedback, it is noted. However, the main objective of this assessment it to determine the therapeutic effectiveness of IAGI in OA patients. In this assessment, the

	is also because injections with PRP, that have been shown to be superior to corticoid injections in mild and moderate OA (ESSKA ORBIT Consensus) are not covered by health insurances in Switzerland.	purpose of the injection is not to determine the cause or source of hip/knee pain, nor to determine if the pain is intra or extra-articular in origin. The patients were diagnosed to have OA with pain as one of the presentations. The diagnostic effect of IAGI is outside the scope of this assessment. No change needed.
4	It also seems important to us that various factors influence the effectiveness and thus also the sense of intra-articular cortisone infiltration: Degree of osteoarthritis, mechanical components (e.g. impacted meniscus, instability), individual factors (BMI, blood pressure, diabetes). A differentiated opinion with the given limitation is not possible, especially since the knee and hip would have to be considered separately.	Thank you for this feedback, it is noted. A number of these factors are included as sensitivity or subgroup analyses, as outlined in section 6.2.6 of the protocol. No change needed.
4	For its part, the Hip Expert Group emphasises that not only the direct costs of treatment but also the indirect cost savings play an important role in the assessment; as mentioned above, diagnostics also play a role in this form of intra-articular infiltration. Potential benefits include pain reduction, postponement of surgical measures, improved function and diagnostic aspects, as well as the alternatives.	A healthcare payer perspective is applied for the economic analysis. Direct healthcare costs will be considered and not indirect costs such as loss of productivity. Cost savings in the healthcare system will be captured by the model. No change needed.