De forskande
läkemedelsföretagen

Comments

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Review of JNHB documents

The possibility for organizations to comment and leave suggestions for improvements of the JNHB documents - JNHB Process Guideline and JNHB Submission Dossier template - is highly appreciated. The Nordic associations had the ambition to give a joint respond but have decided to submit national responses. The reason being that the presented JNHB documents are a compilation of present national demands rather than the joint Nordic approach expected.

From a Swedish perspective, the JNHB documents presents stricter demands than the possibility for HTDs to form a Swedish dossier and TLV´s pragmatic approach which is appreciated.

The relaunch of FINOSE as JNHB is of significance for Lif member companies. It presents a possibility to include a Nordic step between the joint EU evaluation and the national decisions that could be attractive if constructed and managed to save time with a true ambition to increase the rate and shorten the time for access within the Nordics. Unfortunately, the incentives for choosing JNHB presented in the documents will most likely not be sufficient to attract a significant proportion of Health technology developers (HTDs) applications. HTDs evaluation of JNHB is further complicated by the close collaboration with the New Expensive Drugs (NED) working group within Nordic Pharmaceutical Forum. An alternative could be a stepwise approach where the JNHB evaluations is first established without emphasising the JNHB-NED collaboration. This would underline that the decision is to be made at the national level. However, JNHB-NED collaboration may of course be possible if the HTD request or accept a joint Nordic negotiation.

It is surprising that JNHB is not more clearly positioned with regards to HTAR. Lif had expected a more in-depth description of JNHB collaboration on PICOs and the process and submission when a JCA is present.

General comments

Lif expected JNHB to be a joint Nordic approach aiming at making it attractive for HTDs to apply in all countries at the same time, but the published documents suggests that a JNHB application might be more complex than separate submissions to each national HTA body (HB). The reason being that each countries demands has been added on top of each other. This approach emphasises that HTD participation in JNHB must be voluntary. Voluntary participation is also essential since some companies have Nordic organisations while others have independent national affiliates. For the latter JNHB may impose a significant internal administrative burden.

It is not evident if an JNHB application must include all five countries especially since all HBs will not participate fully in all evaluations due to differences in the national set up. It is therefore

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important that HTDs also can decide which of the Nordic countries to include in the JNHB application and to suggest a specific assessing HB even if such request may not always be possible to meet. It also needs to be clarified how HBs acting as observers will use the JNHB evaluation in assessments of national evaluations.

The development of JNHB may take a best-case and a worst-case direction. Actions that can be taken to promote a best-case development and give HTDs incentives to test JNHB include:

- a guarantee HTDs have the possibility to have dialogue meetings with the actual assessors during the evaluation to discuss issues that arise during the assessment,
- that it is clearly expressed that the best method dependent on data will be used,
- that all methods to estimate relative effect relevant and solid for the specific case will be accepted,
- that analyses with an external RWD arms solid enough for the specific case will be accepted,
- that evaluations will consider both positive and negative impact of uncertainties,
- that the most relevant extrapolation - not the most conservative – will be used.

One of the most important incentives for HTDs to use JNHB is time. If the time from application to patient access will become shorter with JNHB it may be an attractive pathway. Another important advantage from a Swedish perspective is if JNHB give HTDs the possibility to initiate evaluations of all hospital products within the same time frame as for reimbursed products, something Lif has proposed for a long time. This would address the present queue for evaluation of hospital products when regions initiate the evaluations. To have the suggested 90 days for JNHB is good and if a timeframe of maximum 90 days for national Swedish decision could be added (a total time of 180 days) it would be a significant improvement if applied for all new products, especially if HTDs also could apply before CHMP opinion with clock start at positive opinion. The JNHB-NED collaboration make it is necessary that participants in the Nordic Pharmaceutical Forum commit to a timeframe that is not longer than any of the country's national timeframes for negotiation/decision. For national processes Lif see a need for a commitment by TLV and regions to stay within or use a short timeframe than used today. A timeframe of 90 days (JNHB) + 90 days (negotiation/decision) would be an important improvement. The possibility to use English both in JNHB applications and national/NED negotiation is also important for HTDs and increase HTDs possibility to adhere to an ambitious timeframe.

Detailed review of JNHB documents

JNHB process guidelines

It would be valuable with a reference to the legal framework for JNHB - such as the transparency directive or other - to make sure that all parties are aware of the regulations under which a JNHB application is handled.

The process when a JCA exists need to be described. Especially which parts of the dossier that can be disregarded when the JCA PICO is aligned with the JNHB PICO. Lif also want to encourage JNHB to adhere to the HTAR principles when it comes to involvement of clinical and patient experts.

It is positive and important that is stated that the use of the JNHB submission dossier is a recommendation and not a requirement. Further, HTDs need a possibility to decide which countries to include to avoid unnecessary delays. Most HTDs for instance use an Icelandic vendor to handle the applications in Iceland.

It is positive that HTDs can propose PICO(s) and that the process starts with a PICO dialogue for the HTD and HBs to agree if the JNHB process should be initiated. Meeting minutes should be taken from the PICO start-up meeting so that the information can be transferred if there is a change of persons assessing the dossier.

The aim must be for assessors to check if the dossier is complete to shorten the time to patient access. That all HBs need to check if the dossier is complete seems ineffective and time consuming.

Further clarification is needed regarding the possibility for HTD to withdraw an JNHB dossier at any time without any negative consequences for future national applications. Clarification is also needed regarding the national step after a JNHB evaluation. For instance, that uncertainty should be described by JNHB but handled nationally and that budget impact analyses – if needed - should only be conducted nationally.

Detailed comments

- It is positive that HTDs can attach a document with comments to the report, but two pages is not enough. A maximum of 10 pages is preferred to allow for a figure or graph when needed to provide relevant comments.
- Timeframes are referred to be in table 2 but no table 2 exist in the document. Figure 2 exist but does not contain timelines.

JNHB submission dossier template

It is positive that it is not mandatory to use the JNHB submission dossier since this allows HTDs to structure the application so that it presents a clear and concise messages.

If HTDs choose to use the JNHB submission dossier, the possibility to delete subheadings and bullet points under each heading is positive as well as the possibility to state “not applicable due to” when a heading is not relevant is appreciated.

Comments on Waiver of Confidentiality

It is not fully clear how the table in section 2.2 works. A description is needed of which document each HB should have access to or if all document specified in the table will be is shared with all HBs.

It should be possible to exclude some of the HBs/negotiation bodies from the waiver if the company include a selection of countries.

Detailed comments

Background and introduction to the submission template + List of required documents

- It is administrative burdensome - compared to Swedish assessments - to include full text for all clinical studies and studies central for the modelling. Inclusion of the most relevant studies and a good reference list with references available on request should be sufficient.
- Excel Macro certification may be administrative burden and is not required in a Swedish application.

Clinical evidence

- Section 2.2 imply that all studies in the NMA should be filled in to table 4 but no timeframe is mentioned. Lif propose that it should be sufficient that studies are summarised and described in the NMA report to avoid double reporting as the data also is requested under section 2.3. It should also be possible to exclude this section if a JCA exist based on a JNHB relevant PICO.
- The request for a *Summary of relevant supportive studies used in health economic modelling* in table format may be unjustified since the sections needed to be filled in may be irrelevant for the assumptions the study support.
- Later planned analyses in Table 4 can be difficult to fill in as information might not be available for affiliates. The assessment needs to be based on available data. An approach to wait for later data-cuts should be avoided in favour of conditional decisions.
- Section 2.4 could include a reference to guidelines for evidence synthesis and indirect comparisons to ensure that good methods standards are applied consistently.

Model requirements

- Other model types than Microsoft Excel - for example R models – need to be accepted.
- Inclusion of data for all countries in the same model will make the model slower and harder to examine due to long and complex formulas. It will also be challenging due to the demands that spreadsheets also should be transparent, fully user modifiable and that changes of input variables automatically should update results.
- The demand for a reset button is not necessary. A more pragmatic approach is that the assessors save an original version of the model.
- Hidden cells or sheets can easily be checked by assessors in Microsoft excel. These should therefore be allowed to make the models easy to follow visually.
- For HTD to provide a large number of Markov-traces and /or other plots for all subpopulations and different setting will increase the size of the model substantially. It should be enough to provide a few key figures/graphs with additional illustrations being done by the assessors themselves.

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Health-related quality of life (HRQoL)

- The template specifies EQ-5D-3L for the Swedish tariff but as EQ-5D-5L exist this should be used in addition to EQ-5D-3L with UK tariffs. In general, up to date national tariffs should be used when possible and JNHB should aim to harmonize the tariff to be used when no national tariffs exist.
- The demand that *treatment specific HSUV may only be considered when differences in HRQoL are documented in clinical studies and have a clinical rationale* is too strict since the rational also can be other reasons such as administration, burdensome testing etc.

Resource use and costs

- The free online tool C-CEMG-EPPI Cost Converter enables the conversion of a cost estimate that is reported in one 'source' currency and price year into its equivalent value in another 'target' currency and price year (https://methods.cochrane.org/economics/workshops) is proposed to replace the demand *to incorporate a feature in the model that allows for conversion between different currencies. All currency conversion rates should be included in the model (DKK, EUR, ISK, NOK, SEK)* to ensure as good quality calculations as possible.

Results

- Section 4.1.1 refers to table 7 which may not be the correct reference.
- It is not clear if Table 10 refers to undiscounted or discounted results.

Probabilistic sensitivity analysis (PSA)

- Should not be a general demand, rather included when deemed relevant.

Budgetary consequences and expected sales

- Should not be a part of the JNHB evaluation, only submitted to countries where it is a requirement.

Joint development

Lif propose that JNHB invite the Nordic trade association on a regular basis with the aim to evaluate and develop JNHBA towards an efficient alternative with high quality that deliver faster access within the Nordics. Topics of special interest for development are:

- Aspects to be considered in the societal perspective.
- A possibility for second opinion from external experts within health economics.
- Further involvement of clinical and patient experts.