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File note

TGA THERAPEUTIC GOODS ADMINISTRATION

Notes from meeting with Johnson & Johnson Pacific Ltd to discuss the proposed submission and the data pack available for a new NRT dose form – a nicotine mouth spray

Date:
30 March 2010 (12:30pm)

Present:
Johnson & Johnson Pacific Ltd: s22 [redacted]

TGA: s22 [redacted]

Location:
Meeting Room 6, TGA Building, Symonston

TGA filenote

Discussion

- The sponsor presented a brief summary of the briefing package dated 9/3/10 that they had supplied prior to the meeting (f.46-187, file 2009/008719). This included some of the graphs and tables from that submission – the sponsor advised no new information was included in the *'Power point'* presentation. The sponsor also provided samples of the proposed product, though these were retained by the sponsor at the conclusion of the meeting.
- The sponsor was advised they would have to submit a 'switch' application to NDPSC **and** have a positive indication that it'll be OTC classified before we begin evaluation. The sponsor was advised that this approach has been handed down to us by TGA management and that if it is retained in S4, then OTCMS will not evaluate the application. The sponsor advised that an application to do this was presented to the February 2010 NDPSC meeting.
- The sponsor was advised that the indication should be for smoking cessation - anything beyond absolute cessation (or with an endpoint to quit) would be novel for the Australian market and would require clinical data.
- The sponsor was also advised that the TGA had a strong preference for clinical data. However, based on the information on the PK data already generated, we could potentially accept the application ….however, certainly no guarantee of success. Would be screened and evaluated in usual manner.
- The sponsor indicated that they would be submitting data on the nicotine nasal spray as part of the clinical package (refer sponsor's *Briefing notes* dated 9/3/10, p7). The sponsor was advised that the nasal spray data could only be considered as supportive data as it is a different route of administration.
- It was noted by the TGA staff that the Phase III study due October 2010. The question was put to the sponsor as to why not wait until this clinical study is available before submitting the dossier. The sponsor replied that the report is now not likely to be finalised until November 2010 and even then would have to be formatted into CTD format and then submitted. The sponsor advised they are not keen on waiting for this and that they are confident in the data package based on the PK data alone. The sponsor indicated that they may consider submitting it when it is available i.e. after the original package had been submitted. The sponsor was advised that while this *may* be acceptable,

there would certainly be no guarantee the TGA would accept data subsequent to the original submission.

- The sponsor advised the directions would be to use the product in place of cigarettes; they advised the proposed directions would be consistent with the approved directions for other NRTs.
- In their presentation, the sponsor stated that there was no indication that the ONS (oromucosal nicotine spray) presented any safety issues. They stated that the pharmacokinetics of nicotine from the ONS compared favourably (from a safety perspective) to that when compared to smoking itself and that the safety of NRT, in general terms, is well established. The sponsor advised that the was advised that the TGA would be interested in a number of safety related issues for this new dosage form: in particular, the sponsor was advised that they could consider addressing in their submission the following points:

  1) safety of the user in normal use
  2) safety of the user in abuse
  3) safety of others, particularly children. It was noted that the spray mechanism has a child resistant feature. However, it was also noted when looking at a sample of the device that, if the spray mechanism was not shut, then this could enable easy access to a child.
  4) In relation to points 2 & 3, could the reservoir of the solution itself be accessed? If so, what could be the implications if taken orally

- It was suggested to the sponsor that, should they make an application for the ONS, they should include a sample of the product – this would be of assistance to the evaluator and an advisory committee (should the application be assessed by such a committee).
- Local tolerance should also be addressed – would expect that such studies would use the same product / frequencies for use etc.

The meeting concluded ~1:45pm

s22 [redacted]
OTC Medicines Section
6 April 2010

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Document 2

Oromucosal Nicotine Spray (aka CORVETTE) TGA/JJP MEETING MINUTES

Meeting at TGA 30 March 2010

Attendees

Johnson & Johnson Pacific:

s22 [redacted]

TGA:

s22 [redacted]

J+J minute

Minutes

Corvette:

1. TGA will accept submission with the PK data and with NNS data as supportive evidence of safety and efficacy, but their preference is to wait for the Phase III data
2. Must be indicated for smoking cessation only
3. Any claims emanating from the PK data should be correctly referenced
4. JJP should provide an update as to the regulatory status in the countries discussed, and copies of the regulatory authority correspondence should be provided
5. JJP should address/include in the submission:
    a. A rationale for our choice of comparators (gum, lozenge) especially in light of the fact that gum etc. are viewed as modified release vs ONS (immediate release)
    b. NNS is viewed as supportive only - the difference between the nasal and oromucosal uptake should be explained
    c. Safety areas: Use; abuse and misuse – specifically in children. s22 [redacted] mentioned the obvious public availability of cigarette butts and gum.
    d. Safety compared with other formats – (we have PSUR's for all formats)
    e. "What if the ONS was left open" and also demonstrate the difficulty to get access to liquid (how hard is it to break it open?) - can reference NNS where possible as a comparator liquid format
    f. Provide local tolerance data –can leverage off NNS where possible. Phase III will have mouth inspection - NNS had ENT inspections
    g. Any difference in method of use vs current formats especially the flexibility vs fixed compared with current registered regimens i.e. use when there is an urge to smoke (every 1 – 2 hours) as an example.
6. No fasttracking to be considered– this would follow normal screening and evaluation process
7. TGA restructure could cause a delay in processing

Other:

8. Combination therapy will be considered provided an acceptable justification is provided (The thinking around NRT has changed over time and there was acknowledgement that people use NRT for temporary abstinence regardless of indication)
9. Open to review labelling warnings - TGA tries to harmonise across sponsers. JJP will be looking to clean up the labels

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Oromucosal Nicotine Spray (aka CORVETTE) TGA/JJP MEETING MINUTES

JJP's response to concerns raised during the meeting.

5.

a. ***A rationale for our choice of comparators (gum, lozenge) especially in light of the fact that gum etc. are viewed as modified release vs ONS (immediate release)***

Gum and lozenge were chosen as comparators in the pharmacokinetic studies since they represent the most common oral NRT products on the intended markets

b. ***NNS is viewed as supportive data only – difference between the nasal and oromucosal uptake should be explained.***

Nicotine from NNS is absorbed mainly via the nasal mucosa whereas ONS is absorbed mainly via the oral mucosa. No direct comparison of the pharmacokinetic profile of NNS and ONS has been made. However, comparing data in between studies (see section 1 module 2.5) it seems as if the plasma concentrations of nicotine during the first few minutes after administration from the ONS is similar or somewhat slower than that from NNS.

c. ***Safety areas: Use; abuse and misuse – specifically in children.***

This is covered in the dossier.
Use: All of Module 2.7.4 and parts of 2.5.
Abuse and misuse: 2.7.4 section 5.7 and 2.5 section 5.7 to 5.9.

The ONS is childproof, but the dispenser is not self-closing. It is therefore the responsibility of the user to make sure the dispenser is securely closed after each use, as is the case with most medicines. The user instruction clearly states that the spray should be kept away from children.

d. ***Safety compared with other formats – (we have PSUR's for all formats)***

This is covered in the dossier
Module 2.5 section 5

e. ***"What if the ONS was left open" and also demonstrate the difficulty to get access to liquid (how hard is it to break it open?) - can reference NNS where possible as a comparator liquid format***

Sponsors can only do so much to help prevent children accessing and using medicinal products. The ONS has a child resistant feature and the labelling clearly states to keep the product out of reach of children, close properly after each use to engage child resistant closure etc. As with all medicines, it is the responsibility of the user to ensure the product is properly closed to engage the child resistant closure and it is also the user's responsibility to ensure that the product is kept out of reach of children. It would be expected that 1-2 sprays of ONS would be enough to

discourage a child from further use, as the ONS has a strong taste and the child is also likely to feel sick. It would take some time to for a child to empty the whole container. The dispenser itself is very difficult to get into if you do not have very strong fingers or have a tool of some sort. Personnel at the lab have a special tool to be able to open without injuring themselves. It could be possible to crush the dispenser with a hammer but this is also likely to destroy the PET bottle and the liquid would spill out.

f. Provide local tolerance data

This is covered in the dossier.
Module 2.5, section 5.3.2 and section 6, third last paragraph. Module 2.7.4, section 2.1.4.1

g. Any difference in method of use vs current formats especially the flexibility vs fixed compared with current registered regimens i.e. use when there is an urge to smoke (every 1 – 2 hours) as an example.

This is covered in the dossier.
Module 2.5, section 4.3.1 and Module 5 Study Report NICTDP2010: