19\textsuperscript{th} Expert Committee on The Selection and Use of Essential Medicines

April 8-12 2013

Expert peer review on oral hypoglycaemic agents; review to update section

The medicines are reviewed in three sections A. Alpha Glucosidase inhibitors and meglitinides B. Glitazones and C. DPP – 4 Inhibitors(Sitagliptin)

A. Alpha glucosidase inhibitors and meglitinides

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes
   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Patients on Metformin and Sulphonyl ureas showed similar HBA1c reduction as compared to those on alpha glucosidase inhibitors and meglitinides.

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes

   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Gastrointestinal side effects were significantly more common with Acarbose than with Metformin and Sulphonyl ureas. Meglitinides have a higher incidence of hypoglycemia than Metformin but lower than Sulphonyl ureas. c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
   a. Have all relevant data on cost been provided
      Yes

   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Acarbose and Meglitinides are much more expensive than Glibenclamide and Metformin. c. Please provide any additional relevant information with reference

   d. Is the product available in several low and middle income countries? No

4. Assessment of public health need
   a. Please provide the public health need for this product (1-2 sentences)
According to the WHO 2010 report, 8 – 10% of the world population suffers from diabetes, with 90 to 95% of the cases being of Type 2 diabetes.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

NICE guidelines – Acarbose recommended for those who cannot tolerate another oral hypoglycaemic agent

American Diabetes Association - Meglitinides

5. Are there special requirements for use or training needed for safe/effective use?
If yes, please provide details in 1-2 sentences

No

6. Is the proposed product registered by a stringent regulatory authority?
Yes

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)

I recommend against inclusion of Acarbose and Meglitinides in the EML. They are only as effective as the drugs currently on the EML. They are also very expensive. Acarbose has significant gastrointestinal side effects.
B. Glitazones – pioglitazone and rosiglitazone

1. Assessment of efficacy
a. Have all relevant studies on efficacy been included
   YES
b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

Metformin and Sulphonyl ureas showed similar HBA1c reduction as glitazones. Weight gain was more with glitazones.

c. Please provide any additional relevant information with reference

2. Assessment of safety
a. Have all relevant studies on safety been included
   No


Rosiglitazone authorisation was withdrawn from the European market after decisions by the EMA and MHRA (UK)\(^1\). Recommendation for its use was withdrawn from the NICE guidelines\(^2\)


In June 2011, based on a French paper\(^3\) and data from California the FDA gave a warning \(^4\) for risk of bladder cancer with prolonged use of or high cumulative dose of pioglitazone. France and Germany suspended use of Pioglitazone based on this data.

Multiple studies have also shown increased risk of osteoporosis and fractures with pioglitazone and rosiglitazone

b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

Pioglitazone and Rosiglitazone confer an increased risk of heart failure, ischaemic heart disease and osteoporosis. Pioglitazone confers an increased risk of bladder cancer. Regulatory bodies have issued warnings and the drugs have been withdrawn from some countries.

c. Please provide any additional relevant information with reference
3. Assessment of cost and availability
   a. Have all relevant data on cost been provided
      Yes
   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      The Glitazones are much more expensive than Glibenclamide and Metformin.
   c. Please provide any additional relevant information with reference
   d. Is the product available in several low and middle income countries? No

4. Assessment of public health need
   a. Please provide the public health need for this product (1-2 sentences)
      According to the WHO 2010 report, 8 – 10% of the world population suffers from diabetes, with 90 to 95% of the cases being of Type 2 diabetes.
   b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable
      FDA – use with caution

5. Are there special requirements for use or training needed for safe/effective use?
   If yes, please provide details in 1-2 sentences
      Yes – Need to be avoided in patients with heart disease, osteoporosis and bladder cancer

6. Is the proposed product registered by a stringent regulatory authority?
   Yes

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)
   I recommend against inclusion of Glitazones in the EML. They have major safety issues and side effects and are only as effective as the drugs currently on the EML. They are also very expensive
C. DPP – 4 Inhibitors (Sitagliptin)

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      YES
   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Metformin showed better HBA1c reduction and greater weight reduction than DPP 4 Antagonists. One study comparing glipizide and sitagliptin showed similar HbA1c reduction. No comparison with glibenclamide was available.

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes
   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Sitagliptin causes less hypoglycemia than sulphophyl ureas (SFU). Diarrhoes is more common with Metformin than with Sitagliptin.

   c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
   a. Have all relevant data on cost been provided
      Yes
   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Sitagliptin is prohibitively expensive costing 5 to 15 times as much as Metformin and Glibenclamide.

   c. Please provide any additional relevant information with reference

   d. Is the product available in several low and middle income countries? No

4. Assessment of public health need
   a. Please provide the public health need for this product (1-2 sentences)

   According to the WHO 2010 report, 8 – 10% of the world population suffers from diabetes, with 90 to 95% of the cases being of Type 2 diabetes.

   b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

   NICE guidelines – DPP 4 antagonists recommended as second or third line drug

   American Diabetes Association
5. Are there special requirements for use or training needed for safe/effective use?
   If yes, please provide details in 1-2 sentences
   
   No

6. Is the proposed product registered by a stringent regulatory authority?
   
   Yes

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)

   I recommend against inclusion of DPP 4 antagonists in the EML. They are prohibitively expensive and only as or less effective as the drugs currently on the EML.