TITLE PAGE

PROPOSAL FOR THE ADDITION OF PREDNISOLONE **1mg** TO THE WHO MODEL LIST OF ESSENTIAL MEDICINES FOR THE TREATMENT OF CHILDREN AND ADULTS WITH ADRENOCORTICAL INSUFFICIENCY.

Applicant:

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Section 1: Summary statement of the proposal (500 words max)

This submission advocates the inclusion of prednisolone **1 mg** tablets to the core list of the EML as an essential, affordable, and effective treatment for children and adults with primary and secondary (pituitary) adrenocortical insufficiency. It should also be included for patients with steroid induced (tertiary) adrenal suppression for slow prednisolone withdrawal.

Recent evidence suggests that patients receiving 3 mg or 4 mg prednisolone once daily for adrenal insufficiency may have clinically important improvements in cardiovascular risk, with a reduction in the risk of osteoporosis and improved quality of life, compared to patients taking hydrocortisone, the traditional glucocorticoid replacement, which is more expensive, or prednisolone 5 mg, which is an excessive, supraphysiological glucocorticoid dose. Prednisolone has the additional advantage of being a once daily tablet compared with multiple-daily doses of hydrocortisone.

Higher, immunosuppressive doses of prednisolone are licenced for numerous clinical indications including many autoimmune diseases, asthma and colitis, and for these indications, multiples of 5 mg are commonly used, for example 40 mg for acute severe asthma. In many countries, the smallest strength of prednisolone tablets available is therefore 5 mg. Some patients can only afford prednisolone, and thus take 5mg daily for adrenal insufficiency. However, this has been demonstrated to be a supraphysiological dose, increasing the risk of long-term glucocorticoid associated morbidity, including increased cardiovascular disease, diabetes and osteoporosis. The literature has many citations of the harm caused by prednisolone, but this is because of the associated adverse effects with high doses of glucocorticoid exposure.

Studies comparing hydrocortisone thrice daily with prednisolone 3 mg to 4 mg once daily have shown that patients taking prednisolone have a lower risk of cardiovascular disease with a loss of weight when switched to prednisolone together with reduced bone turnover and a reduced risk of osteoporosis.

In Sri Lanka where the lowest dose prednisolone tablet is 5 mg, patients taking three quarters of a 5 mg tablet of prednisolone (i.e. 3.75 mg daily) has demonstrated improved cardiovascular risk[1]. Hydrocortisone is less affordable in many low-income countries. Pharmaceutical firms in Sri Lanka are currently considering manufacturing 1 mg prednisolone tablets; having prednisolone 1 mg on the EML will help encourage companies to make this very affordable drug available to patients in countries where there are few alternatives to prednisolone 5 mg. Enabling cost-effective prescribing of lower doses of prednisolone can significantly improve patient morbidity and mortality by avoiding the chronic use of higher doses of prednisolone (5mg) due to a lack of alternatives.

Section 2: Consultation with WHO technical departments: Not applicable

Section 3: Other organization(s) consulted and/or supporting the submission

Pakistan Endocrine Society

National Hospital Kandy, Sri Lanka

President of the Thai Endocrine Society

National Hospital, Singapore

ISE, the International Society of Endocrinology, federating 48 national endocrinology societies representing 25,000 members worldwide.

SAFES (South Asian Federation of Endocrine Societies)

Endocrine Society of India

Section 4: Key information summary for the proposed medicine

INN		Prednisolone (Prednisone)	
ATC code		H02AB06 (H02AB07)	
Indication		Primary and secondary adrenocortical insufficiency in adults and children. Prednisolone withdrawal in patients with glucocorticoid-induced adrenal insufficiency	
ICD-11 code		4A74 Adrenocortical insufficiency	
Dosage form	**Strength**	**EML**	**EMLc**
Tablet	1 mg	Yes	Yes

Section 5: Listing as an individual medicine or representative of a pharmacological class / therapeutic group

Listing is proposed for prednisolone with a square box as the representative medicine, with prednisone as a therapeutic alternative.

Section 6: Information supporting the public health relevance

Primary adrenal insufficiency has an estimated worldwide prevalence of 1 in 10,000. In Western countries, this is most commonly due to autoimmune-mediated adrenal failure. Other causes include tuberculosis and infectious diseases, which are more common in low-income countries.

Secondary adrenal insufficiency, with an estimated worldwide prevalence of 1 in 4,000, is caused by adrenocorticotropic hormone (ACTH) deficiency. This is secondary to hypothalamo-pituitary disease and is often associated with other pituitary hormone deficiencies.

Tertiary adrenal failure (called glucocorticoid-induced adrenal insufficiency or suppression in some publications) is caused by long term glucocorticoid exposure at supra-physiological doses and is the most common cause of adrenal insufficiency. Up to 1 in 100 people worldwide are taking glucocorticoids long term at doses that cause adrenal suppression doses[2-4].

For immunosuppression, patients typically start taking high doses of prednisolone such as 40mg daily with the aim of reducing the dose as the autoimmune disease comes under control. In countries where the lowest strength prednisolone tablet available is 5mg daily, patients are often left taking this dose lifelong due to the lack of any lower doses to use to try to wean the patient gradually off prednisolone. These patients will have adrenocortical suppression due to chronic use of supraphysiological doses of prednisolone and hence, will be unable to suddenly stop the prednisolone. If they do, such patients with adrenal suppression are at risk of an Addisonian adrenal crisis, which is cause of death worldwide every year.

Thrice daily hydrocortisone is a commonly used glucocorticoid replacement regimen for patients with adrenal/adrenocortical failure, although this may also be supraphysiological. Furthermore, there is an increased mortality associated with adrenal insufficiency despite glucocorticoid replacement therapy with a standardised mortality ratio greater than two[5,6]. The cause of the increased mortality is yet to be definitively elucidated, but may be due to excess glucocorticoid exposure, or replacement regimens that are uncoupled from the normal physiological cortisol profile. In some countries, prednisolone 5 mg once daily has been used as glucocorticoid replacement. This dose is also supraphysiological and may also be associated with increased mortality[7,8]. However this is not the case when lower prednisolone glucocorticoid replacement doses are used[9].

More recent evidence suggests that prednisolone 3 mg to 4 mg once daily has lower cardiovascular risk and side effects than hydrocortisone. It will also have a lower risk than prednisolone 5 mg tablets.

Section 7: Treatment details

Primary and secondary adrenal insufficiency.

Patients with autoimmune primary adrenocortical insufficiency or secondary pituitary induced adrenocortical insufficiency will need lifelong glucocorticoid treatment. Patients should take a median dose of 3 mg[10] rather than 5 mg. The 1 mg tablets are required to optimise and minimise the dose of prednisolone for this lifelong condition[10].

Prednisolone or other glucocorticoid induced (tertiary) adrenal suppression.

Low dose prednisolone can also help patients who have previously been taking higher doses of prednisolone for other conditions and require safe tapering of the dose when their primary condition is in remission. For example, some patients with severe chronic asthma spend over a year taking prednisolone at doses well above 10mg. Once their asthma is in remission, discontinuing the prednisolone can be difficult. Reducing or stopping the dose too quickly can cause a life-threatening adrenal crisis.

The new NICE guidelines now recommend a very slow reduction over 21 weeks from 5mg to none.

https://www.nice.org.uk/guidance/ng243/chapter/Recommendations#managing-glucocorticoid-withdrawal-to-prevent-adrenal-insufficiency

The NICE guidelines refer to the Imperial guidelines below. This details an example protocol that can be followed to slowly reduce the dose of prednisolone and encourage endogenous cortisol production.

https://www.impendo.co.uk/prednisolone/prednisolone-withdrawal

Patients who previously had Cushing's syndrome

The protocol can also be used for patients who have had pituitary tumours producing ACTH or adrenal tumours producing cortisol. These patients are exposed to very high levels of cortisol over a prolonged period. Following surgery, a rapid reduction in cortisol levels can cause glucocorticoid withdrawal syndrome[11]. These patients require generous replacement with higher doses of prednisolone such as 6mg once daily and can start the regimen in table 1 below once they are on prednisolone 5mg.

Table 1:

NICE approved weaning protocol for steroid withdrawal aimed at avoiding adrenal crisis and glucocorticoid withdrawal syndrome.

Available at https://www.impendo.co.uk/prednisolone/prednisolone-withdrawal

Week	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
0	5	5	5	5	5	5	5
1	5	4	5	4	5	4	5
2	4	4	4	4	4	4	4
3	4	3	4	3	4	3	4
4	3	3	3	3	3	3	3
5	3	3	3	2	3	3	3
6	3	2	3	3	2	3	3
7	3	2	3	2	3	2	3
8	2	3	2	3	2	3	2
9	2	3	2	2	3	2	2
10	2	2	2	3	2	2	2
11	2	2	2	2	2	2	2
12	2	2	2	1	2	2	2
13	2	1	2	2	1	2	2
14	2	1	2	1	2	1	2
15	1	2	1	2	1	2	1
16	1	2	1	1	2	1	1
17	1	1	1	2	1	1	1
18	1	1	1	1	1	1	1
19	1	1	1	0	1	1	1
20	1	0	1	1	0	1	1
21	1	0	1	0	1	0	1
22	0	1	0	1	0	1	0
23	0	1	0	0	1	0	0
24	0	0	0	1	0	0	0

Section 8: Review of evidence for benefits and harms

Strategy: All publications reviewed by the NICE committee on the development of the guidelines for adrenal insufficiency were reviewed. A summary of the evidence considered can be found here:

https://www.nice.org.uk/guidance/ng243/evidence

The currently available formulation of prednisolone with a minimum dose of 5mg may be effective for autoimmune diseases, where large doses are required, but the inability to use smaller doses is harmful. Many patients worldwide are continued on a "maintenance dose" of 5mg, a supraphysiological glucocorticoid dose, and this is likely to be the reason that the standardised mortality ratio for patients with adrenocortical failure taking glucocorticoid replacement is over two[5-8]. This risk often goes unnoticed by clinicians, as stopping glucocorticoid replacement in these patients can trigger adrenal crisis, and therefore many patients are simply maintained on a small, but nevertheless excessive, dose of prednisolone or hydrocortisone.

Recent work has shown the reduced cardiovascular risk of lower doses of prednisolone (3mg or 4mg once daily, but this regimen is only feasible in countries where 1mg tablets are available. In other countries, patients either remain on 5mg once daily, or switch to multiple daily doses of hydrocortisone, which also has adverse effects at the current doses and timings used. A soon to be published randomised, blinded cross-over study comparing lower doses prednisolone (3 mg to 5 mg) to standard regimens of hydrocortisone, has demonstrated weight loss, improvements in bone markers, reductions in risk of developing diabetes, associated with prednisolone use (https://www.isrctn.com/ISRCTN41325341).

Plenadren, a recently developed dual-release hydrocortisone formulation combining immediate and sustained release hydrocortisone, offers no advantage over low dose prednisolone[12], but is more expensive at £224 for 50 tablets in the UK (5mg), and only available in a few countries. Plenadren cannot be split due to its dual-release design, limiting its flexibility for dose adjustments. Prednisolone, at £1.31 for 28 tablets (5 mg), is more affordable. The availability of 1 mg tablets enables gradual dose reductions in countries where this is available. A pharmacokinetic study of prednisolone revealed that a mean dose of 3.86 mg provides effective replacement in adrenal insufficiency, with peak concentration at 1.43 hours[14]. Once-daily prednisolone offers a glucocorticoid profile similar to dual-release hydrocortisone, supporting its use as a more widely-available alternative, especially for dose adjustments at low levels.

The involvement of endocrinologists and the use of short synacthen tests (SSTs) to assess patients with potentially reversible adrenal insufficiency slows adrenal recovery in patients who are on hydrocortisone thrice daily. Even with a 30-minute cortisol levels above 350 nmol/L recovery took up to four years. Patients on higher doses had levels

below 350 nmol/L and only had a 49% recovery rate[13]. The use of prednisolone weaning regimens without endocrinology involvement is more effective but requires the use of 1mg tablets of prednisolone.

For conditions such as congenital adrenal hyperplasia secondary to 21-hydroxylase deficiency (21OHD), prednisolone may be more effective than thrice-daily hydrocortisone. A one-year study of 44 patients taking prednisolone (2.4–3.5 mg/m^2 BSA) showed stable bone maturation, growth rates, and height gains, compared to those on thrice-daily hydrocortisone (10–15 mg/m^2 BSA), achieving effective control of androgen suppression at lower doses[15].

Low-dose prednisolone (2–4 mg) is safe and effective for the management of adrenal insufficiency. In a study of 76 individuals, prednisolone day curves helped establish therapeutic levels, allowing precise dose titration. Most patients stabilised on a 4 mg median dose, with some reduced to 2 mg[10]. The aim in patients with adrenal insufficiency should be to use the lowest, effective glucocorticoid dose to ensure adequate glucocorticoid replacement without risk of the negative effects of chronic, high dose glucocorticoid exposure.

Interim results from several centres in the ongoing HYPER-AID Study (NCT03608943) indicate that once-daily prednisolone is a safe and effective alternative to twice or thrice daily hydrocortisone for adrenal insufficiency[16-19]. At one centre, 13 of 15 patients who completed the switch from hydrocortisone to prednisolone showed minor yet significant reductions in BMI and waist circumference, with no adverse effects on cardiovascular or metabolic markers. At the other centre, 17 patients maintained stable BMI, HbA1C, and cardiovascular health after switching from 20-30 mg/day hydrocortisone to 3-5 mg prednisolone. All patients at both centres chose to remain on prednisolone due to its convenience and well-being benefits.

Section 9: Summary of recommendations in current clinical guidelines

European Society and American Society

This guideline between the American and European Societies on the slow reduction of glucocorticoids for patients who have previously been on high doses who no longer need them for a resolved autoimmune disease. In the US, it recommends a reduction by 1mg steps of prednisone. It also suggests hydrocortisone (20mg with 5mg decreases) as an alternative if low dosage prednisolone or prednisone preparations are not available.

https://academic.oup.com/ejendo/article/190/5/G25/7663654

This is a link to the European Society of Endocrinology and Endocrine Society Joint Clinical Guideline: Diagnosis and therapy of glucocorticoid-induced adrenal insufficiency | European Journal of Endocrinology | Oxford Academic (oup.com)

NICE

Because 1mg tablets of prednisolone are available in the UK, the recommendation requires 1mg tablets and suggests the protocol in table 1 above.

https://www.nice.org.uk/guidance/ng243/chapter/Recommendations#managing-glucocorticoid-withdrawal-to-prevent-adrenal-insufficiency

The NICE guidelines refer to the Imperial guidelines below.

Imperial College

https://www.impendo.co.uk/prednisolone/prednisolone-withdrawal

Section 10: Summary of available data on comparative cost and cost-effectiveness

In the **United Kingdom**: BNF accessed 31st October 2024:

Medicinal forms | Prednisolone | Drugs | BNF | NICE

https://bnf.nice.org.uk/drugs/prednisolone/medicinal-forms/#oral-tablet

Prednisolone 1mg daily costs £0.71 for a months supply in the UK, so 3mg daily using 1mg tablets costs **£2.13 (minimum cost in the UK)**

A 3mg tablet is now available in the UK at £5.50 per month.

A 4mg tablet is available in the UK at £5.75 per month

A 5mg tablet has always been available at £0.77 per month.

Hydrocortisone in the UK

A 10mg tablet can be split up to 10mg in the morning, and then half at noon and half in the evening, and this formulation costs **£3.84** per month, by using two 10mg tablets each day. The timing is important and if patients combine two doses for convenience, they might increase their long term cardiovascular risk. £3.84 is thus the minimum cost in the UK for hydrocortisone replacement.

Lower strength tablets are available, but at a higher cost:

Hydrocortisone 10mg once daily for 1 month: £1.92

Hydrocortisone 5mg daily for 1 month: £26.28

Hydrocortisone 2.5mg daily for 1 month: £25.11

We are in the unusual situation of having a treatment (prednisolone) that is cheaper, and more effective, with fewer side effects (than hydrocortisone).

Australia: pbs.gov.au

In Australia, the dispensed price for 100 x 1 mg **prednisolone** is **AU$ 16.56** which will last a month at 3mg daily.

Hydrocortisone costs AU$ 42.39 for 100 tablets, so, if patients are given **hydrocortisone** 12mg + 4mg + 4mg daily, then they will need five 4mg tablets daily, so 150 tablets for a month would cost **AU$63.58**

For information, 120 x 20 mg tablets of hydrocortisone is AU$ 54.75 in Australia.

Pakistan (see letter of support from the President of the Pakistan Endocrine Society).

Prednisolone 5mg costs between **PKR 45** and PKR 110.

Lower doses are not available.

Hydrocortisone 10 + 5 + 2.5 costs PKR 252 for generic hydrocortisone, and for branded hydrocortisone, between PKR: 5300 PKR and PKR 10,500

Sri Lanka (see letter of support from the National Hospital, Kandy, Sri Lanka).

Prednisolone 5mg costs between **SLRs 3 and SLRs 14 per day**

Lower doses are not available.

Hydrocortisone 10 + 5 + 5 costs SLRs 64 to SLRs 96 for generic hydrocortisone per day (as a 20mg tablet broken up).

Thailand (see letter of support from the President of the Thai Endocrine Society).

Hydrocortisone not generally available and less affordable than prednisolone 5mg.

Singapore (see letter of support).

International Society of Endocrinology (see letter of support)

SAFES (South Asian Federation of Endocrine Societies) (see letter of support)

ESI (Endocrine Society of India) (see letter of support)

Section 11: Regulatory status, market availability and pharmacopeial standards

Prednisolone 5mg tablets are widely available in all countries for many indications, but not for adrenal insufficiency. The 5mg strength is already on the EML. The indications on the 23rd list of prednisolone 5mg (in section 8.2.4) are as follows, and does not currently include adrenal insufficiency:

– Acute lymphoblastic leukaemia – Anaplastic large cell lymphoma – Burkitt lymphoma – Chronic lymphocytic leukaemia – Diffuse large B-cell lymphoma – Follicular lymphoma – Hodgkin lymphoma – Langerhans cell histiocytosis – Metastatic castration-resitsant prostate cancer – Multiple myeloma

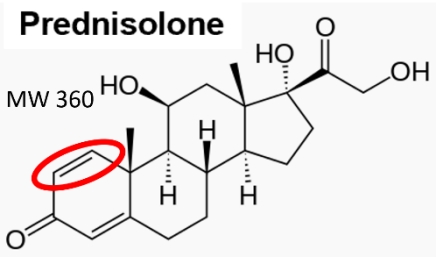
Prednisolone 1mg tablets are available in the United Kingdom, New Zealand and Australia, and Prednisone 1mg is available in the United States, but I have not found it in any other countries.

International pharmacopoeia – yes
(https://digicollections.net/phint/2022/index.html#d/b.6.1.285

Prednisolone (Prednisolonum)

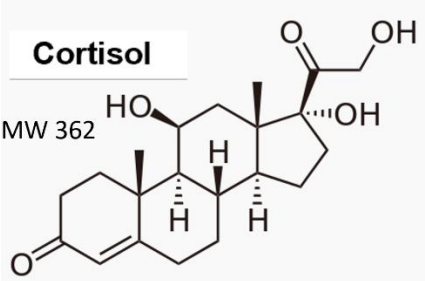
Molecular formula. $C_{21}H_{28}O_5$ **Relative molecular mass.** 360.5

Chemical name. 11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione; CAS Reg. No. 50-24-8.



The double bond highlighted here is the difference between cortisol (hydrocortisone) and prednisolone. The double bond results in a molecule that is more potent and has a longer half life, so that once daily administration is suitable. We just now need to get the dose right.

Hydrocortisone is recommended in section 18.1 of the EML 2023 for adrenal replacement therapy given thrice daily (10mg in the morning, 5mg at noon, and 5mg in the afternoon). However this is more expensive than prednisolone in most countries.



Hydrocortisone (cortisol) has too short a half life for once daily administration, and so needs to be administered twice or thrice daily.

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PAKISTAN ENDOCRINE SOCIETY

Date: October 29, 2024

The Secretary
WHO Expert Committee on Selection and Use of Essential Medicines
Department of Health Products Policy and Standards
World Health Organization, Geneva

Dear World Health Organization,

Re: **Adding Prednisolone 1mg tablets to the Essential Medicines List**

We are writing in support of the submission put forward from Professor Karim Meeran from Imperial College London to include Prednisolone 1mg tablets for patients with primary, secondary and tertiary adrenocortical insufficiency.

Currently hydrocortisone is on the list for these indications.

The cost of hydrocortisone for a months' supply is higher than prednisolone, and many countries are using prednisolone 5mg tablets off licence. Prednisolone is licenced at higher doses for autoimmune diseases, but we need lower doses for adrenal insufficiency. Emerging evidence suggests that lower doses pose less cardiovascular risk than higher doses. The availability of 1mg tablets will allow careful and more accurate replacement.

In Pakistan, access to hydrocortisone remains a significant challenge due to limited availability and high costs. A monthly supply of Hydrocortisone at a dose of 10 mg +5 mg + 2.5 mg costs 5300 PKR to 10,500 PKR. A monthly supply of generic hydrocortisone in the same dose (available by the name of Corticort in Pakistan) currently costs approximately 252 PKR. While prednisolone is widely available, it is limited to doses of 5 mg, with monthly costs ranging between 45 PKR and 110 PKR for standard tablets and 117 PKR to 123 PKR for the enteric-coated version (Deltacortril-EC). Splitting 5 mg prednisolone tablets to achieve lower doses results in erratic dosing, creating both safety and efficacy concerns. Therefore, the inclusion of a 1 mg prednisolone tablet on the Essential Medicines List would address this gap, allowing for precise, low-dose therapy that is both affordable and accessible to patients in Pakistan with adrenal insufficiency.

Kindest Regards

Dr. Aisha Sheikh

FCPS (Medicine), FACE (USA)
Fellowship Diabetes, Endocrionology & Metabolism (AKUH)
PG Dip Endocrinology (Glamorgan, UK), PG Dip Diab (Cardiff, UK)
Lecturer and Consultant Endocrinologist,
Section of Endocrinology, Department of Medicine
The Aga Khan University Hospital, Karachi, Pakistan.
Recognized tutor, University of South Wales, UK
President - Pakistan Endocrine Society

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30th of October, 2024

The Secretary
WHO Expert Committee on Selection and Use of Essential Medicines
Department of Health Products Policy and Standards
World Health Organization, Geneva

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Re: Adding Prednisolone 1mg tablets to the Essential Medicines List

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Prednisolone 5 mg is the only dose tablet of Prednisolone available in Sri Lanka, and therefore is a limitation in prescribing patients who require lower doses of Prednisolone.

Oral Hydrocortisone 10 mg costs Rs 32-48 and Prednisolone 5 mg costs only Rs 3 - 14.
The average cost per day per patient is as follows:
Oral Hydrocortisone 20 mg - Rs. 64 – 96 per day
Prednisolone 5 mg - Rs 3- 14 per day

If we switch our patients with adrenal insufficiency to Prednisolone from Hydrocortisone the cost will be roughly 5 -15 % of the current expense for steroid replacement. This will save a significant amount of cost on the healthcare burden in Sri Lanka being a resource poor developing country.

Thanking You

Dr. Charles Antonypillai
MBBS, MD, MRCP (UK)
MRCP (Diabetes & Endocrinology (UK)
FSLCE, FACE (USA), FRCP (London)
Consultant Endocrinologist
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October, 29th 2024

Dear The WHO Essential Medicines Committee,

On behalf of the Endocrinology and Metabolism Unit at Prince of Songkla University, Thailand, I write to strongly support the inclusion of 1 mg and 3 mg prednisolone tablets on the WHO Essential Medicines List. Our unit's experience with adrenal insufficiency (AI) management in Thailand and the ASEAN region highlights the urgent need for these lower-dose formulations. Below, I outline three key issues impacting patient care and outcomes:

1. Limited Availability of Low-Dose Prednisolone: In Thailand, and broadly across Asia, prednisolone is only available starting at a 5 mg dose. This limitation hinders precise dose tapering, leading to unnecessary side effects and making it difficult for clinicians to provide individualized treatment, particularly for AI patients who require gradual tapering under close supervision.

2. Accessibility and Cost of Hydrocortisone: While hydrocortisone is an alternative for AI management, it remains expensive and difficult to obtain in the necessary therapeutic doses in Thailand. Consequently, prednisolone is often the more practical option for patients, yet the lack of smaller dose options restricts optimal dosing flexibility.

3. Local Cost Disparities: Prednisolone is generally affordable compared to hydrocortisone, which can be several times more expensive per therapeutic dose. In the context of limited healthcare resources, particularly in Thailand and surrounding ASEAN countries, the cost barrier for hydrocortisone reinforces the need for accessible, lower-dose prednisolone formulations.

To address these challenges and improve healthcare outcomes across underserved populations, we strongly encourage the WHO to prioritize prednisolone 1 mg and 3 mg tablets on the Essential Medicines List.

Thank you for your attention to this urgent matter. We look forward to collaborating to improve global access to critical, effective AI treatment solutions.

Warm regards,

(Padiporn Limumpornpetch)
Head of Endocrinology and Metabolism Unit

Department of Internal Medicine
Songklanagarind Hospital
Faculty of Medicine, Prince of Songkla University
Email: padiporn@gmail.com

National University Hospital

The Secretary
WHO Expert Committee on Selection and Use of Essential Medicines
Department of Health Products Policy and Standards
World Health Organization, Geneva
Dear World Health Organization,
Re: Adding Prednisolone 1mg tablets to the Essential Medicines List

We are writing in support of the submission put forward from Professor Karim Meeran from Imperial College London to include Prednisolone 1mg tablets for patients with primary, secondary and tertiary adrenocortical insufficiency.

Currently hydrocortisone is on the list for these indications.

The cost of hydrocortisone for a months supply is higher than prednisolone, and many countries especially countries in ASEAN do not have prednisolone at 1 mg or 3 mg and only have prednisolone 5mg tablets. However, we need lower doses for adrenal insufficiency. Emerging evidence suggests that lower doses pose less cardiovascular risk than higher doses. The availability of 1mg tablets will accurate cortisol replacement and weaning.

Yours sincerely

Dr Eng Pei Chia
Consultant Endocrinologist
National University Hospital
Singapore

Thursday, October 31, 2024

To: The Secretary
WHO Expert Committee on Selection and Use of Essential Medicines
Department of Health Products Policy and Standards
World Health Organization, Geneva

Dear World Health Organization,

Re: **Adding Prednisolone 1mg tablets to the Essential Medicines List**

We are writing in support of the submission put forward from Professor Karim Meeran from Imperial College London to include Prednisolone 1mg tablets for patients with primary, secondary and tertiary adrenocortical insufficiency.

Currently hydrocortisone is on the list for these indications.

The cost of hydrocortisone for a months supply is higher than prednisolone, and many countries are using prednisolone 5mg tablets off licence. Prednisolone is licenced at higher doses for autoimmune diseases, but we need lower doses for adrenal insufficiency.

Emerging evidence suggests that lower doses pose less cardiovascular risk than higher doses. The availability of 1mg tablets will allow careful and more accurate replacement.

Yours sincerely`,

Syed Abbas Raza
President

South Asian Federation of Endocrine Societies

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To
The Secretary
WHO Expert Committee on Selection and Use of Essential Medicines
Department of Health Products Policy and Standards
World Health Organization, Geneva

01 Nov 2024

Re: Adding Prednisolone 1mg tablets to the Essential Medicines List

Dear World Health Organization,
We are writing in support of the submission put forward from Professor Karim Meeran from Imperial College London to include Prednisolone 1mg tablets for patients with primary, secondary and tertiary adrenocortical insufficiency.

Currently hydrocortisone is on the list for these indications. The availability of the Hydrocortisone is always a challenge in the member countries of SAFES and many times patients miss their doses due to non-availability. This puts their life in danger as regular consumption of glucocorticoids is essential and lifesaving for patients with Primary Adrenal Insufficiency.

In addition to the availability, another major challenge is the cost of Hydrocortisone in comparison with Prednisolone. The cost of hydrocortisone for a month's supply is higher than prednisolone, and many countries are using prednisolone 5mg tablets off licence. Prednisolone is licenced at higher doses for autoimmune diseases, but we need lower doses for adrenal insufficiency. Emerging evidence suggests that lower doses pose less cardiovascular risk than higher doses. The availability of 1mg tablets will allow careful and more accurate replacement.

Regards,

Dr KVS Hari Kumar
Secretary, SAFES

ENDOCRINE SOCIETY OF INDIA

(Registration No 115A of 1971 under Registration of Societies Act XXL of 1860)

Affilated to South Asian Federation of Endocrine Societies

&

International Society of Endocrinology

To
The Secretary
WHO Expert Committee on Selection and Use of Essential Medicines
Department of Health Products Policy and Standards
World Health Organization, Geneva

Sub: Adding Prednisolone 1mg tablets to the Essential Medicines List

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Currently hydrocortisone is on the list for these indications. The availability of the Hydrocortisone is always a challenge in a vast country like India and many times patients miss their doses due to non-availability. This puts their life in danger as regular consumption of glucocorticoids is essential and lifesaving for patients with Primary Adrenal Insufficiency.

In addition to the availability, another major challenge is the cost of Hydrocortisone in comparison with Prednisolone. The cost of hydrocortisone for a month's supply is higher than prednisolone, and many countries are using prednisolone 5mg tablets off licence. Prednisolone is licenced at higher doses for autoimmune diseases, but we need lower doses for adrenal insufficiency. Emerging evidence suggests that lower doses pose less cardiovascular risk than higher doses. The availability of 1mg tablets will allow careful and more accurate replacement.

Regards,

Place: HYDERABAD
Date: 01 Nov 2024

Dr. K.V.S. Hari Kumar
Honorary Secretary
Endocrine Society of India

contact@endocrinesocietyindia.org www.endocrinesocietyindia.org
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